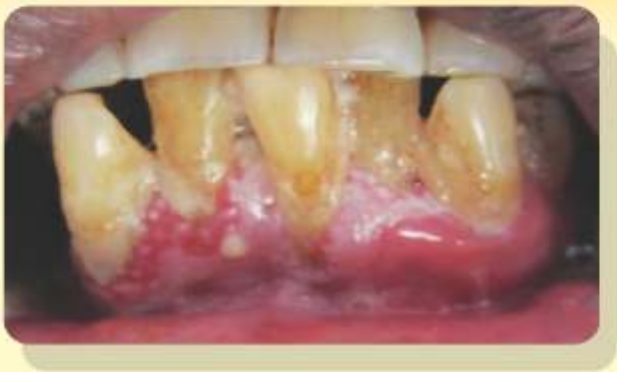
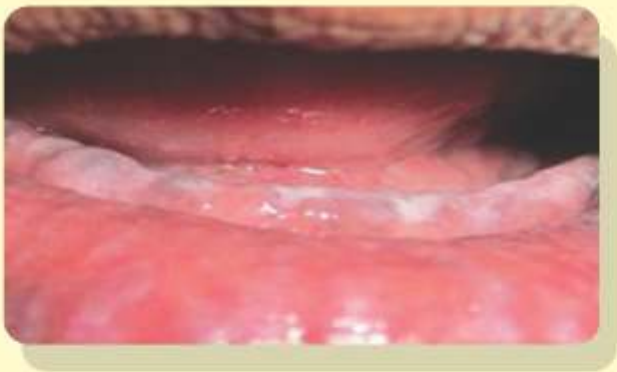
ISSN 2348 - 1374

IJWDC

INTERNATIONAL JOURNAL OF WOMEN'S DENTAL COUNCIL

VOL 2 No 1 Jan - June 2014





website : www idakerala.com
email : rreditorijwdc@gmail.com

wdc
Women's Dental Concil

The official publication of Women's dental council, IDA, Kerala State.

ISSN 2348 - 1374

INTERNATIONAL JOURNAL OF WOMEN'S DENTAL COUNCIL

IJWDC

Editorial Board

Editor in Chief : Dr. R. Rathy
Associate Editors : Dr. Praveena.G
Dr. Indu.M
Dr. Annie George

Indian Advisory Board

Dr. Anita Balan
Dr. Kunjamma Sebastian
Dr. Rosamma Joseph
Dr. Prasanthila janam
Dr. Mini Jose
Dr. Elizabeth Koshi

International Advisory Board

Dr. Hari . S. Prasad, USA

Office bearers IDA Kerala State

President :Dr. Nizaro Siyo
IMM Past president :Dr. Antony Thomas
President Elect : Dr. Thomas K.C.
Vice President : Dr. Mohammed Sameer P.T
: Dr. Ciju. A. Poulose
: Dr. Fazil.V. Hassan
Hon. Secretary:Dr. O.V. Sanal
Joint Secretary:Dr. Anil Kumar P.K.
Asst. Secretary:Dr. Naveed Sait
Treasurers:Dr. T.V. Rameshan
Editor: Dr. K Nandakumar
CDE Convener :Dr. Anil G
CDH Chairman :Dr. Joji George

Office bearers WDC Kerala State

Chair person : Dr.Anjana.G
PAST Chair person : Dr.Thaj.S.Prasad
Chair person elect : Dr.Merly Joji
Vice chairperson : Dr.Sudha Santhosh
: Dr.Rani Thambi
: Dr.Susha.C.N
Secretary : Dr.Shoma Anil
Joint secretary : Dr.Elsy Bijoy
Treasurer : Dr.Jayashree Ajith
Editor : Dr.R.Rathy

Editorial Office:

PRESIDENT'S MESSAGE

Dear Colleague,

The International Journal of WDC enters the second year....Join with me to congratulate the meticulous efforts of our Editor Dr Rathy R Ravindran in bringing out this issue.

As you all know ,we are professionals from the cream of the society and we have a lot of responsibilities to our community. As an association, we achieve many things than what an individual can.Each one of us have a lot of capabilities and when we put it together in the right way it results in everyone's development and eventually the up gradation of the society we live in.

Women's Dental Council under the active leadership of Dr Anjana. G is doing extremely well this year.Let me end by wishing WDC to move forward with more enterprising visions.

Dr.Nizar S
President
IDA Kerala State

SECRETARY'S MESSAGE

Dear member,I consider it a privilege indeed to address you in the second issue of International Journal of Women's Dental Council.Dentistry as of now is the digital transformation of healthcare, and it will redefine virtually every dimension of health care.With the advent of sophisticated methods and procedures numerous options for new applications are open to the dental professionals which were not even heard of a decade ago.Hence we need to update ourselves of these advancements in order to achieve clinical excellence.I take this opportunity to appreciate the efforts of Team WDC especially the editor Dr Rathy Ravindran in bringing out this issue of IJWDC. In this expanding world of dental science,let this journal offer the means to improve your clinical practice.

Dr Sanal.O.V
SecretaryIDA
Kerala State

WDC CHAIR PERSON'S MESSAGE

It is indeed a great pleasure to write a foreword to the Second Edition of IJWDC, Kerala State.

I would like to thank the Chief Editor Dr. Rathy Raveendran, members of the editorial board and all the contributors who made this journal a success.

There is an upward trend in the number of Women Dentists world wide as this profession offers unique opportunities for women to exercise a high degree of flexibility and autonomy as health care providers.

But there are many practical obstacles for women entering this career as in all other careers when they want to pursue and advance their career ambitions. The significance of a Women Dental Council is to help women dentists face these unique challenges in achieving professional excellence. Global attention, concepts and strategies are needed for the advancement of women in academic and research careers.

WDC, Kerala State being a scientifically oriented community had brought out its first scientific journal in 2013. Now the second edition has been published. May the texts published here inspire new research and new findings.

Dr. Anjana G
Chairperson
WDC
Kerala State

IJWDC
Vol 2/No1/ Jan-June 2014

CONTENTS

Review Article

CORRELATION OF CHRONIC PERIODONTITIS AND ORAL CANCER –IS THERE ANY LINK ?: A REVIEW

DR.RATHY R.*, DR. SRUTHY K., DR. SRUTHI A.K.*****

Dept of Oral & Maxillofacial Pathology, Azeezia College of Dental Science & Research, Meeyannoor, Kerala State, India

ADDRESS FOR CORRESPONDENCE

Dr. RATHY R. MDS.
Professor and HOD,
Dept of Oral and Maxillofacial Pathology,
Azeezia College of Dental Science & Research,
Diamond Hills, Meeyannoor, Kollam,
Kerala State – 691537,
E-mail:rathyravindran27@gmail.com

ABSTRACT :

Infections are considered as potential trigger for carcinogenesis apart from other risk factors like tobacco . Recent evidence suggests that extent and severity of periodontal disease and tooth loss may be associated with an increased risk of malignant disease .Biologic mechanism underlying association of periodontal disease with cancers remain unclear.Studies suggest persistent inflammation functions a driving force to cancer. Several pro inflammatory cytokines have been shown important in both periodontitis and oral cancer .This is brief review on the link between chronic periodontitis and oral cancer.

KEY WORDS : Chronic periodontitis, Oral cancer, Inflammatory cytokines

INTRODUCTION

Oral cancer is one of the most dreadful health problem in terms of morbidity and mortality ,faced by mankind today.[1] Squamous cell carcinomas encompass 90 % of all oral malignancies .Oral cancer holds eight position in the incidence of cancer in worldwide with variation between geographic areas [2]. In India and most South-East Asian countries it is the most common malignancy.Worldwide five year survival rate of head and neck cancer has remained below 50 % over last decades in spite of advances in treatment modalities .[3] Development of new therapeutic strategies with improved treatment options or possible prevention of oral squamous cell carcinoma requires a more understanding of its etiology .

Important risk factors of multistep carcinogenesis model are genetic predisposition ,presence of premalignant lesions and environmental triggers like tobacco usage and heavy use of alcohol .[4] The increasing incidence rates of oral cancer pleads for the presence of other etiologic factors like human papilloma virus infection, immunosuppressive therapy , poor oral hygiene and some infections .[5] Recently the influence of infection and inflammation for cancer developments have been discussed .Many tumors arise from the sites of chronic irritation ,infections and inflammation.[6] There are some latest studies showing possible association between the history of chronic periodontitis and oral cancer independent of other factors [5].

*Professor & Head **Senior Lecturer ***Postgraduate student

Periodontal disease is a chronic destructive disease ,which occurs in children , young people and adults.[7] Chronic periodontitis is an infectious inflammatory disease caused by bacteria of the dental plague , resulting in the progressive destruction of tissues that support the tooth ie gingival, periodontal ligament ,cementum and alveolar bone [8] .It is caused by anaerobic bacteria in the dental biofilms .[9] Recent studies suggests that viruses has some role in initiation and progression of periodontitis [10] . The role of bacteria in the initiation of periodontitis is well reported . Bacteria induce tissue destruction indirectly by activating host defense cells producing and releasing mediators that stimulate the effectors of connective tissue breakdown .[11] Periodontitis is associated with many systemic conditions like cardiovascular diseases, low birth weight complications in pregnancy , diabetes and pulmonary disease .[12] Chronic inflammation increases the chance of severe cancers and inflammation resulting in breakdown of connective tissue that surrounds the tooth[13.]

Chronic inflammation has been the rationale behind the association looking both at cancers and periodontal disease. Periodontitis characterized by epithelial proliferation and migration results in chronic release of inflammatory cytokines ,chemokines ,prostaglandins ,growth factors and enzymes all of which are closely associated with carcinogenesis [14] .These by products of periodontal disease might account for the relationship between these two diseases. Microbial components have the capacity to activate macrophages to synthesize and secrete a wide array of molecules including cytokines .IL-1, and TNF –α , prostaglandins , especially PG E2 and hydrolytic enzymes [11] . The progression and extent of tissue destruction to be determined by relative concentration and half life of IL -1 ,TNF α and related cytokines . As periodontitis progresses ,.the pocket epithelium is characterized by continuing proliferations , formation of rete ridges and ulcerations . In connective tissue there is angiogenesis ,chronic inflammatory infiltrate ,fibrosis and tissue loss . Further more periodontal pathogens and inflammatory mediators travel with saliva and blood from the affected tissues to distant sites and adversely affecting systemic health. Same mechanism plays a role in field of cancerisation of oral cancer.Chronic inflammation plays a multifactorial role in carcinogenesis and there are evidence that suggests persistent inflammation function as a driving force in the journey of cancer. Overexpression , elevated or abnormal action of proinflammatory mediators facilitate tumor progression [15,16] .The specific markers of inflammation can be studied to know the association between chronic inflammation and cancer [17]. Screening and examination of oral cancer can be targeted in order to improve prevention and early detection of oral cancer if periodontal diseases is found to be a significant risk and warning sign.

INFLAMMATORY CYTOKINES AND ITS RELATION IN CHRONIC PERIODONTITIS AND ORAL CANCER:

Inflammation is a critical component of tumor progression [18.]Tumor cells have co-opted some of the signaling molecules of innate immune system, such as selectins , chemokines and their receptors form invasion , migration and metastasis.[6] Local host responses to periodontal pathogens release inflammatory mediators and cytokines , which play a cruial role in the pathogenesis of periodontal diseases .[19] They mediate different steps in pathway leading to tumorigenesis.

Cytokines are small soluble proteins produced by a cell that alter the behavior or properties of another cell locally or systematically . Cytokines include interleukins ,interferons ,growth factors , colony stimulating factors and intercrines. Inflammatory cytokines is the cytokine induced during the course of inflammatory response . IL-1 , IL -6 , IL-8 and TNF- α are generally classified as inflammatory cytokines [20] .They are produced by locally infiltrated immunocompetent cells such as T cells and monocytes at the diseases sites .Fibroblasts, epithelial cells and endothelial cells are also involved in cytokine production during inflammatory process.[21]

INTERLEUKIN-1 (IL-1)

IL-1 is a polypeptide produced by mononuclear phagocytes induced by bacterial products .It acts as a mediator of host inflammatory response to stimuli and work together with TNF in innate immunity and inflammation .There are two forms of IL-1 called IL-1α and IL1-β that are less than 30 % homologous to eachother [20.] It has been demonstrated IL 1α remains largely cell associated where as IL-1 β is released from cell. IL-1 stimulates the proliferation of keratinocytes , fibroblasts and endothelial cells and enhance fibroblast synthesis of type 1 collagen ,collagenases, hyaluronate ,fibronectin and PG E2.[21] It also play a role in bone diseases like periodontitis.[22,23.]

INTERLEUKIN 6 (IL-6)

IL -6 is a cytokine influencing immune responses and inflammatory reactions . Produced by stimulated monocytes , fibroblasts and endothelial cells.[20] IL-6 induces the final maturation of B cells into immunoglobulin secreting plasma cells. [21] It also plays a role in local regulation of bone turn over and also stimulates bone turnover .[24]

INTERLEUKIN 8 (IL-8)

Il-8 is a potent chemotactic factor for leukocytes .It is sereted by variety of cell including monocytes , fibroblasts , lymphocytes and endothelial cells .It has proinflammatory and neutrophil chemotactic properties [21] .Excessive IL -8 mediated chemotactic activation effects on inflamed gingival and contributes tissue destruction .[25]

TUMOR NECROSIS FACTOR α (TNF-α)

TNF –α is a proinflammatory cytokine secreted mainly by monocytes and macrophages. They stimulate the secretion of collagenase by fibroblasts ,resorption of cartilage and bone and implicated in the destruction in periodontitis .[21] In macrophage they induces the synthesis of IL-1 and PG E2.They have synergistic effects with bone resorptive action of IL-1 .[26] It is also produced by tumor cells and reported to mediate macrophage –induced angiogenesis , proliferation, cellular transformation and metastasis .

Inflammatory responses in periodontal tissues are regulated by cytokine network. IL-1 ,IL-8 and TNF- α can be detected in GCF. It has been proved that cytokines like IL-1, IL-6, IL-8 and TNF are also produced by tumor cells. [27]A role of cytokines in angiogenesis and tumor progression have been suggested .[28] Studies have been reported that IL-1 ,IL-6 IL-8 in saliva is increased with periodontal infection ; however oral cancer associated increase may be correlated with development of age , smoking status and number of teeth .Thus the association between periodontitis and oral cancer has been evaluated by several studies .[31,32,35.]

ASSOCIATION BETWEEN ORAL CANCER AND CHRONIC PERIODONTITIS : -

On literature review many studies linking oral cancer and chronic periodontitis are noted. In a prospective study by Michaud et al a significant association was found between the history of periodontitis and the risk of developing lung, kidney, pancreas and haematological cancers.[30]

More consistent risk was noted in the studies of oral cancers and periodontal diseases.[8]

Study by Mine Tezal represents an association between tongue cancers and periodontal diseases after adjusting other factors including effects of age, smoking status and number of teeth. Study by Eunice et al concluded that chronic periodontal disease indicated by extracted or extruded molars associated statistically with elevated incidence of cancer. Bundgaard et al. reported results of a study where ,subjects with 15 teeth and less showed a two-fold increase risk in cancer. Dr Rezende compared dental health and periodontal status (CPITN) of 50 untreated oral squamous cell carcinoma and 50 healthy subjects and clarified that, 76% of subjects with cancer had periodontal pocket depths of 6 mm or greater but in the control group 10% of the subjects had periodontal pockets.Garrote in his study found that poor oral conditions and number of missing teeth were 4.6 times more in oral cancer compared to control. Guha et al did a

study comparing condition of mouth, toothbrush use and daily mouth wash use in oral cancer patients and found rate of poor oral hygiene was higher in test group.Marshell et al in his study found that loss of 11 or more teeth showed 2.7 fold increased risk of oral cancer.Rosenquist et al study in Sweden concluded that subjects who had lost more than 20 teeth , had 3 fold increased risk of cancer.

Thus the association between periodontal diseases and cancer has been evaluated by several studies.[31,32,35,36]

CONCLUSION :-

Additional studies are needed to confirm periodontal disease as a risk factor for various types of cancers. Chronic periodontitis itself would trigger the development of oral squamous cell carcinoma.[32] Malignant transformation may be due to immune responses between macrophage and T cell activation and cytokine release like IL-1,IL-8 and TNF-α. Osteoclastic activity by these proinflammatory molecules constitute a potential route for invasion of an adjacent tumor.[5] Specific association of chronic periodontitis and oral cancer need to be explored.[33,34] More studies are needed to clarify the exact mechanisms involved.

REFERENCES

1. Koshy AV, Rao NN, Kamat SS, Kiswani, Expression of extracellular matrix- laminin in oral squamous cell carcinoma : an immunohistochemical study, J Contemp Dent Pract 2012 Mar 1; 13(12): 194 – 200
2. Doshi Neena P, Shah Siddharth A, Patel Keyuri B, Jhabuawala Munira F, Histological grading of oral cancer : a comparison of different systems and their relation to lymph node metastasis, National Journal of Community Medicine 2011; Vol(2) : 136 -142
3. Tarig A Osman, Daniela E Costea, Anne C Johannessen, The use of salivary cytokines as a screening tool for oral squamous cell carcinoma : A review of literature Journal of Oral and Maxillofacial Pathology 2012, Vol 16 : 256 – 261
4. Andrea Tannapfel, Anette Weber, Tumor markers in squamous cell carcinoma of the head and neck : clinical effectiveness and prognostic value, Eur Arch Otorhinolaryngol 2001;25 (8) : 83 – 88
5. Maximilian Kruger, Torsten Hansen, Adrian Kasaj, Maximilian Moergel, The correlation between chronic periodontitis and oralcancer, Case reports in Dentistry, 2013; 1 – 8
6. Coussenlm, Werb Z, Inflammation and cancer : Review, Nature 420, 2002; 860 – 867
7. Papapanau PN, Periodontal disease, epidemiology, Ann Periodontol ,1996; 1: 1-36
8. Abrodun O, Arigbede, B Osagbemiro, Kolude, Periodontitis and systemic diseases : A literature review, 2012; 16(4) : 487 – 491
9. Jemin Kim, Solomon Amae, Periodontal diseases and systemic conditions : bidirectional relationship, Odontology, 2006; 94(1); 10 -21
10. Tezal M, Sullivan MA, Danial L Stoler, Thomas Melendy, Chronic periodontitis : human papilloma virus synergy in base of tongue cancers, April 2009; Vol 135: 391 -396
11. Roy C Page, Role of inflammatory mediators in the pathogenesis of periodontal disease, J Periodontol Res 1991; May 26: 230 – 42
12. Rose LF, Sternberg BJ, Minsk L, The relationship between periodontal disease and systemic diseases, Compend Contin Educ Dent 2000; 21: 870 – 77
13. Farzeen Tanwir, Dua Shaukat, Relationship between periodontal disease, tooth loss and

caner, Pakistan Oral & Dental journal Vol 32; 2012: 62 – 65

14. Bharat B Aggarwal, Shishodia S, Santosh K Sandur, Manoj K Pandey, Gautam Sethi, Inflammation and Cancer how hot is the link ? Biochemical pharmacology 72,2006;1605 - 1621

15. Joydeb Kumar Kundu, Young-Joon Surh, Inflammation : Gearing the journey to cancer, Mutation research 2008;659(1-2):15-30

16. Ben Bainch A, Inflammation associated immunosuppression in cancer : the roles played by cytokine, chemokine, additional mediators, Seminar cancer biology 2006;16(1):18-52

17. Wing TY Loo, Lyan, Epigenetic changes on E cadherin and cox_2 to predict chronic periodontitis, Journal of translation mediators 2010; 8 -10

18. Gods,land, Johiston, BV North, Simple indices of inflammation as predictor of death for cancer or cardiovascular disease in a prospective cohort after two decades of follow up, QJM, Vol 104 2011; 384 – 394

19. Deo V, Bhongade ML, Pathogenesis of periodontitis : Role of cytokine in host response, Dent today 2010; 9: 60 – 66

20. H Okada, S Murakami, Cytokine expression in periodontal health and disease, Critical reviews in oral biology & medicine 1998;9(3);248 -266

21. Abul K Abbas, Andrew H Lichtman, Cellular and molecular immunology, fifth edition, Saunders publication

22. Grigoriadou ME,Koutayas SO, Madianus ,Strub, Interleukin 1 as a genetic marker for periodontitis: Review of literature, Quintessence Int 2010 : 517 – 525

23. Chen CC, Chanq KL, Huang, Correlation of IL-1β, IL-6 and periodontitis, Kaoshsiunq J Med Sci 1997(10) 609-17

24. Sha MY, Huanq P, Chinq R, Hu T, Interleukin-6 polymorphisms modify the risk of periodontitis : a systematic review and meta analysis, J zheijianq Unn Sci B, 2009(12),920 – 927

25. Houshmand B, Hayiloui Reflei A ,Bidqoli M ,Scheilif S ,Evaluation of IL-8 gene polymorphism in patients with periodontitis in Iran ,Dent Res J, 2012; 4: 427-432

26. Graves DT, Cochran D , The contribution of IL-1 and TNF to periodontal tissue destruction ,J Periodontol,2003 ; 41: 391-401

27. Zhong Chen , Peanut S , Giovana ,Expression of proinflammatory and proangiogenic cytokines in patients with head and neck cancer, Clinical cancer research,2013;19(24)

28. Gareema Prasad,Michael Mc Cullough , Chemokines and cytokines as salivary biomarkers for the early diagnosis of oral cancer ,1999; 5:1369-1379

29. Akira Katakura, Isao Kamiyama , Nobuo Takano , Takahiko Shibahara , Takashi M uramatsu, Kazuyuki Ishihara , Ryo Takaji ,Takehiro Shouno, Comparison of salivary cytokine levels in oral cancer patients and healthy subjects,Bull Tokyo Dent coll,2007; 48(4):199-203

30. Dominique S Michaud, Yan Lu, Periodontal disease, tooth loss and cancer risk in a prospective study of male health professionals, Lancet Oncol, 2008 June;9(6): 550 – 558

31. Mine Tezal, Maureen Sullwaan, chronic periodontitis and the risk of tongue cancer, Arch Otolaryngol head and neck Sug 133, 2007

32. Seymour RA ,Is oral health a risk for malignant disease? ,Dent update, 2010 ; 37(5):282-3

33. Sadigi Shamani, Amini, Periodontol disease and tooth loss as risk for cancer : A systematic

review of literature. SID 2011,189 -194

34. Manish Arora, Jennifer, An exploration of shared genetic risk factors between periodontal diseases and cancedr : A prospective co-twin study AJE, 2009;171:253 -259

35. Michael Karin, Toby Lawrence, innate immunity gone awry : linking microbial infections to chronic inflammation and cancer, Cell 124;2006;823-835

36. Eunice Virtanen, Per-Osten Soder,Jukka H Meurman, Leif C Anderson, Birgitta Soder,Chronic periodontal Disease : A proxy of increased cancer risk ,International journal of cancer research , 2013;47:1127-1133

Source of Support: Nill Conflict of Interest: None declared

Review Article

Incipient non-invasive chair side diagnostic aids for oral cancer.

Dr.Indu.M**** Dr.Rathy.R*, Dr.Sunil S**, Dr.Harish RK***, Dr.Neethu Oomen****, Dr.Aswathy kutty*****
Dept of Oral Pathology, Azeezia College of dental sciences and research, Meeyannoor P.O, Kollam, Kerala.

ADDRESS FOR CORRESPONDENCE
Dr.INDU.M
Senior lecturer, Dept of Oral Pathology,
Azeezia College of dental sciences and research
Meeyannoor P.O, Kollam, Kerala.
Indumohan2011@gmail.com

Abstract

Oral cancers are extremely fatal disease conditions which are usually neglected at initial stages. Early detection and treatment gives the best chance for its cure. Several diagnostic aids have been developed over the years for early detection of oral cancer. The purpose of this article is to review the non invasive chair side diagnostic adjuncts for the detection of oral cancer.

Key words: Oral cancer, Dysplasia, Diagnostic aids, Cytology, Tissue fluorescence.

Introduction

The key factor in the lack of improvement in the prognosis of oral cancers is that a significant proportion of cases are not diagnosed and treated until they reach an advanced stage. Incipient non-invasive chair side diagnostic aids can change the scenario to a certain extent.

Incipient non-invasive diagnostic methods

Incipient non-invasive diagnostic methods can be generally divided into standard screening test, established diagnostic adjuncts and light-based detection systems.[1] **(Table 1)** Early stage carcinoma may not be detected by standard screening test. [1]

Other newer techniques include Tissue Fluorescence Spectroscopy, ***Identafi 3000,*** *In Vivo Confocal Microscopy, Colposcopy,* narrow band imaging, Raman spectroscopy etc.

Established diagnostic adjuncts

Vital staining

Staining of cells or tissues in living state is called vital staining. In intra vital staining, staining is done directly on living body and in supra vital staining, stain is applied on slide preparation of

*Professor & Head **Professor ***Reader****Sr. Lecturer*****Intern

detached cells[1,2] TB which is used for vital staining is a cationic metachromatic nuclear stain that selectively binds to acidic tissue component (sulphate, carboxylate, phosphate radicals) of DNA, RNA.[3]

Table 1: Types of incipient noninvasive methods [1]

Methods	Example
Standard screening test	Conventional oral examination (COE)
Established diagnostic adjuncts	Oral cytology Vital staining by Toluidine Blue (tolonium chloride) / TB
Light-based detection systems	ViziLite Plus MicroLux DL VELscope

Table 2: Inoue's classification of IPCL[17]

Type	Appearance	Interpretation
type I	Regular brown dots	Normal mucosa
type II	Dilation and crossing	Normal / progressing into carcinoma
type III	Elongation and meandering	Progressing into carcinoma
type IV	Pattern destruction and angiogenesis large vessels with no loops at the terminal branches	Carcinoma

It stains dysplastic cells more intensely because dysplastic cells contain quantitatively more nucleic acids than normal epithelium. More than that greater penetration and temporary retention of the stain occur in the intercellular spaces of rapidly dividing cells.[3,4]

Dark royal blue colour of mucosa upon TB staining is suggestive of dysplasia. This appearance is significantly related to the nuclear uptake of stain. Pale royal blue staining may be unrelated to dysplasia.[5]

Vital staining is an easy, less technique sensitive and cost effective procedure. But methods of application of stain are not standardised. There is still confusion regarding inclusion of pale blue staining as positive or negative result. Detection of mild dysplasia has been less consistent. Epithelial hyperplasia, hyperkeratosis, inflammatory and traumatic lesions show false positive results.Second examination of inflammatory lesions after 14 days can eliminate reduce false positive results associated with vital staining.[1] *According to Scully the sensitivity and specificity of this procedure ranges from 93.5 to 97.8% and 73.3 to 92.9% respectively.*[6]

Brush biopsy

It is the method of collecting a trans-epithelial cells from a mucosal lesion with representation of the superficial, intermediate and parabasal/basal layers of the epithelium.[7] Brush biopsy is an adjuvant to scalpel biopsy and can be used for evaluating benign-looking lesions, medically compromised patients and when patient refuses to have a biopsy performed.[8,9]

Brush biopsy can be done using Oral CDx Brush Test kit .The obtained epithelial cells are stained by papanicolaou method. Slides are evaluated by an automated computer-driven microscope.[7,8]

Brush biopsy is a relatively painless procedure which requires minimum technical skills and has low inter observer variability. But inadequate sampling may produce false-negative results. Air drying the smear or using wrong fixatives produce artefacts and alterations in the cellular morphology.[7]In a study conducted by Scheifele et al., sensitivity and specificity of brush biopsy were 92.3% and 94.3% respectively. [10]

Light based detection systems (VELscope, ViziLite Plus, MicroLux DL) VELscope (Tissue Fluorescence Imaging/ Wide-field Narrow-emission tissue fluorescence imaging)

Tissue Fluorescence can be used for screening precancers and early cancers of the uterine cervix, skin and oral cavity.[9]

Autofluorescence of tissue alters with epithelial changes like hyperkeratosis, hyperchromatism and cellular and nuclear pleomorphism. Changes in composition of collagen, elastin and changes in concentration of flavin adenine dinucleotide [FAD] and nicotinamide adenine dinucleotide (NAD) also alter tissue fluorescence. [9] Normal mucosa emits a pale green autofluorescence with an intense blue light excitation. Abnormal tissue exhibits decreased autofluorescence and appears darker with respect to the surrounding healthy tissue. Based on autofluorescence technology LED Medical Diagnostics Inc. in partnership with the British Columbia Cancer Agency marketed VELscope system. It is a portable device that allows direct visualization of the oral lesions.[9]

VELscope identifies dysplastic/ malignant lesions (or lesion's margins) that are not visible to the naked eye under white light. But inflammation, ulceration or pigmentation demonstrated a loss of fluorescence on VELscope examination, potentially making it difficult to distinguish them from neoplastic lesions. VELscope system demonstrated 98% sensitivity and a 100% specificity for discriminating dysplasia and cancers.[11]

High-resolution optical techniques

High-resolution imaging can visualize morphologic and architectural features of the epithelium like changes in nuclear size, shape. It may provide a tool to discriminate benign changes from neoplasia with better specificity than wide-field imaging which mainly captures autofluorescence generated primarily in the stroma.[11]

Combination of wide-field and high-resolution systems

Wide-field imaging enables rapid inspection of large mucosal surfaces and high resolution imaging can probe epithelial changes with sub cellular details. Once suspicious regions are identified with wide-field images, these areas could be imaged with sub-cellular resolution using a high-resolution system potentially improving specificity.[11]

Tissue Fluorescence Spectroscopy (auto fluorescence spectroscopy)

The autofluorescence spectroscopy system consists of a small optical fiber that produces various excitation wavelengths and a spectrograph that receives and analyzes the spectra of reflected fluorescence from the tissue.

This technique eliminates the subjective interpretation of tissue fluorescence and has high sensitivity and specificity. But it is not suitable for demarcating large lesions as the optical fiber can sample only a small mucosal area.[9]

Other tests based on tissue Autofluorescence

Identafi 3000, from Trimima Remicalm of Houston uses white, violet and amber light. It allows clinicians to perform the conventional examination with the white light, to observe the changes in tissue autofluorescence with violet light and to examine the areas of loss of autofluorescence with amber light.

The amber light illumination enhances the reflectance property of normal tissue which will assist differentiation of vasculature in normal and abnormal tissues. The vasculature in normal tissue is well defined in contrast to the abnormal tissue which shows a diffuse vasculature.[12]

Chemiluminescence (reflective tissue fluorescence)

Chemiluminescence technique improves identification of mucosal abnormalities with respect to the use of normal incandescent light. They are marketed under the name ViziLite plus and MicroLux Dl. ViziLite uses disposable chemiluminescent light packet. ViziLite Plus also provides a tolonium chloride solution (TB). MicroLux unit offers a reusable, battery-powered light source.[1]

Blue/white light of wavelength 490 to 510 nm is used. Normal healthy tissue will absorb the light and appear dark, abnormal tissue will appear white due to higher nuclear cytoplasmic ratio of epithelial cells.[9]

ViziLite is simple to use, non invasive, no need of special reagents and detect most of mucosal lesions. It needs only short training and has limited operated variability. But ViziLite is expensive and need dark environment. It leaves no permanent record unless photographed. Low specificity for dysplasia may lead to over treatment. In addition there is an inability to measure the results objectively. [9]According to K.H.Awan etal Sensitivity is 77.3 %, specificity is 27.8%.[13]

In vivo Confocal Microscopy (optical biopsy)

Confocal microscopy provides the advantages of optical sectioning and high resolution imaging, by blocking the light originating from tissue layers above and below the focal plane. In Vivo Confocal Microscopy provides images of tissue architecture and cell morphology. It has optical sectioning ability, so no need of surgical procedure, sectioning or staining. But further optimization of the instrument and validation of the data is still needed. [12]

Colposcopy (direct intra oral microscopy)

Colposcopy assesses abnormal vascular pattern, colour tone change and irregular surface contour of tissues. Halogen lamp emit blue/ green filtered light to examine vascular structure.[14]

Normal mucosa exhibit network of hair pin capillaries. As degree of dysplasia increases intercapillary distances increases.In dysplasia, punctate, mosaic, atypical types of capillary networks can be seen. Punctate and mosaic pattern indicates carcinoma insitu. Even if the test is non invasive, painless; vascular patterns could not be visualized if keratinization is present. In addition instrument is expensive. According to Abhishek etal sensitivity of Colposcopy is 68% and specificity of is 54%.[15]

Raman Spectroscopy

Raman spectroscopy is laser-based technique that enables chemical characterization and structure of molecules. Raman spectroscopy has the distinct advantage over other optical techniques that it provides information on molecular composition and structure of living tissue. Raman spectroscopy has been successfully applied for the diagnosis of OSCC in the hamster cheek pouch model. But overlapping of Raman bands occur due to biological constitutes, making it difficult to identify individual components correctly. Signals produced by the Raman Effect are inherently weak. Biomedical samples usually produce a strong fluorescent background which may completely obscure the true Raman signals. The applications of Raman spectroscopy in the life sciences are still in the early stages of development. [16]

Narrow band imaging (NBI)

It is an endoscopic technique that uses special optical filters that narrow the light bandwidth to enhance the visualization of the mucosa surface and microvasculature. NBI checks intrapapillary capillary loops (IPCL).[17]

Morphological changes to the IPCL are useful for diagnosing early cancers, and determining the depth of invasion and the margin of resection. Types of capillary forms and their appearances are summarized in **Table 2**. NBI Xenon light source produce light rays of shorter wavelength (blue

light) and longer wavelength (red light). Shorter wavelength light is absorbed selectively by haemoglobin, providing good contrast for the mucosa microvasculature, mainly the capillary loops. Longer wavelength light penetrates deeper into the tissues revealing the sub mucosal vessels. Each reflected light spectral feature is captured by a charge-coupled device chip at the tip of the endoscope. A unique high-resolution, contrast image is reconstructed at the monitor from the structures.

NBI can be used for follow up of pre-malignant lesions. Visualization of the IPCL alterations surrounding a lesion is useful for establishing the surgical margin. But visualization of the capillaries was limited in areas of hyperplasia and it is difficult to analyze the vasculature in the central areas of mucosal erosion due to IPCL destruction.[17]

Optical coherent tomography (OCT)

OCT is a non invasive high-resolution imaging modality. It is analogous to ultrasound imaging except that it uses light rather than sound. OCT penetration depth is limited to 2 to 3 mm, but this penetration depth sufficient to evaluate macroscopic characteristics of epithelial and sub epithelial structures. [18]

The average scattering coefficients reported here show an increase from 27 cm^{-1} in normal tissue to 39 cm^{-1} in dysplastic tissue to 60 cm^{-1} in SCCs. Increased scattering in abnormal tissue is due to changes in nuclear morphology.But OCT-based early cancer detection is limited by the low contrast levels in biological tissues. [18,19]

Conclusion

Screening and early detection in populations at risk have been proposed to decrease both the morbidity and mortality associated with oral cancer. Several diagnostic adjuncts for detecting early changes for OSCC are currently available. The non invasive diagnostic aids along with mechanism of action and interpretation is summarized in **Table 3.**

Table3: Non invasive diagnostic aids, mechanism of action and interpretation

Diagnostic aid	Mechanism of action	Sign of dysplasia
Vital staining	Affinity for nuclear material	Dark Royal Blue staining
Brush biopsy	Analysis of trans-epithelial cells.	Clinician receives atypical or positive/ negative results in a digitized format
VELscope	Tissue fluorescence	Abnormal tissue exhibits decreased auto fluorescence and appears darker
ViziLite, MicroLux	Chemiluminescence	Abnormal tissue will appear white due to higher nuclear-cytoplasmic ratio.
Colposcopy	Vascular pattern	Punctate, mosaic, atypical types of capillary networks.
NBI	Capillary structure	Type III& IV capillary structure.
OCT	Scattering co efficient of light	Increased scattering coefficient.

REFERENCES

1. Lingen MW, Kalmar JR, Karrison T, Speight PM. Critical Evaluation of Diagnostic Aids for the Detection of Oral Cancer. Oral Oncol. 2008; 44(1): 10–22.
2. Upadhayay J. Asian Pacific Journal of Cancer Prevention 2011; 12: 1757- 1759.
3. K.H.Awan, YH Yang, P.R.Morgan and S.Warnakulasuriya. Utility of toluidine blue as a diagnostic adjunct in the detection of potentially malignant disorders of the oral cavity – a clinical and histological assessment. Oral Diseases 2012; 18: 728–733.
4. Mashberg A: Toluidine blue. J Can Dent

Assoc 1995, 61(11):922-944.

5. Sergio Gandolfo et al. Toluidine blue uptake in potentially malignant oral lesions in vivo: Clinical and histological assessment. Oral Oncology 2006; 42 1: 88–94.

6. Scully C, Bagan JV, Hopper C, Epstein JB. Oral cancer: Current and future diagnostic techniques. American journal of dentistry 2008; 21(4):200-209.

7. Babshet M, Nandimath K, Pervatikar SK, Naikmasur VG. Efficacy of oral brush cytology in the evaluation of the oral premalignant and malignant lesions. J Cytol. 2011 ; 28(4): 165–17

8. Alfred B,Sproll B, Stocklein N, Rita D,Kubler NRK,Handschel J.Role of brush biopsy and DNA cytometry for prevention, diagnosis, therapy and follow up care of oral cancer. Journal of Oncology 2011: 1 -7.

9. Fedele S. Diagnostic aids in the screening of oral cancer. Head & Neck Oncology 2009; 1(5): 1 -6.

10. Scheifele C, Schmidt Westhausen AM, Dietrich T, Reichart PA. The sensitivity and specificity of the OralCDx technique: evaluation of 103 cases. Oral Oncol 2004; 40(8):824–8.

11. Shin D, Vigneswaran N, Gillenwater A, Kortum RR. Advances in fluorescence imaging techniques to detect oral cancer and its precursors Future Oncol. 2010; 6(7): 1143–1154.

12. Cheng, Wright. Advances in diagnostic adjuncts for oral squamous cell carcinoma. The Open Pathology Journal 2011; 5: 3-7.

13. Awan KH, Morgan PR, Warnakulasuriya S. Utility of chemiluminescence (ViziLite) in detection of oral potentially malignant disorders and benign keratosis. J Oral Pathol Med 2011; 40(7): 541 -544.

14. Shambulingappa et al.Colposcopy: A new ray in diagnosis of oral lesions. Indian Journal of dental research 2011; 22(6): 810 -815.

15. Nayyar AS, Gayitri HC,Khan M,Bafna UD, Ahmed S. Colposcopy and carcinoma buccal mucosa: finding significance, a pilot study. International Journal of Scientific and Research Publications 2012, 2(6): 1-7.

16. Oliveira AP, Bitar RA, Silveira L, Zângaro RA, Martin AA. Near-infrared Raman spectroscopy for oral carcinoma diagnosis. Photomed Laser Surg 2006; 24:348-353.

17. Takano JH,Yakushiji T,Kamiyama I,Nomura T,Katakura A,Takano N etal Detecting early oral cancer: narrowband imaging system observation of the oral mucosa microvasculature. Int. J. Oral Maxillofac. Surg. 2010; 39: 208–213.

18. Ahn YC, Chung J, Wilder-Smith P, Chen Z.Multimodality approach to optical early detection and mapping of oral neoplasia. Journal of Biomedical Optics 2011; 16(7):76007-7.

19. Clark AL, Gillenwater A, Alizadeh-Naderi R,

El-Naggar AK, Richards-Kortum R. Detection and diagnosis of oral neoplasia with an optical coherence microscope. J Biomed Opt. 2004; 9(6): 1271–1280.

Source of Support: Nill Conflict of Interest: None declared

Review Article

REVIEW ON HISTOPATHOLOGICAL ASPECTS AND MOLECULAR PATHOGENESIS OF AMELOBLASTOMA

DR. ANILA K.*, DR. MRUDULA K.**
Department Of Oral Pathology And Microbiology,kannur Dental College , Anjarakandy, Kannur, Kerala, India

ADDRESS FOR CORRESPONDENCE
DR. ANILA K.
Professor,
department Of Oral Pathology And Microbiology,
Kannur Dental College,
Anjarakandy, Kannur,
Kerala, India
e-mail: dranila_opath@yahoo.com

ABSTRACT

Ameloblastoma represents 1% of all tumors and cysts of the jaws and remains the most frequently encountered odontogenic tumor. The histological alterations occurring during early ameloblastomatous transformation need to be well elucidated to prevent underdiagnosis of ameloblastoma developing in cysts of the jaws. This article attempts to review the histological aspects, biological behavior of the various types and molecular pathogenesis of ameloblastoma.

Key words: Ameloblastoma, Histopathology, Pathology

1.INTRODUCTION

Odontogenic tumors are lesions derived from the epithelial /mesenchymal remnants of tooth bearing apparatus. Ameloblastoma belongs to the group of tumors arising from odontogenic epithelium with mature fibrous stroma without odontogenic ectomesenchyme. It accounts for 1% of all tumors in head and neck region and around 11% of all odontogenic tumors. The W.H.O. Monograph on International Histologic Classification of Tumors defines ameloblastoma as "an invasive, potentially malignant neoplasm consisting of proliferating odontogenic epithelium supported by fibrous stroma"[1]. Robinson has defined it as a unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent lesion.

2.HISTORY

Gorlin identifies Cusack as the first person to describe ameloblastoma in 1827. Falkson gave a detailed description in 1879. The first histopathologic description was given by Wedl (1853) who called the tumor cystosarcoma or cystosarcoma adenoids and thought that it could have arisen from tooth bud/dental lamina. Wagstaffe (1871) is credited with the first histological drawing. In 1885 Malassez introduced the term adamantinomaepithelioma while Derjinsky (1890) called it adamantinoma[2].Ivey and Churchill in 1930 changed the name to ameloblastoma[1].

*Professor & Head **Postgraduate student

to evaluate objectively, this being a frequently observed phenomenon in neoplasms. Nuclear hyperchromatism is not a cytologic feature routinely encountered in dental cysts though nuclear hyperchromatism has been observed in odontogenic keratocysts (Fig 1)

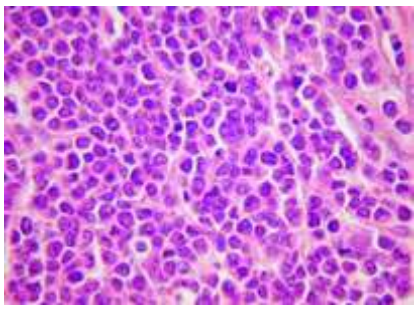


Fig 1Nuclear hyperchromatism(40X)

Palisading with polarization of basal cell nuclei –It is more readily observed and evaluated.It has been a relatively constant feature of ameloblastoma and was the principal histologic factor that led to identification of ameloblastoma as a neoplasm resembling the fetal, tooth-forming structure, the dental organ.(Fig 2)

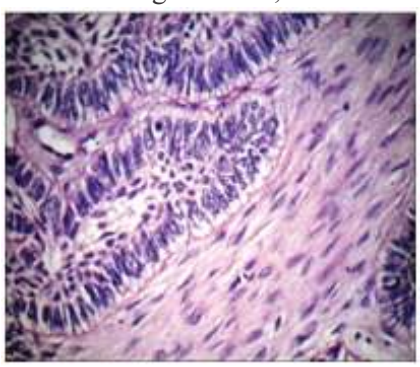


Fig 2

Cytoplasmic vacuolization with intercellular spacing is an additional consistent histopathologic feature and has been frequently pictured in photomicrographs in the literature.It could be easily observed in the basal cells ofthe epithelial lining and were most prominent in that portion of the cell approximating the basement membrane.This has been observed in ameloblastomas and postulated to represent evidence of abortive dentin formation. It can be observed in other odontogenic lesions. Further investigation and amplification of this phenomenon is required.

FOLLICULAR AMELOBLASTOMA:These are most readily recognizable and common type of ameloblastoma histologically. The follicular pattern consist of islands of epithelial cells with a central mass of polyhedral cells or loosely arranged angular cells resembling stellate reticulum.The peripheral cell layer tends to show cytoplasmic vacuolization. Surrounded by well organized single layer of cuboidal or tall columnar cells with nuclei placed at the opposite pole of basement membrane resembling pre-ameloblasts.(Fig 3)

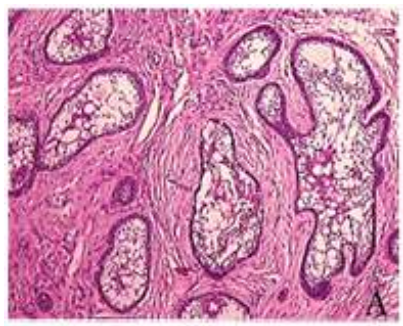


Fig 3

PLEXIFORM AMELOBLASTOMA: The tumor epithelium is arranged in form of network/trabeculae which is bound by a layer of cuboidal or columnar cells and stellate reticulum like areas are usually minimal. Cyst formation occurs but is usually due to stromal degeneration rather than cystic change in the epithelium. The stroma consists of loose, vascular sparsely cellular connective tissue. Arranged as a network of interconnecting strands of cells bounded by a layer of columnar cells, double layer of columnar cells are lined up back to back.

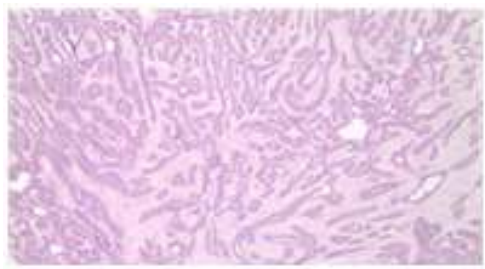


Fig 4

parts of the body especially the pituitary gland

Origin from dental cysts-Cahn in 1983 reported a case of ameloblastoma originating in the wall of a dentigerous cyst,and numerous cases have subsequently developing in this fashion. Stanley and Diehl after reviewing 641 cases found out that 17% of the cases are associated with impacted tooth and dentigerous cyst. Becker described a dental cyst that demonstrated a tendency to form a tumor. The "pavement epithelium" of the cyst sac that was retained gave off "sprouts" of ameloblastomatous character[4].Thoma and Goldman also noted a cystic lesion that demonstrated histologic signs of ameloblastomatous transformation.There have also been proven examples of ameloblastoma that were associated with **odontogenic keratocysts.** Pincock illustrated a cyst with developing ameloblastoma in a patient with multiple jaw cysts and other stigmata of the multiple nevoid basal cell carcinoma syndrome.

Misdiagnosed as origin from cysts-Kramer noted 3 common sources of error when interpreting ameloblastomas as arising in follicular cysts: 1. Epithelial rests may be found in cyst walls;2. There may be cystic, acanthomatous epithelium in granulomatous areas of cysts 3. Ameloblastomas may undergo cystic degeneration[4].

Macroscopy: Mural nodules within lumens of cystic jaw lesions and irregularities of cyst walls have been considered macroscopic evidence of ameloblastoma. There is little advantage of microscopic examination of those specimens without such distinguishing characteristics. Grossly, the typical lesion appears as firm, yellow, with areas of necrosis and cystic degeneration. Some were predominantly cystic, while others were solid.

6.HISTOPATHOLOGY

Although only about 11 % of odontogenic tumors and cysts are estimated to be ameloblastomas, the lesion has continued to fascinate pathologists because of diversity of microscopic features.

Epithelial extensions of cyst linings -Because there is no other absolute way of making diagnosis of ameloblastoma, careful histologic examination of the lining of all odontogenic cysts has been repeatedly emphasized.Outward reaching extensions of the epithelial lining, so-called sprouting or budding, and protruding epithelial islands have been considered histologic evidence of neoplastic transformation[4]. Several histologic variants of growth patterns were noted. The most common types were follicular and plexiform. Multiple sections of these tumors revealed an overlap in the patterns of neoplastic growth. Squamous metaplasia was especially associated with the follicular and granular cell varieties.Out of all,the one which requires special attention is desmoplasticameloblastoma. It has unusual histomorphology with extensive stromal collagenization or desmoplasia. Subclassification of ameloblastoma has not proven practical, however, since it has been determined that 2 or more histologic types may be observed in the same tumor, and there has been little evidence to suggest there are significant differences in bioIogicaI behavior.

Vicker and Gorlin[4] introduced a criteria for diagnosing ameloblastoma in which hyperchromatism of basal cell nuclei, palisading with polarization of basal cells and cytoplasmic vacuolization with intercellular spacing of the lining epithelium were required to be observed *together.*No single histologic alteration of the **3** appeared more significant than the other on the basis of the present analysis and, therefore, all should be observed prior to consideration of cystic lesions of jaws as early ameloblastomas

Hyperchromatic staining reactions of nuclei is difficult

3.CLASSIFICATION

According to the World Health Organization (WHO) Classification of Odontogenic Tumors in 2005.

Ameloblastoma is divided into 4 types: Solid/ multicystic(intra –osseous), Peripheral(extra-osseous), Unicystic and Desmoplastic[3]

Histopathologic Classification

A.The solid/multicystic ameloblastoma can be divided into a follicular and a plexiform type

1.The follicular type2.The plexiform type

1.a Spindle cell type,

1.bAcanthomatous type

1.c Granular type

1.d Basal cell type

B. The unicystic ameloblastoma represents an ameloblastoma variant that presents as a cyst. Two histopathological variants are recognized--luminal variant and mural variant

C.The peripheral type shows the histopathogical cell types and patterns as seen in the solid/multicystic type.

D.In the desmoplastic type the stromal component dominates, compressing the odontogenic epithelial components

Classification of Unicystic Ameloblastoma

Ackermann classified this entity into the

Group I: Luminal unicystic ameloblastoma-tumor confined to the luminal surface of the cyst

Group II: Intraluminal/plexiform unicystic ameloblastoma-nodular proliferation into the lumen without infiltration of tumor cells into the connective tissue wall

Group III: Mural unicystic ameloblastoma-invasive islands of ameloblastomatous epithelium in the connective tissue wall not involving the entire epithelium.

The classification has been modified by Philipsen and Reichart as follows:

Subgroup 1: Luminal

Subgroup 1.2: Luminal and intraluminal

Subgroup 1.2.3: Luminal, intraluminal andintramural

Subgroup 1.3: Luminal and intramural.

4.GEOGRAPHIC VARIATION

Only the mandibular predilection and the two most common histopathologic patterns (follicular and plexiform) seem to be agreed on by most reported series. The clinicopathologic features of ameloblastomas from some countries in Asia differ from those in North America with respect to age, gender, and radiographic features. The differences may be partially accounted for by ethnic influences, accessibility to medical facilities, documentation, and the availability of data. Histopathologically, the distribution of tumors were as follows:Solid/multicystic type -75.02%, Unicystic - 20.71%,Desmoplastic -4.34%,Peripheral ameloblastomas -4.27%[3]

Of particular interest is that the incidence of unicystic ameloblastoma was remarkably higher in Asia than in North America, whereas the opposite was true for peripheral ameloblastoma. In most of the countries the most common histopathologic pattern is the follicular pattern .The second most common histopathologicpatterninNorth America is mixed follicular and plexiform pattern (in solid/multicystic ameloblastoma),closely followed by the pure plexiform pattern. In Asia theplexiform pattern is followed by the acanthomatous pattern.

5.ORIGIN

The possible sources of cells forming these lesions are epithelial lining of odontogenic cysts, especially dentigerous cysts, disturbances of developing enamel organ, reduced enamel epithelium, stratified squamous epithelium of the oral cavity, displaced dental epithelial remnants or cell rests,heterotrophic epithelium in other

ACANTHOMATOUS AMELOBLASTOMA-- It resembles a typical follicular ameloblastoma except that it shows extensive squamous metaplasia sometimes with keratin formation within the central portion of epithelial islands. Central area of follicles show extensive squamous metaplasia

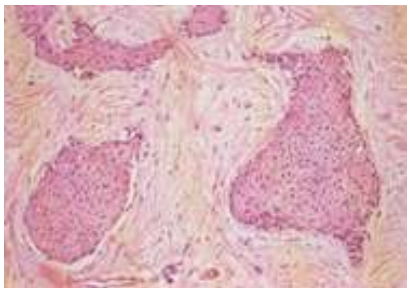


Fig 5

GRANULAR CELL AMELOBLASTOMA:When the central stellate reticulum cells show extensive granular cell transformation i.e. in the form of sheets of large eosinophilic granular cells, the tumors are referred to as granular cell ameloblastoma. Sometimes this change may be so extensive that the peripheral columnar cells may also be replaced making the diagnosis difficult espesially in a small biopsy. Ultrastructurally, it is seen that the granules consist of pleomorphic, osmiophilic, lysosome like organelles

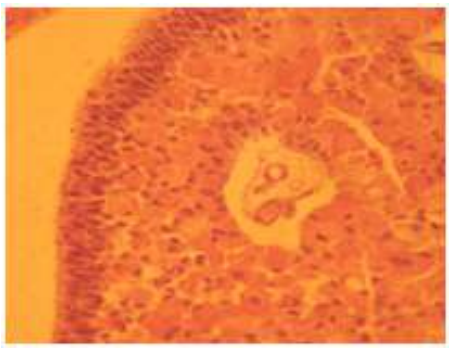


Fig 6

CLEAR CELLAMELOBLASTOMA:They show unusual histologic biphasic patterns with areas of acceptable ameloblastoma (follicular, basaloid cells, acanthomatous) together with the conspicuous clear cell component in the ameloblastic follicles. The presence of clear cell component may represent a sign of dedifferentiation and possibly a malignancy with or without metastases. [5]

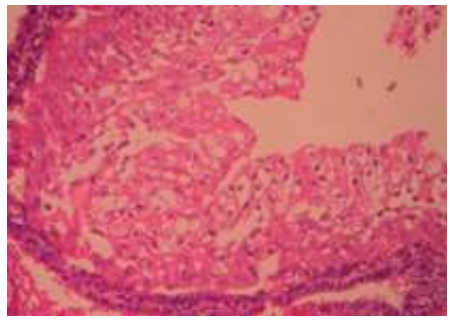


Fig 7

BASAL CELL AMELOBLASTOMA: Basal cell variant of ameloblastoma is the least common type.This variant shows predominant basaloid pattern consisting of darkly stained cells with minimal cytoplasm and little evidence of palisading at the periphery resembling those seen in basal cell carcinoma.These lesions are composed of nests of uniform basaloid cells and are histopathologically very similar to basal cell carcinoma of skin. No stellate reticulum is present in the center portion of the nest. The peripheral cells around the nest tend to be cuboidal rather than columnar

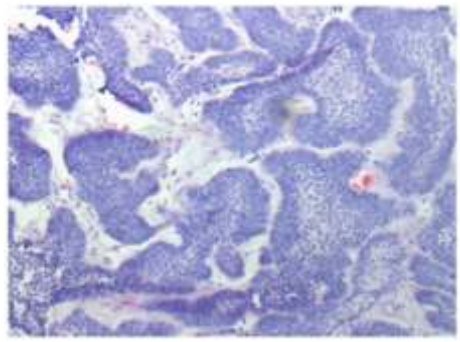


Fig 8

DESMOPLASTIC AMELOBLASTOMA:First described in detail by Eversole et al. in 1984 .Characterized by extensive stromal collagenization or desmoplasia surrounding compressed small/irregular islands of odontogenic epithelium making it a distinct entity. Cyst formation is common and ameloblast like areas are present only in small foci. Calcification in the

fibrous stroma and occasional bone formation can also be seen. Extensive stromal collagenization or desmoplasia surrounding compressed small/irregular islands of odontogenic epithelium

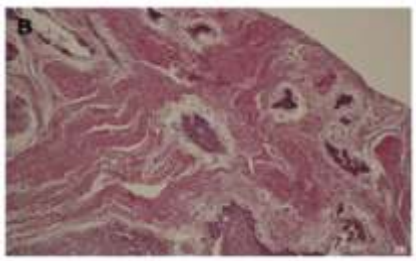


Fig 9

UNICYSTIC AMELOBLASTOMA:Unicystic ameloblastoma refers to those cystic lesions that show clinical, radiographic or gross features of a jaw cyst but on histologic examination show a typical ameloblastomatous epithelium lining the cyst cavity, with or without luminal and/or mural tumor proliferation

1.Luminal UA-Cystic lesion lined by epithelium which exhibits columnar differentiation and reverse polarization of the basal cell layer.The connective tissue adjacent to the epithelium often exhibits a uniform, thin band like area of hyalinization.

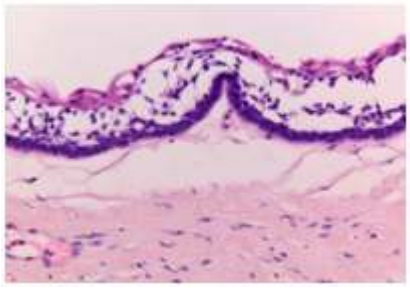


Fig 10

Unicystic ameloblastoma (luminal type), showing ameloblastomatous epithelium lining the "cyst" wall

1.2 Luminal And Intraluminal --Is the simple type but exhibits one or more nodules projecting into the lumen.No extension is seen into the surrounding connective tissue wall. Occasionally, this form of UA can produce an intraluminal plexiform pattern of odontogenic epithelium that lacks typical ameloblastomatous differentiation and is called as unicystic plexiformameloblastoma.

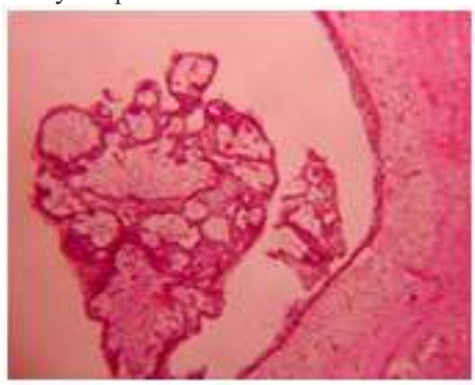


Fig 11

Nodules projecting into the lumen.

1.2.3. Luminal, Intraluminal And Intramural :Here there is occurrence of intramural proliferation of ameloblastoma along with subgroup 1.2 features.

1.3. Luminal and intramural UA:Exhibits a cyst with a luminal lining in combination with intramural nodules. The intramural ameloblastoma tissue may be seen as an infiltration from the cyst lining or as free islands of follicular ameloblastoma.

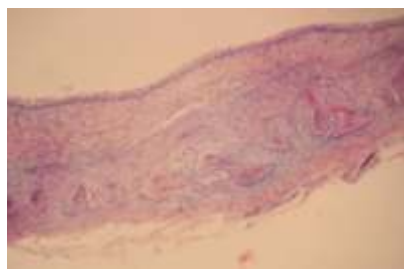


Fig 12 *Extensions of tumor cells into the underlying connective tissue*

PERIPHERAL AMELOBLASTOMA-- Can be defined as an odontogenic tumor with the histologic characteristics of an intraosseous ameloblastoma but occurring solely in the soft tissues covering the tooth-bearing parts of the jaws.The most common histological pattern is acanthomatous.PA should be differentiated from peripheral reactive lesions such as pyogenic

granuloma, epulis, papilloma,fibromaperipheral giant-cell granuloma,peripheral odontogenic fibroma,peripheral-ossifying fibroma,Baden's odontogenic gingival epithelial hamartoma and basal cell carcinoma of the gingiva(features showing resemblance are the peripheral palisading of cell,hyperchromatic nuclei and minimal atypia)

MOLECULAR PATHOGENESIS

1.Clonality
2.Cell cycle proliferation
3.Apoptosis
4.Tumor suppressor genes
5.Signaling pathways
6.Ameloblastin and other enamel matrix proteins
7.Osteoclastin mechanisms and matrix metalloproteinases

Clonality-The etiology of the ameloblastoma has not been clarified yet. An essential step in the study of the pathogenesis of tumors is the determination of its clonal pattern.An initial mutation/molecular alteration is the first event in the development of the tumor[6]. Although molecular alterations were detected in ameloblastoma, the sequence of events remains unknown.

Cell cycle proliferation-The Ki-67 protein (also known as MKI67) is a cellular marker for proliferation. Ki67 positive nuclei in the ameloblastoma are mainly located in peripheral ameloblast-like cells in the follicular as well as in the plexiform areas of the solid ameloblastoma and in the basal cells of unicystic ameloblastoma[7].This staining pattern indicates that the cellular proliferation and consequently the ameloblastoma growth are concentrated in the peripheral areas composed by ameloblast-like cells[8].Desmoplasticameloblastoma had a lower cellular proliferation index (1.5%) than peripheralameloblastoma.A higher Ki67 staining in the solid/multicystic follicular subtype in comparison with other types of ameloblastomas was observed in some studies .The great body of evidence support an overall low cellular proliferation index in ameloblastoma. The influence of such low index on the lesion's behaviour still needs to be clarified. However, a higher cellular proliferation index was found in the recurrent samples of ameloblastomas when compared with primary lesions[9,10].

An interesting fact is the demonstration that telomerase activity, which is linked to cell immortalization, is associated with the proliferative potential of ameloblastomacells . According to these authors,the telomerase activity detected in ameloblastoma reflects tumour characteristics such as ability of local invasion and high recurrence rates.

Apoptosis-Two distinct patterns of ameloblastoma cells are observed .An anti-apoptotic proliferating area correspondent to its peripheral basal cell layer and a pro-apoptotic site in the central layers of the tumourislands . A different expression pattern of apoptosis-related proteins could not be demonstrated between primary and recurrent ameloblastomas, which means that apoptotic activity is not a predictive marker of recurrence[11].The peripheral basal cell layer of ameloblastomas are responsible for the progression of this neoplasia, as they express anti-apoptotic proteins (such as Bcl-2) together with cell proliferation markers (such as Ki67/MIB1).

Tumor Markers And Tumorigenesis

Important genes involved in the initiation of tooth development,morphogenesis, and cytodifferentiation and tooth patterning includeSonic hedgehog (*SHH*),Patched (*PTCH*),*WNT* ,Activin,ßaP53, P63 andP73. Also found are the growth factors like bone morphogenetic proteins (*BMP2* and *BMP4*) and fibroblast-growth-factor (*FGF*) and proteins such

asameloblastin,enamel matrix proteins,calretinin,syndecan-1, proteinase like MMP.There are specific pathways through which the proteins coded by these genes act to bring about the process of tooth development. Alterations in these genes will result in significant alterations in its function resulting in aberrant tooth development

Tumour suppressor genes -p53 is the most widely mutated gene across all cancer types .Mutations of the p53 do not seem to play an important role in ameloblastoma pathogenesis. Allelic losses of tumor suppressor genes were demonstrated in a high proportion of ameloblastoma cases[12] .Kumamoto et al. demonstrated positive expression of p63 and p73, which are p53 homologues, in tooth germs as well as in ameloblastomas[13]

Signaling Molecules-The PTCH1 gene encodes a transmembrane receptor for Sonic Hedgehog (SHH) and other Hedgehog proteins.It was suggested that the deregulation of genes involved in odontogenesis might play a role in ameloblastomahistogenesis. A high expression of SHH (Sonic Hedgehog), SMO (Smoothened) and GLI protein was reported in ameloblastoma using immunohistochemistry[14]. PTEN (Phosphatase And Tensin Homologue)protein functions as an inhibitor of Akt signaling pathway, leading to cell cycle arrest and apoptosis. A significant reduction of PTEN immunoexpression was observed in ameloblastomas compared with tooth germs .Whether the decreased PTEN expression is a phenomenon involved in the transformation of the odontogenic epithelium needs further investigations.

Syndecan-1 (CD138) is known to regulate many biological processes, including odontogenesis, and it was suggested to participate in the Wnt- induced tumourigenesis in odontogenicepithelium .Decreased expression of syndecan-1 was observed in the ameloblast-like cells of ameloblastomas .There is also loss of this protein in malignant epithelial neoplasms and it was associated with parameters such as tissue invasion, metastasis and poor prognosis Hence syndecan-1 might be involved in promoting local invasiveness of ameloblastomas[15]

Ameloblastin and other enamel matrix proteins- Ameloblastin is the most important protein involved in dental cytodifferentiation and is highly expressed during the inner enamel epithelium differentiation.As ameloblastoma shows ameloblast-like cells, the ameloblastin protein has been immunohistochemically investigated in these tumours.[16,17]Ameloblastin has a central role in the ameloblastoma pathogenesis.Enamelin and sheathlin proteins were not expressedin ameloblastoma, whereas amelogenin and ameloblastin (involved in dental cytodifferentiation)secreted by differentiated ameloblasts, was expressedby ameloblastoma epithelial cells.Mutations of ameloblastin gene were also detected in other epithelial odontogenictumours, this alteration is not a specific molecular signature of ameloblastomadevelopment.

Osteoclastic mechanism and matrix metalloproteinases-The most controversial characteristic of ameloblastomais its invasiveness into surrounding bone via osteoclastic bone destruction, despite its benign nature.Ameloblastoma could induce osteoclastogenesis by secreting (RANKL) and TNFalpha. This osteoclastogenesis, in turn, provides the space for ameloblastoma to expand in the bone[18]. Matrix metalloproteinases are important in matrix degradation during tumour growth, invasion and induction of angiogenesis. MMP-2 has an important function as it can degrade type IV collagen, resulting in the promotion of tumour invasion and metastasis

As mRNA levels of TIMP-2 and MMP-14 were

significantly higher in recurrent and solid/multicystic ameloblastoma tissues than in primary and unicystic ameloblastoma tissues, respectively, the local invasive capacity of ameloblastoma may be related to the expression of these MMPs.Mechanism by which ameloblastoma gain growth and invasion advantages include overexpression of TNF –alpha,anti apoptotic proteins [bcl2 and bcl-x1] and interface proteins [FGF and MMPS] .Caspase 3 an enzyme in the apoptosis-inducingprotease is associated with cell death. Ameloblastoma showed positivity for Caspase 3, in the central area of tumor islands.

Loss of chromosome 22 and 10 has been seen inameloblastoma which leads to oncogenesis.TWIST is a transcription protein which works as an epithelial-mesenchymal transition promoter and has been expressed in ameloblastoma playing a role in tumor development[7]. Nuclear accumulation of b-catenin was demonstrated in ameloblastomas and it seemed to be associated with tumourigenesis and cell proliferation .Calretinin (calb2) is a protein expressed diffusely and intensely in the inner enamel epithelium and presecretoryameloblasts during odontogenesis .This protein is strongly expressed only in ameloblastomas compared with other odontogenic tumours.This protein may play a role in the transition of the dental lamina remnants to ameloblastoma[19]

CONCLUSION:Despite advances in the field of genetic or epigenetic alterations in ameloblastoma, the genes responsible for the susceptibility of the disease are not known.Moreover, a great effort should be made to establish theprofile of up and down regulated genes in ameloblastomausing microarrays analysis. Molecular studies could set up new predictive markers for ameloblastoma evolution and to establish new paradigms for the differential diagnosis of unicystic and multicystic clinical variants

REFERENCES

1. Sehdev MK, Huvos AG, Strong EW, Gerold FP, Willis GW (1974) Proceedings: ameloblastoma of maxilla and mandible. Cancer 33(2):324–333
2. Head and neck:odontogenic tumor :Ameloblastoma
3. Ameloblastoma: a multicentricstudy,OOO, *Vol. 113 No. 6 June 2012*
4. Ameloblastoma: delineation of early histopathologic features of neoplasiaroberat. Vickersd, ds, msd," and roberjt. Gorlind,d s, m s . CANCER*September*1970. Vol. 26
5. Reichart PA, Philipsen HA –Odontogenic tumors
6. Current concepts of ameloblastoma pathogenesis .Carolina Cavalieri Gomes1, Alessandra Pires Duarte2, Marina Gonc¸alves Diniz2, Ricardo Santiago . J Oral Pathol Med (2010) 39: 585–591
7. The molecular and genetic aspects in the pathogenesis and treatment of ameloblastoma,Journal of dr.ntr universty of helath sciennces,2013:2:157-161
8. Ja¨a¨ skela¨ inen K, Jee KJ, Leivo I, Saloniemi I, KnuutilaS,Heikinheimo K. Cell proliferation and chromosomalchanges in human ameloblastoma. Cancer Genet Cytogenet2002; 136: 31–7.
9. Piattelli A, Fioroni M, Santinelli A, Rubini C. Expressionof proliferating cell nuclear antigen in ameloblastomas andodontogenic cysts. Oral Oncol 1998; 34: 408–12.
10. Hirayama T, Hamada T, Hasui K, Semba I, Murata F,Sugihara K. Immunohistochemical analysis of cell proliferation and suppression of

ameloblastoma with special reference to plexiform and follicular ameloblastoma. ActaHistochemCytochem 2004; 37: 391–8.

11. Luo HY, Yu SF, Li TJ. Differential expression ofapoptosis-related proteins in various cellular componentsof ameloblastomas. Int J Oral MaxillofacSurg 2006; 35:750–5.
12. Nodit L, Barnes L, Childers E, Finkelstein S, Swalsky P,Hunt J. Allelic loss of tumour suppressor genes inameloblastictumours. Mod Pathol 2004; 17: 1062–7.
13. Kumamoto H, Ohki K, Ooya K. Expression of p63 andp73 in ameloblastomas. J Oral Pathol Med 2005; 34: 220–6.
14. Kumamoto H, Ohki K, Ooya K. Expression of Sonichedgehog (SHH) signaling molecules in ameloblastomas.J Oral Pathol Med 2004; 33: 185–90.
15. Leocata P, Villari D, Fazzari C, Lentini M, Fortunato C,Nico` tina PA. Syndecan-1 and Wingless-type protein-1 inhuman ameloblastomas. J Oral Pathol Med 2007; 36: 394–9.
16. Saku T, Okabe H, Shimokawa H. Immunohistochemicaldemonstration of enamel proteins in odontogenictumours. J Oral Pathol Med 1992; 21: 113–9.
17. Takata T, Miyauchi M, Ogawa I, et al. Immunoexpressionof transforming growth factor beta in desmoplasticameloblastoma.Virchows Arch 2000; 436: 319–23.
18. Sandra F, Hendarmin L, Kukita T, Nakao Y, NakamuraN, Nakamura S. Ameloblastoma induces osteoclastogenesis:a possible role of ameloblastoma in expanding in thebone. Oral Oncol 2005; 41: 637–44.
19. Mistry D, Altini M, Coleman HG, Ali H, MaioranoE.The spatial and temporal expression of calretinin in developing rat molars (Rattusnorvegicus). Arch Oral Biol 2001; 46: 973–81

Source of Support: Nill Conflict of Interest: None declared

Review Article

REJUVENATE THE PULP: REVITALISATION

Dr. Praveena G* Dr. Ajay Varghese Kurien** Dr. Arun M.**
Dept of Conservative dentistry, Azeezia College of Dental Science & Research, Meeyannoor, Kerala State, India

ADDRESS FOR CORRESPONDENCE

Dr. Praveena G. MDS,
Professor, Dept. of Conservative dentistry,
Azeezia College of Dental Science & Research
Diamond hills, Meeyannoor,
Kollam, Kerala, India
E-mail: pravi_geetha@gmail.com

Abstract

The field of Regenerative endodontic*s* makes use of tissue engineering, to regenerate functional and healthy pulp-dentine complex.Regenerative procedures have diverse applications and in endodontics, it includes direct pulp capping, revascularization, apexogenesis, apexification, and even stem cell therapy and tissue engineering.It involves the triad of appropriate stem cells, scaffolds, and the growth factors to form a functional tissue or organ.The process of revascularization takes place by various mechanisms and it has its own advantages and limitations.

Intracanal medicaments like triple antibiotic paste have a significant role to create a sterile environment, which is mandatory in regenerative endodontic procedures like revascularization. Tooth discolouration is a major disadvantage ofTriple antibiotic paste.Augmentin is a suitable alternative to triple antibiotic paste which does not imparts any tooth discolouration.

Conclusion:
The rapid scientific advancement in the field of regenerative endodontics will allow the dentists to perform *'regeneration of tooth'* as a routine treatment optionin the near future.

Introduction

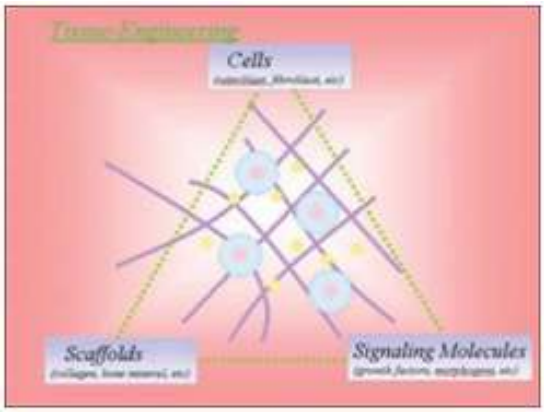
The field of Regenerative endodontics is quite interesting and rapidly advancing. It makes use of tissue engineering, to regenerate functional and healthy pulp-dentine complex.Regenerative endodontic procedures can be defined as biologically based procedures designed to predictably replace damaged, diseased, or missing structures, including dentin and root structures as well as cells of the pulp–dentin complex, with live viable tissues, preferably of the same origin, that restore the normal physiologic functions of the pulp–dentin complex.[1] It involves the spatial delivery of appropriate stem cells, scaffolds, and the growth factors to form a functional tissue or organ.Regenerative endodontic procedures are diverse and can include direct pulp capping, revascularization, apexogenesis, apexification, and even stem cell therapy and tissue engineering. Revascularisation is a beneficial procedure to the patients that can re-establish the vitality in non-vital teeth. This article describes the various components and procedures of Revacularisation, its biological mechanisms, advantages and limitations, and the future of regenerative endodontics.

Triad of Regenerative Endodontics[2]

It includes Stem cells, Growth factors and

*Professor **Post Graduate Student

Scaffold.



Stem Cells

Pulpal mesenchyme stem cells are thought to be localized in the perivascular region and the cell-rich zone adjacent to the odontoblastic layer; both have been proposed to serve as cell sources for replacement odontoblasts. At least five different types of postnatal mesenchymal stem cells have been reported to differentiate into odontoblast-like cells, including dental pulp stem cells (DPSC),stem cells of human exfoliated deciduous teeth (SHED),stem cells of the apical papilla (SCAP),dental follicle progenitor cells (DFPC),and bone marrow-derived mesenchymal stem cells (BMMSC).

Growth Factors/ Morphogens

Growth factors trigger the differentiation of selected mesenchymal stem cell populations into odontoblast-like cells. They include corticosteroids, statins, demineralized human bone, TGF-β-3, Nerve growth factor (NGF), Fibroblast growth factor 2 and so on. Moreover, the application of ethylenediamine tetraacetic acid (EDTA) strongly exposed immunoreactive TGF from human dentin, with appreciably smaller activities released after treatment with $Ca(OH)_2$, sodium hypochlorite (NaOCl), mineral trioxide aggregate (MTA), or citric acid.

Scaffolds

An important component of tissue engineering is a physical scaffold. Tissues are organized as three-dimensional structures, and appropriate scaffolding is necessary to provide a spatially correct position of cell location and regulate differentiation, proliferation, or metabolism. It is known that extracellular matrix molecules control the differentiation of stem cells and an appropriate scaffold might selectively bind and localize cells, contain growth factors, and undergo biodegradation over time.

Scaffolds can be classified as either natural or synthetic. Natural scaffolds include collagen, glycosaminoglycans, demineralized or native dentin matrix. Platelet-rich plasma (PRP) is first generation platelet concentrate autologous, fairly easy to prepare in a dental setting, rich in growth factors. But Platelet-rich fibrin is second generation platelet concentrate, which has better handling properties, ease of preparation, greater amount of growth factors and no use of anticoagulants as in the case PRP.

Chitosan, chemically similar to cellulose, has been investigated for use as a scaffold for dental pulp regeneration. Direct pulp capping with chitosan monomer in rats showed that chitosan monomer induced minimal inflammatory cell infiltration after 1 day, promoted proliferation of pulp fibroblasts after 3 days, and induced mineralization by odontoblastic cells after 5 and 7 days.[3]

Synthetic Scaffolds include polylacticacid(PLA), polyglycolic acid(PGA), polylacticcoglycolic acid (PLGA), hydroxyapatite/tricalcium phosphate, bioceramics and polyethylene glycol (PEG). Moreover, the combination of scaffolds with certain growth factors/ morphogens appears to be an important combination for optimal generation of an odontoblast-like cell.

Intracanal Medicaments

The development and progression of endodontically induced periapical lesion is clearly associated with polymicrobial infection in the root canal system.Because of the complexity of the root canal infection, it is unlikely that any single antibiotic could result in effective sterilization of the canal.. Majority of bacteria in the infected root canal dentin are obligate anaerobes. Hence, metronidazole was selected as the first choice among antibacterial drugs. Even at a high concentration, it cannot kill all the bacteria, indicating the necessity for combination of other drugs. Triple Antibiotic Paste appears to be most promising consists of metronidazole, ciprofloxacin, and minocycline. Propylene glycol can be used as a vehicle for the delivery of this paste.

The triple-antibiotics regimen was first tested by Sato *et al.,* which is a combination of 500 mg metronidazole, 200 mg ciprofloxacin and 100 mg minocycline for the disinfection of root canal system. It was used in the ratio of 1:1:1 or 1:3:3.Metronidazole is a nitroimidazole compound that exhibits a broad spectrum of activity against protozoa and anaerobic bacteria[4]. Minocycline is a semisynthetic derivative of tetracycline with a similar spectrum of activity. Ciprofloxacin, a synthetic fluoroquinolone, has a bactericidal mode of action.

Ruparel et al[5] reported that both Triple Antibiotic Paste and Augmentin have serious detrimental effects on Stem Cells of Apical Papilla in concentrations 10 times lower than its clinical dose. They also noted that Calcium hydroxide is biocompatible with Stem Cells of Apical Papilla. But long-term use of calcium hydroxide has several disadvantages such as multiple treatment appointments, probable recontamination of the root canal system during treatment period, and increased brittleness of root dentin which increases the risk of future cervical root fractures. Recently, mineral trioxide aggregate (MTA) has been used in one-step apexification procedures to create an artificial apical barrier on which the obturation material can be compacted. Although clinically successful for treatment of apical periodontitis it does not help to strengthen the root, and in the absence of continued development of the root, the roots remain thin and fragile. Recent studies had shown that both grey and white MTA discolour the tooth structure.

The main disadvantage of Triple Antibiotic Paste is tooth discolouration. It is mainly related to minocycline in the antibiotic paste. One option to prevent this discolouration is to replace minocycline by Cefaclor or Fosfomycin. Augmentin can be used as another good alternative to Triple antibiotic paste to prevent the tooth discolouration[6]. Hoshino *et al*. performed an *in vitro* study testing the antibacterial efficacy of these drugs alone and in combination against the bacteria of infected dentin, infected pulps, and periapical lesions. Alone, none of the drugs resulted in complete elimination of bacteria. However, in combination, these drugs were able to consistently sterilize all samples[7].

Platelet rich plasma (PRP) and Platelet rich fibrin (PRF)[8]

Platelet rich plasma and Platelet rich fibrin have been used for pulp regeneration. Platelet rich plasma (PRP), first generation of autologous platelet concentrate, has complex preparation protocol and moderate benefits limit its usage in regenerative surgeries .Platelet rich fibrin (PRF), introduced by Choukroun et al. in the year 2001, is a second-generation platelet concentrate enriched with platelets and growth factors which promote periapical tissue regeneration and healing. Unlike PRP, it is obtained from a anticoagulant and thrombin free blood harvest making it free from the risk of disease transmission. Both PRP and PRF have been successfully used with bone grafts like

v. Blood clot itself, being a rich source of growth factors, might plat an important role in regeneration.These include platelet-derived growth factor, vascular endothelial growth factor, platelet derived epithelial growth factor and tissue growth factor.

Advantages:

1. The biggest advantage is the continued root development and strengthening of the root.
2. Obturation of the root canal is not required.
3. After the control of infection, it can be completed in a single visit.

Limitations:

1. Long term clinical results are not yet available
2. The entire canal might be calcified; compromising esthetics and potentially increasing the difficulty in future endodontic treatment, if required.
3. Case wherein post and core are the final restorative treatment plan, revascularization can't be attempted because the vital tissue in apical two-thirds of the canal cannot be violated for post placement.

Future of Regenerative endodontics[10]

Now the regenerative endodontics emphasize on *recreation* of the genetic odontogenic program using stem cells. Numerous genes control embryonic tooth development and define the various dental territories (i.e., incisors, canines, premolars and molars) in the mouth, as well as the number, shape, size and color of the teeth. A stem cell strategy for tooth regeneration must combine stem cell populations with adequate signaling molecules. The existing challenges include the need to determine consistent protocols to control the size, shape and color of teeth, as well as to considerably shorten the time of enamel and root formation and tooth eruption. Furthermore, the use of culture-expanded stem cell populations needs to take into account the possibility of genetic and epigenetic instability. We hope that the rapid scientific and technological advancement will provide new information and solutions that will allow regenerated teeth to become a routine treatment for individuals with missing teeth.

Conclusion

Tooth regeneration provides an attractive alternative to existing tooth restoration therapies. Endodontists' knowledge in the fields of pulp biology, dental trauma and tissue engineering can be applied to deliver biologically based regenerative endodontic treatment of necrotic immature permanent teeth resulting in continued root development, increased thickness in the dentinal walls and apical closure. These developments in regeneration of a functional pulp-dentin complex have a promising impact on efforts to retain the natural dentition, the ultimate goal of endodontic treatment.

References

1. Garcia-Godoy F, Murray PE. Recommendations for using regenerative endodontic procedures in permanent immature traumatized teeth. Dent Traumatol 2012;28(1):33–41.
2. Hargreaves KM, Cohen S. Cohen's pathways of the pulp. 10th edition. St Louis (MO): Mosby Elsevier; 2011. p. 602–19
3. Jeremy J. Mao, Sahng G. Kim,JianZhou,Ling Ye, Shoko Cho,Takahiro Suzuki, Susan Y. Fu,Rujing Yang and Xuedong Zhou. Regenerative Endodontics:Barriers and Strategies for

β-TCP for bone regeneration in the treatment of periodontal defects.

Revascularization Protocol

At the first appointment, the treatment alternatives, risks, and potential benefits should be described to the patient and guardian after collecting clinical information and establishing pulpal and periradicular diagnoses. Then the tooth is anesthetized and isolated. After access opening, minimal instrumentation should be accomplished, but the use of a small file to "scout" the root canal system and determine working length is important. The root canal system is copiously and slowly irrigated with 20 ml of NaOCl followed by 20 ml of 0.12% to 2% chlorhexidine (CHX). The root canal system is then dried with sterile paper points, and the antimicrobial medicament is delivered into the root canal space. Both triple antibiotic paste or Ca(OH)2 medicaments have been shown to be effective. The triple antibiotic paste has the advantage of being a very effective antibiotic combination against odontogenic microorganisms.Ca(OH)2 has the advantage of being widely available and is a commonly used medicament, but it may be cytotoxic to stem cells.After antimicrobial medicament is placed, the tooth is then sealed with a sterile sponge and a temporary filling (e.g., Cavit), and the patient is discharged for 3 to 4 weeks.

At the second appointment, the patient is evaluated for resolution of any signs or symptoms of an acute infection (e.g., swelling, sinus tract pain, etc.) that may have been present at the first appointment. The antimicrobial treatment is repeated if resolution has not occurred.In most cases, the acute signs and symptoms have resolved. Since revascularization-induced bleeding will be evoked at this appointment, the tooth should not be anesthetized with a local anesthetic containing a vasoconstrictor. Instead, 3% mepivacaine can be used, which will facilitate the ability to trigger bleeding into the root canal system.93 Following isolation and reestablishment of coronal access, the tooth should be copiously and slowly irrigated with 20 ml NaOCl, possibly together with gentle agitation with a small hand file to remove the antimicrobial medicament. After drying the canal system with sterile paper points, a file is placed a few mm beyond the apical foramen, and the apical tissue is lacerated with bleeding up to 3 mm from the CEJ. A small piece of Colla-Plug may be inserted into the root canal system to serve as a resorbable matrix to restrict the positioning of the MTA. About 3 mm of MTA is then placed, followed by a restoration. A 12- to 18-month recall should be considered as the earliest time point to conduct the clinical examination and evaluate continued radiographic improvement in root development.

Mechanism of Revascularisation[9]

According to Shah.N, the five possible mechanisms by which the process of revascularization takes place are:

i. A few vital pulp cells in apical end of the root canal might proliferate into the newly formed matrix and differentiate into odontoblasts under the organizing influence of the cells of Hertwig's epithelial root sheath. These cells are quite resistant to destruction, even in the presence of inflammation.

ii. Multiotent dental pulp stem cells, which are present in permanent teeth and immature teeth might be seeded on to thr existing dentinal walls and differentate into odontoblast like cells.

iii. Periodontal ligament stem cells can proliferate and grow into the apical end of root canal and deposit hard tissue.

iv. Stem cells from the apical papilla or the bone marrow migh have excellent proliferating capacity to deposit dental hard tissues.

Clinical Translation.DentClin N Am 56 (2012) 639–649.

4. Bansal R, Khursheed I, Bansal T. Endodontic Management of a Periapical Cyst- A Review. J Adv Med Dent Scie 2013;1(1)

5. Ruparel NB, Teixeira FB, Ferraz CC, Diogenes A.Direct effect of intracanal medicaments on survival of stem cells of the apical papilla. J Endod. 2012 Oct;38(10):1372-5

6. Ali Nozart,KevinL.Li,KunwarVir,M Lamer Hicks, Ashraf F Fouad. Is Pulp Regeneration Necessay for Root Maturation? J Endod 2013;;39:1291-1295

7. RangasamyVijayaraghavan, Veerabathran Mahesh Mathian, AlagappanMeenakshiSundaram,Ramachandran Karunakaran, and SelvarajVinodh. Triple antibiotic paste in root canal therapy. J Pharm Bioallied Sci. Aug 2012; 4(Suppl 2): S230–S233

8. K. B. Jayalakshmi,ShipraAgarwal,M. P. Singh,B. T. Vishwanath,Akash Krishna,and RohitAgrawal. Platelet-Rich Fibrin with β-Tricalcium Phosphate—ANoval Approach for Bone Augmentation in Chronic Periapical Lesion: A Case Report. Case Rep Dent. 2012

9. Shah.N. Efficacy of Revascularization to induce Apexification/ Apexogenesis in infected non-vital immature teeth: A Pilot study.JEndod 2008;34:919-925

10. Thomas A Mitsiadis.Regenerated teeth: the future of tooth replacement? Regen. Med. (2011) 6(2), 135–139

Source of Support: Nill Conflict of Interest: None declared

Review Article

EFFECT OF CELL PHONE RADIATION ON OROFACIAL REGION- A REVIEW

Anuradha S.E.*, Neethu K.**, Smitha S.G.***

Dept of Oral & Maxillofacial Pathology, Royal Dental College, Challisery, Palakkad, Kerala State, India

ADDRESS FOR CORRESPONDENCE

Dr. ANURADHA S.E.
Professor and HOD,
Dept of Oral and Maxillofacial Pathology,
Royal Dental College,
Challisery, Palakkad,
Kerala State, India.
E-mail:anuradhasunil@gmail.com

Abstract : There has been much debate and anxiety in the general public regarding the effect of cell phones on health in both adults and children. Considering that a population of 6 billion out of a total of 7 billion individuals on this planet use cell phones, this is certainly a concern. The addition of various interesting features on cell phones including a high gigabyte storage capacity, games and even movies requiring perhaps 2 - 3hours of viewing is another reason for anxiety. This article attempts to review the effects of cell phone radiation on skin, teeth, salivary glands, oral epithelium and also to evaluate cancer risk and genotoxicity. Studies of various investigators have been compiled and presented in this article.

Keywords: Mobile phones, cell phone radiation, RF-EMF, SAR, effects on human tissues, genotoxicity, cancer risk, steps to reduce RF exposure.

Introduction:

Mobile phones were first introduced in Denmark & Sweden in the late 1980's. The current number of mobile phone users worldwide is about 6 billion.

Transmission and reception of mobile telephone signals take place through electromagnetic wave radiation of RF fields between the mobile phone and the emitting station. There has been much speculation that exposure of the human body to electromagnetic radiation is not safe and may cause skin, ear and brain cancers.

The WHO International Agency for research on cancer classified radiofrequency fields as possibly carcinogenic to humans in 2011.Radiofrequency fields fall in Group 2B of their classification of environmental factors that can increase the risk of cancer in humans, which means that there is limited evidence showing radiofrequency carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals.

The electromagnetic fields of frequencies between 300MHz and 300GHz are the carrier waves (microwaves) that are used by all mobile phone systems. Exposure to EMF in the range 100 kHz to 10GHz results in absorption of part of the energy carried by waves within the body. Within a given volume of body tissue this rate of energy absorption is proportional to the square of internal field strength. It is denoted as SAR (Specific Absorption Rate).

In simpler words the SAR is a measure of the rate at

*Professor, HOD & Principal, ** Senior lecturer, Department of Oral Pathology & Microbiology, Royal Dental College, Chalissery, Kerala. *** General Dental Practitioner, Seventh-Day Adventist Hospital, Ottapalam, Kerala

which energy is absorbed by the human body when exposed to a radiofrequency electromagnetic field such as a mobile device/ cell phone, the unit of which is watts/kilogram (W/kg) of body weight.

Various governments have defined maximum SAR levels for radiofrequency energy emitted by cell phones[1].

US: Phones sold should have SAR level at/below 1.6W/kg per gram of tissue absorbing the most signal.

EU:SAR limits for mobile phones within the European Union are2W/kg averaged over the 10g of tissue absorbing the most signal.

India: Switched from EU limits to US limits for mobile handsets in 2012. In India, random compliance tests are also done by a government run Telecom Engineering Centre and all handsets are supposed to have handsfree mode.

The analog handheld devices of the early 1980's were pioneer models and had higher levels of SAR than the ones that are available today. Comparative values of SAR of cell phones available in the Indian market are shown in the table.

Ï Õ Ö	Brand of Cell phone	Ï Ë Ï Q Ñ
Ê	Ë Ó Ó Ñ Ö Ó Ö Ñ Ċ G Ï	Ó Ë D E
Č	Ë Ó Ó Ñ Ö Ó Ö Ñ Ç Ï	Ê Ê Ê
Ċ	Ë Ó Ó Ñ Ö Ó Ö Ñ D Ï	Ê Ê Đ
Ç	Ġ Ö Ö Ñ Ö Ï Ñ Ŕ Þ Ó Ç	Ó Ë D D
D	Ç ì F Î Õ Ñ Ĵ	Ó Ë Ď Đ
Ď	Ç ì F J Ø Ö Ñ Ö R Ó Ī Ó Ö Ö Ñ Đ Ĵ	Ó Ë D Đ
Đ	Ç ì F G Ñ Ø Ø Ñ	Ê Ç Đ
Đ	Ç ì F Î Õ Ñ I J	Ó Ç D
E	Ħ M Ø Ñ Ö Ö Ō Œ Ö M Ø Þ Ó Ö Ö Ō Ñ Œ	Ó Ë D Ć - 0.99
Ê Ć	I M Q M Ő Ö Ö Ō Ñ Œ	Í ot Available
Ê Ê	I Ñ Ō Ö Ø Ö Ï Đ Ö Ć	Ó Ë D Ç
Ê Č	I Ñ Ō Ö Ø Ö Ï Đ Œ Ć	Ó Ë Ç Ê
Ê Ċ	I Ñ Ō Ö Ø Ö Ï E Ö Ć	Ó Ë Ç Ď
Ê Ç	I Ñ Ō Ö Ø Ö Ï Ď Ö Ć	Ó Ë Ċ Đ
Ê D	I Ñ Ō Ö Ø Ö Ï Đ Ö Ć	Ó Ë Ď D
Ê Ď	Ì Ø M Ő Ö M Ŕ Ő Ö Ō Ñ Œ	Ê Ď Č - 1.97
Ê Đ	Í Ö Ø M Þ Ö Ø M Ď Ć Ć	Ê Ê Ê
Ê Đ	Í Ö Ø M Þ Ö Ø M Đ Ê Ć Ć	Ê Ë Ć
Ê E	Ï M Ö Œ Ō N Ĵ Ö Þ Ñ H H	Ó Ë Ç Č
Č Ć	Ï M Ö Œ Ō N Ġ M Ø M Ŕ Ř Ï H H H	Ó Ë Ç Ć
Č Ê	Ï M Ö Œ Ō N Ġ M Ø M Ŕ Ř Ï H H	Ó Ë Ċ Ç
Č Č	Ï M Ö Œ Ō N Ġ M Ø M Ŕ Ř Ï G Þ Ö Œ	Ó Ë Ç Đ
Č Ċ	Ï Ö Ō Ř Ĵ Ō N Ø M Ï Ñ Ø Ō Œ	Ó Ë D Ç - 1.22

Effects of RF-EMF on Teeth

Various studies have been undertaken to study the effects of exposure to cell phone use on teeth. It is a well-known fact that amalgam restorations and metallic implants in the mouth can create galvanism with the help of saliva as the conductor.

Galvanism results in fluctuation of normal oral electric current up to 1000mV or higher (battery mouth). This current causes amalgam levels (mercury vapour) to rise in surrounding tissues e.g.,gingiva, oral mucous membrane[2].Significant amounts of silver, tin and copper with their own toxic effects are also released. Amalgam containing Zinc produces even higher galvanic currents.

Electric currents and ionic flow between various dental alloys have been shown to cause irritation to trigeminal nerve. These currents also can cause headaches, migraine, dizziness, nausea etc. Removing the amalgam filling, metal fixture or dental repair eliminated the problem.

Studies have also been done on the release of mercury from dental amalgam restoration after exposure to cell phones. It was found that microwave radiation emitted from mobile phones significantly releases mercury from dental amalgam restorations[3].

Another study in 2014 found that enamel microhardness of rats' teeth was not altered after exposure to 900 MHzradio frequency radiation for 2 hours/day for 10 months[4].

Effects on Skin

Molecular level changes might take place in human volunteers in response to exposure to RF-EMF.

A pilot human volunteer study examined whether local exposure of human skin to RF-EMF causes changes in protein expression in living people[5].This was done by taking punch biopsies from non-exposed areas of skin and areas exposed to SAR 1.3 W/kg of RF-EMF. Analysis identified 8 proteins that were significantly affected with 2 of the proteins present in all volunteers.

Studies on temperature changes in soft tissues around the facial nerve led to discovery that the average temperature of surrounding soft tissues was significantly higher than pre-exposure values, during the exposure and immediately after turning off the mobile phone and decreased to normal levels 25

minutes after the exposure. However, there were no adverse effects due to the rise in temperature[6].

Effects on Salivary Glands

A study on the functional and volumetric changes in the parotid glands associated with mobile phone use was conducted in which bilateral parotid ultrasonography was performed to evaluate gland volume.

It was found that there was a significant increase in salivary flow rate along with increase in blood flow rate and increase in the volume of parotid glands at the site where mobiles are frequently placed in heavy users of mobile phones[7].

Another study was undertaken to evaluate physiologic changes in the parotid gland on the side of use(dominant side) of handheld mobile phones. The rate of secretion and protein levels in the saliva secreted by both parotid glands on both sides was studied[8].

It was found that there was a significantly higher saliva secretion rate and lower total protein concentration in the dominant side compared to the other side. It was concluded that parotid glands adjacent to the handheld cell phone in use respond by elevated salivary rates and decreased protein secretion reflecting continuous insult to the glands.

A third study to compare salivary outcomes (secretion, oxidative damage indices, flow rate, composition of saliva) between mobile phone users and non- users was conducted[9]. A significant increase in all salivary oxidative indices was reported in mobile phone users. Salivary flow, total protein, albumin and amylase activity were decreased in mobile phone users. These observations have suggested that the use of mobile phones may cause oxidative stress and modify salivary function.

CANCER RISK

Evaluation of carcinogenicity in humans relies on these sources of data- epidemiological, experimental animal and in vitro genotoxicity data.

There have been innumerable studies to establish a link between use of mobile phones and tumours of the brain and salivary glands. With mobile telephone use prevalent among approximately 6 billion users worldwide today, this is definitely a concern[10].

However, almost all of these studies have not found any significant relation between mobile phone use and carcinogenicity.

The International Commission for Non-Ionising Radiation Protection (ICNIRP) has recommended a basic restriction for SAR localised in the head to 2 W/kg averaged over 10g of tissue.

Long exposures to mobile phone radiation (>1 hour at a time) are not safe and may cause skin, ear and brain cancers[11]. RF is mostly absorbed by mobile phones but some frequencies are absorbed by salivary glands, external ear and brain. In the brain, these frequencies are absorbed by glial and meningeal tissues located in the outermost part of the frontal, parietal and temporal lobes on the side of the head where the mobile phone is used.

According to Swedish researchers the risk of brain cancer is 5 times greater in children as compared to adults[12]. This is because the brain and nervous system in children are in the developmental stages and radiation can disturb this development leading to abnormalities.

Genotoxic effects

Many publications have been reviewed to investigate the genotoxic effect of RF-EMF but there are conflicting reports. Some studies have shown that RF-EMF can enhance the genotoxic effect of other agents.In the studies that show possible positivity of genotoxiceffect of RE-EMF, chromosomal aberration, DNA fragments and gene mutations have been listed[13].

Effects on Oral Epithelium:

A small number of studies have shown genomic alteration in oral epithelial cells in response to mobile phone exposure. Most common alterations observed were increased frequency of nuclear abnormalities such as micronucleus, broken egg etc indicating chromosomal damage.[14]

When frequency of micronucleated exfoliated cells based on duration of mobile phone radiation exposure was studied a positive correlation between 0–1, 1–2, 2–3 and 3–4 years of exposure and the frequency of MNC was found[15]. Other similar studies have shown such changes were significantly greater in subjects who spent more than 5 hours per week on mobile phones.[16]On other hand, some investigations have shown no alterations.[17]

Conclusion:

Many people are concerned that cell phone radiation will cause cancer or other serious health hazards. The weight of scientific evidence has not linked cell phones with any health problems.Many studies conducted to date indicate that there is not much connection between health problems and exposure to Radio Frequency fields by using cell phones.

Cell phones emit low levels of RF energy in the microwave frequency range.

They also emit RF at substantially reduced time intervals (30-40 seconds) when in the standby mode. While high and very high levels of RF and EMF (for example X- rays and Gamma rays) can produce permanent damage by ionizing biological tissues including genetic material like DNA,lowlevels of RF phones produce no known adverse health effects.

The steps that can be taken to reduce RF exposure:

1) Reduce time spent on cell phones as there is a microwave effect (especially if ears become warm while listening)
2) Use speaker mode or wired headset (not Bluetooth) to place more distance between head and cell phones.
3) During a call, keep phone at least 15mm away from head/ear.
4) Avoid carrying cell phone on the body (e.g. in a pocket or bra).
5) Use cell phone on speaker setting or with an "air tube" headset.
6) Avoid using wireless device in cars,trains or elevators (to prevent rebound from the metallic roofs).
7) Avoid keeping cell phones near the head during the night while sleeping. If alarm needs to be set, do so in airplane mode.
8) While charging, phone is to be kept away from the body. Calls should not be answered while charging.
9) Whenever possible, connect to the internet with wired cables.
10) When using Wi-Fi, connect only to download, then disconnect.
11) Avoid prolonged or direct exposure to Wi-Fi routers.
12) Unplug home Wi-Fi router when not in use(that is, at bedtime).
13) When signals are weak or low, cell phone should not be used.
14) Sleep as far away from wireless utility meters ("smart" meters) as possible.
15) Replace amalgam fillings with other materials.
16) Use cell phone with SAR limit below 2 W/ Kg.
17) Use RF safe cell phone accessories (RF safe radiation shield or covers) to reduce radiation.
18) Since mobile towers also emit high amounts of radiation it is advised to avoid residing near them for prolonged periods.
19) Children/toddlers should not be left to play with cell phones as there could be danger from RF EMF during the development of the brain and facial tissues.

References:

1)Wikipedia:http://en.wikipedia.org/w/index.php?title=Specific_absorption_rate&oldid=624137200

2) Metal-Free Dental Implants in Maryland | Dental Implants and Cell Phones - What's The Real Risk? Source: http://www.milesofsmilesdental.net/1792/dental-implants-and-cell-phones-whats-the-real-risk/

3) Mortazavi SMJ, Daiee E, Yazdi A, Khaibani K, Kavousi A, Vazirinejad R et al. Mercury release from dental amalgam restorations after magnetic resonance imaging and following mobile phone use. Pak.J.Biol.Sci 2008;11(8):1142-1146.

4) Dasdag S, Yavuz I, Bakkal M, Kargul B. Effect of Long Term 900 MHz Radiofrequency Radiation on Enamel Microhardness of Rat's Teeth. OHDM 2014;13(3): 749-752.

5) Karinen A, Heinävaara S, Nylund R, Leszczynski D. Mobile phone radiation might alter protein expression in human skin. BMC Genomics. 2008 Feb 11;9:77

6) Acar GO, Yener HM, Savrun FK, Kalkan T, Bayrak I,

Enver O. Thermal effects of mobile phones on facial nerves and surrounding soft tissue. The Laryngoscope 2009;119:559-562

7) Goldwein O, Aframian DJ, Effect of handheld mobile phone use on parotid gland salivary flow rate and volume, Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology; Volume 114, Issue 2, August 2012, Pages 200–206

8) Hashemipour MS, Yarbakht M, Gholamhosseinian A, Famori H. Effect of mobile phone use on salivary concentrations of protein, amylase, lipase, immunoglobulin A, lysozyme, lactoferrin, peroxidase and C-reactive protein

9) Hamzany Y, Feinmesser R, Shpitzer T, Mizrachi A, Hilly O, Hod R. Is human saliva an indicator of the adverse health effects of using mobile phones? Antioxid Redox Signal. 2013 Feb 20;18(6):622-7

10) Environmental Health Perspectives, 11/1/2011, Vol. 119, Issue 11, Page 1534-1538

11) Royal Society of Canada ,1999; Rothman et al,1996; Wiart et al, 1998; Dimbylow and Mann,1994.

12) Social Aspects of Cancer Genesis, Cancer Therapy Vol , 6-14, 2011.

13) Ruediger HW. Genotoxic effects of radiofrequency electromagnetic fields. Pathophysiology. 2009 Aug;16(2-3):89-102.)

14)Gandhi G, Singh P. Cytogenetic damage in mobile phone users: preliminary data.Int J Hum Genet 2005;5(4):259-265.)(Souza Lda C, Cerqueira Ede M, Meireles JR. Assessment of nuclear abnormalities in exfoliated cells from the oral epithelium of mobile phone users. ElectromagnBiol Med. 2014 Jun;33(2):98-102.

15. Yadav S, Sharma MK. Increased frequency of micronucleated exfoliated cells among humans exposed in vivo to mobile telephone radiations. Mutat Res 2008;650(2):175-180.

16.Souza Lda C, Cerqueira Ede M, Meireles JR. Assessment of nuclear abnormalities in exfoliated cells from the oral epithelium of mobile phone users. ElectromagnBiol Med. 2014 Jun;33(2):98-102.

17. Hintzsche H, Stopper H. Micronucleus frequency in buccal mucosa cells of mobile phone users. ToxicolLett 2010; 193(1): 124-130.

Ros-Llor I, Sanchez-Siles M, Camacho-Alonso F, Lopez-Jornet P. Effect of mobile phones on micronucleus frequency in human exfoliated oral mucosal cells. Oral Dis. 2012 Nov;18(8):786-92.

****

.

Source of Support: Nill Conflict of Interest: None declared

Review Article

Is it time to stop the interruption of antiplatelet therapy for dentoalveolar surgery?

Dr. Ajoy V.* Dr. Joy R. Dr. Archana S.*****
Professor & Head of the Department, Oral & Maxillofacial Surgery, Kannur Dental College, Anjarakandy, Kannur: 670612
Dept of Oral & Maxillofacial Surgery, Kannur Dental College, Anjarakandy, Kannur: 670612

ADDRESS FOR CORRESPONDENCE

Dr. Ajoy Vijayan
Professor & Head of the Department
Oral & Maxillofacial Surgery
Kannur Dental College
Anjarakandy
Kannur: 670612
Contact number:
9895414244 (mob)
0497- 2851255
Email id: vjynjy@gmail.com

Abstract: Dental patients presenting for treatment may have cardiovascular diseases necessitating modifications in treatment with respect to drug therapy. The practitioner must be prepared with current trends in the management of patients with cardiovascular diseases, especially with respect to medications acting upon the coagulation cascade. With increase in the number of patients with cardiovascular diseases seeking dental care, the clinician is confronted with a dilemma whether to continue antiplatelet therapy or not prior to surgical procedure. The incidence of post operative hemmorrhage on continuing antipatelet therapy as well as the danger of thrombo- embolic events in case of its discontinuation have been well documented in the literature. This article aims to review the current literature and trends in the management of patients with antiplatelet therapy.

Key words: antiplatelet therapy, thrombo embolic events, risk of hemorrhage,dentoalveolar surgery

Introduction

Cardiovascular diseases form one of the primary causes of mortality and morbidity in the world. Coronary heart disease represents the most frequent indication for antiplatelet therapy. Antiplatelet therapy is indicated for secondary prevention in cases of acute coronary syndrome, myocardial infarction, myocardial revascularisation, ischemic stroke or chronic peripheral arterial insufficiency as it has been found that it reduces the incidence of cardiovascular events in these patients by about 25 to 35%.[1,2]

A considerable number of patients presenting before a dentist are on antiplatelet therapy. Thus the fear of excessive bleeding often prompts the physician to stop antiplatelet therapy before any surgical procedure. But discontinuity of antiplatelet drugs subjects the patient to an increased risk of thrombo-embolic episodes by suppression of antiplatelet protection and by a rebound platelet activity and could bring about fatal cardio-vascular consequences. On the other hand, continuation of therapy may still carry the inherent risk of hemorrhage intra operatively or post operatively.Thus a clinical dilemma of whether to continue or discontinue these agents confronts the surgeon.

Physiology of platelet function:

Platelets are small anucleated cell fragments of megakaryocytes that circulate in blood which play a crucial role in managing vascular integrity and regulating hemostasis. The disc-shaped platelets circulate in an inactive state as long as the endothelial lining of the blood vessel is intact and remain in circulation for about 10 days before being removed

*Professor & Head **Sr. Lecturer***PG Student

from circulation by the spleen. When the endothelium is damaged, the blood is exposed to the subendothelial layer of the vessels. The platelets become spherical and extend pseudopods, which adhere to vessel walls and each other, and release cytoplasmic granules with biochemical mediators which bring about hemostasis. These events lead to the formation of a temporary platelet plug which in conjunction with activation of coagulation cascade stops bleeding from the injured vessel.

When platelets encounter the atherosclerotic eroded endothelial surface which mimics an endothelial injury, platelets are activated initiating the aggregation followed by definitive fibrin clot formation. Also, the atherosclerotic plaques can rupture, attracting platelets to the site, again initiating the formation of a thrombus. This can lead to cardiac event with complete or near complete blockade of the coronary artery leading to ischemia and infarction of the myocardium. A similar event can occur if the blockade of artery occurs in the brain, leading to transient ischemic attack or stroke.

Mechanism of action of commonly used antiplatelet agents:

The commonly used antiplatelet agents are aspirin, clopidogrel or a combination of the two.

Aspirin

Aspirin is the most commonly used antiplatelet agent which brings about its antiplatelet action by decreasing platelet aggregation by irreversibly inhibiting cyclooxygenase-1, thus blocking the synthesis of thromboxane A2, a potent platelet-activating agent. This action lasts for the life span of platelets i.e., 7 to 10 days.

A low dose of aspirin (around 0.5-1 mg/kg body weight, 75-150mg/patient) is generally used.

Clopidogrel

Clopidogrel is another antiplatelet drug which binds to adenosine diphosphate platelet receptor and irreversibly inhibits platelet aggregation.

It is given in a dose of 75mg orally.

A combination of aspirin and clopidogrel has also been used to prevent stroke and produce better results than with each drug alone especially in acute coronary syndrome, post intra coronary stenting and following coronary angioplasty.

Risk of adverse cardiovascular events following discontinuation of antiplatelet therapy

Collet JP et al conducted a retrospective analysis on 475 patients, hospitalized in intensive care for myocardial infarction and reported that, in 11 patients (2.3%), aspirin interruption was seen 15 days prior to the infarction. These patients on long term aspirin had been stable and symptom free for 10 years but suffered myocardial infarction after stopping aspirin therapy. [3]

Ferrari E et al conducted a retrospective study of 1236 patients hospitalized for acute coronary syndrome and found that 51 patients (4.1%) were shown to have interrupted their aspirin intake, 10 ± 1.9 days before the occurrence of the coronary attack.[4,5]

Vaclavik J et al conducted a meta-analysis involving 50,279 patients taking aspirin for secondary prevention and showed that the risk of developing major cardiovascular events after aspirin withdrawal was 3 times higher than in those who did not discontinue aspirin therapy.[6]

Rossini et al found that patients, who had stopped antiplatelet therapy early after drug-eluting stent implantation, experienced a greater incidence of major adverse cardiac events (28.6%) and stent thrombosis (7.6%). Mortality (13.4%) and cardiovascular death (5%) were also significantly higher among patients with early discontinuation.[7]

Risks of bleeding associated with continuing antiplatelet therapy in dentoalveolar surgery:

Ardekian L et al conducted a comparative, randomized, single blinded trial, on 39 patients, who were divided into 2 groups: 20 patients stopped the aspirin treatment at a dose of 100mg; 7 days prior to the dental extractions, and the other 19 pursued it. In both groups, no persisting postoperative bleeding was observed.[8]

Madan GA et al conducted a study on 51 patients on long term low dose aspirin who underwent minor oral dental surgical procedures under local anesthesia without discontinuing aspirin and reported that none of the patients experienced intra-operative or post-operative excessive bleeding.[9]

Garnier et al conducted a descriptive and retrospective

analysis on 52 patients taking antiplatelet agents. Out of 218 extractions performed without stopping the antiplatelet agent treatment, three hemorrhagic sockets were reported (1.3%). One patient presented with persistent bleeding (1.9%) in whom a local hemostatic measure in the form of compression and sutures was used, which stopped the bleeding.[10]

Krishnan B et al conducted a study on eighty-two patients requiring dental extractions, of whom 57 were on antiplatelet therapy (aspirin), and were divided into 3 groups, Group 1 consisting of 25 patients in whom antiplatelet therapy was interrupted, group 2 consisted of 32 patients continuing their medication, and group 3 comprised 25 healthy patients not on antiplatelet therapy , when preoperative bleeding time and clotting time were determined, the mean bleeding times in groups 1, 2, and 3 were 3 minutes, 2 minutes and 45 seconds, and 1 minute and 49 seconds, respectively and no patient in any group had any episode of prolonged or significant bleeding from the extraction sites.[11]

Napenas et al conducted a retrospective study on 43 patients on single or dual anti-platelet therapy who underwent minor dental surgical procedures and concluded that the risk of bleeding complications after invasive dental surgical procedures was negligible.[12]

Cardona-Tortajada et al. monitored 155 patients on antiplatelet therapy who underwent dental extractions. 26 patients had minor bleeding complications which were controlled by local haemostasis measures.[13]

Canigral A et al performed surgical and multiple teeth extractions in patients on aspirin and clopidogrel. In majority of cases (92%), bleeding was mild and subsided within 10 minutes with gauze pressure. In 8% cases, bleeding was moderate and easily controlled by local hemostatic measures.[14]

Mahn-Won Park et al conducted a study on 100 patients having a Drug Eluting Stent who were on long term aspirin clopidogrel therapy and reported only 2 excessive intra extraction bleeding cases that continued at the extraction site for 4 and 5 hours, respectively, and 1 excessive intraextraction bleeding case that continued for 3 hours in the control patients which was controlled by local hemostatic means.[15]

Bajkin BV et al conducted a prospective study on 213 patients on oral anticoagulant and aspirin therapy who were divided into 3 groups with 71 participants in each, group-A patients receiving combined oral anticoagulant and aspirin therapy, group-B oral anticoagulant therapy and group-C receiving aspirin only. It showed that three (4.2%) patients in group A, two (2.8%) in group B and none (0.0%) in group C presented with postoperative bleeding which was easily controlled by local hemostatic measures.[16]

Discussion:

In dentoalveolar surgery, major blood vessels are unlikely to be encountered and bleeding sites are usually accessible and local hemostatic methods can be easily employed to arrest bleeding.

Even though, until recently, it was recommended to discontinue antiplatelet therapy in patients on long term antiplatelet therapy before any surgical procedures due to the fear of intra operative and post operative hemorrhage,[17] the current recommendations and consensus favour no discontinuation of antiplatelet therapy provided proper hemostatic measures are cautiously undertaken.[8,9,10,11,12,13,14,15,16]

The American and European guidelines recommend continuing aspirin in the perioperative period, unless the risk of bleeding is clearly higher than the risk of cardiovascular events.[18,19]

It should be noted that on discontinuing the antiplatelet therapy, only the newly formed platelets overcome the inhibitory effects. Therefore the risk of increased bleeding persists for some days even after discontinuation of the therapy. Although, it takes longer time for local hemostasis to occur when platelet functions are inhibited, since the clotting time is not impaired, the bleeding time remains within normal or slightly outside the normal range as the clotting agents bring about hemostasis by forming a more stable fibrin clot and prevent further bleeding. Also, no case of permanent disability or death has been reported as a consequence of post operative hemorrhage associated with continued therapy with antiplatelet agents following extractions contrary to 40 % of arterial thromboembolism leading to serious permanent disability and 20% of these being fatal.[20]

Concomitant use of low-dose clopidogrel (2×75 mg) and aspirin (150 mg) has been shown to significantly increase the bleeding time from 7.6 minutes to 17.5 minutes, probably through a synergistic antiplatelet action. It is recommended that, in these patients, aspirin can be continued whereas clopidogrel discontinued at least 5 days (preferably 10 days) prior to the procedure in patients not at high cardiac risk.[21]

The CHEST 2012 guidelines make the following recommendations:

1. Many dental procedures (e.g., minor surgery, teeth cleaning, and tooth extraction) can be performed while patient is on single or dual antiplatelet therapy without a significant increase in bleeding.
2. Elective procedures with significant risk of bleeding should be postponed, if possible, until patients have completed full course of antiplatelet therapy.
3. Patients should be educated to contact their cardiologist before stopping any antiplatelet therapy, even if instructed to stop by another healthcare provider.
4. Patient specific management plans, including holding therapy, should be made in consultation with the patient's prescribing physician and dentist performing the procedure and communicated.

Thus, when planning dental procedures for a patient on antiplatelet drugs, several important factors must be considered:

Is the surgery urgent or elective?

Is the patient at high or low risk of thrombo-embolism if the drug is discontinued?

Can the procedure be done safely without discontinuing the drug? Does the patient understand the nature of the dental procedure and the risks associated with continuing or discontinuing the drug?

What degree of risk are the patient and the provider willing to accept?

Finally, is the patient on a single antiplatelet drug or on combination therapy with another drug.[22]

Conclusion

The dental and medical literature shows only a minimal risk of bleeding complications in patients with continued use of antiplatelet medication and intra operative or post operative hemorrhage if encountered, can be effectively and efficiently controlled by various local measures like pressure with a gauze plug, placing sutures or use of absorbable hemostatic dressings in the socket or by oral or topical hemostatic agents. Moreover, bleeding complications, while inconvenient, do not carry the same risks as thrombo-embolic complications. Also, no cases of transfusion, re-hospitalization for bleeding or major cardiovascular events have been reported in the literature.

Even though a combination therapy was shown to increase bleeding tendency, aspirin alone did not cause any bleeding complications.

When balancing benefits and risks of continuing versus discontinuing the antiplatelet medications peri-operatively, the existing data supports the continuation of antiplatelet therapy throughout the routine and invasive dental procedures and prevents the increased risks of potentially life-threatening complications. Also, most of the cardiovascular physicians would leave continuation of antiplatelet therapy on the confidence of the operating surgeon in terms of achieving control of post extraction hemorrhage.

References

1. Bell AD, Roussin A, Cartier R, et al. The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society Guidelines. Can J Cardiol 2011; 27 (Suppl A):S1–S59

2.Collet JP, Montalescot G. Premature withdrawal and alternative therapies to dual oral antiplatelet THERAPY. Eur Heart J 2006;8:46-52.

3.Collet JP, Himbert F, Steg PG. Myocardial infaction after aspirin cessation in stable coronary artery disease patients. Int J Cardiol 2000; 76 : 257-8.

4. Ferrari E, Benhamou M, Cerboni P, Baudouy M. Coronary syndromes following aspirin withdrawal. Chest 2003; 124 : 148S.

5. Ferrari E, Benhamou M, Cerboni P, Baudouy M. Corony syndromes following aspirin withdrawal, A special risk for late stent thrombosis, J Am Coll Cardiol 2005; 45: 456-9

6. Vaclavik J, Taborsky M.Antiplatelet therapy in theperioperative period. Eur J Inter Med.2011 Feb;22(1):26–31

7. Rossini R, Capodanno D, Lettieri C, et al. Prevalence, predictors, and long-term prognosis of premature discontinuation of oral antiplatelet therapy after drug eluting stent implantation. Am J Cardiol 2011; 107:186–194

8. Ardekian L, Gasper R, Peled M, etal. Does low dose aspirin therapy complicate oral surgical procedures? J Am Dent Assoc 2000; 131:331-5

9. Madan GA, Madan SG, Madan G, Madan AD, Minor oral surgery withoutstopping daily low-dose aspirin therapy: a study of 51 patients, J Oral Maxfac Surg 2005;63:1262-5

10. Garnier J[1], Truchot F, Quero J, Meziere X, Clipet F, Alno N, Frachon X, Delanoue O, Bader G, Lejeune S, Limbour P, De Mello G, 218 tooth extraction in patients taking platelet aggregation inhibitors, Rev Stomatol Chir Maxillofac. 2007 Nov; 108(5):407-10. Epub 2007 Apr 25

11. Krishnan B, Shenoy NA, Alexander M, Exodontia and antiplatelet therapy, J Oral Maxillofac Surg. 2008 Oct;66(10):2063-6. doi: 10.1016/j.joms.2008.06.027

12. Napenas JJ, Hong CH, Brennan MT, Furney SL, Fox PC, Lockhart PB. The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual anti-platelet therapy. J Am Dent Assoc. 2009;140(6):690-5.

13. Francisco Cardona-Tortajada, Esther Sainz-Gómez, Jorge Figuerido-Garmendia, Ana Lirón de Robles-Dental extractions in patients on antiplatelet therapy, SpainMed Oral Patol Oral Cir Bucal. 2009 Nov 1,14 (11):e588-92.

14. Canigral A, Silvestre FJ, Canigral G, Alos M, Garcia-Herraiz A, Plaza A. Evaluation of bleeding risk and measurement methods in dental patients. Med Oral Pathol Oral Cir Bucal. 2010;15(6):e863-e868

15. Mahn-Won Park, MD; Sung-Ho Her, MD; Jong Bum Kwon, MD, Safety of Dental Extractions in Coronary Drug-Eluting Stenting Patients Without Stopping Multiple Antiplatelet Agents, ClinCardiol. 35, 4, 225–230 (2012)

16. Bajkin BV, Bajkin IA, Petrovic BB. The effects of combined oral anticoagulant-aspirin therapy in patients undergoing tooth extractions: A prospective study. J Am Dent Assoc. 2012;143(7):771-6.

17. Jafri SM, Zarowitz B, Goldstein S, Lesch M. The role of antiplatelet therapy in acute coronary syndrome and for secondary prevention following myocardial infarction. Prog Cardiovasc Dis. 1993;36(1):75-83

18. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: J Am Coll Cardiol 2007; 50:1707–1732.

19. Guidelines for preoperative cardiac risk assessment and perioperative cardiac management in noncardiac surgery. Eur Heart J 2009; 30:2769–2812.

20. Anderson C.S. Jamrozik KD, Broadhurst R.J, Stewart- Wynne EG(1994) predicting survival for 1 year among different subtypes of stroke. Stroke 25, 1935- 1944

21. Randall C, editor. Surgical management of primary care dental patient on antiplatelet medication.

22. Aubertin MA. The patient taking antiplatelet drugs: A review with dental management considerations. Gen Dent 2008; 5:363-9.

Source of Support: Nill Conflict of Interest: None declared

Review Article

Diabetic relation of periodontal diseases and vice versa

Dr.Harish Kumar. MDS*
Deptartment of periodontics, KMCT Dental College, manassery, mukkam, Calicut - 673602 email: perioking@hotmail.com

ADDRESS FOR CORRESPONDENCE
Dr.HARISH KUMAR. MDS
Professor and HOD,
Dept of periodontics,
KMCT Dental College,
Manassery,
Mukkam,
Calicut - 673602
email: perioking@hotmail.com

Abstract :

It has always been an establishes fact that periodontal diseases were having a direct and influential effect on various systemic conditions and diseases. In this article the relationship of periodontal infections and daibetes is analysed and reviewd. This is not an attempt to go into the details of diabetic disease. But an analysis of the diseases to understand them better.

(Key words : Diabetes, Periodontitis, Systemic relation, Risk factor)

There has always been and it is a known fact that periodontal diseases have their influence on systemic diseases or vice versa. Periodontitis is an independent risk factor for atherosclerosis including stroke (Wu et al .2000), coronary heart disease (Bahekar et al. 2007 , Humphry et al .2008) , adverse pregnancy outcomes (Chambrone et al . 2011), and diabetes (Allen et al.2011 , Preshaw et al 2012).

Periodontal diseases have a major influence on diseases and conditions , that have a major impact on public health, including respiratory disease, chronic renal disease, rheumatoid arthritis, cognitive impairment, obesity, metabolic syndrome and cancer.

Here the focus will be on one of the major systemic diseses.. Diabetes. We will explore their known inter relationships, and discuss the scientific evidence.

The impact of periodontal treatment on the glycemic control in the diabetic has not been fully elucidated. and vice versa, ie, the effect of glycemic control on periodontal status.

The impaired metabolism of glucose, lipids and proteins in diabetes produces alterations in macro and micro vascular circulation that are associated with the five classic complications of the disease, namely retinopathy, neuropathy, nephropathy, cardio vascular complications and delayed wound healing[1.] Periodontal diseae has been proposed as the sixth complication of daibetes, based on the highly frequent presence of both in the same patient [2,3].

Here we dont intend to go into the classification details of different diabetic patterns. The following mechanisms have been proposed to explain the classic

*Professor & Head

complications of diabetes.

1) Polyol pathway
   According to this theory, glucose is converted to sorbitol , by the action of aldose reductase, which is implicated as the toxin in almost all of these complications.
2) Production of Advanced Glycation Endproducts (AGE s).
   the second theory proposed the binding of glucose to proteins, lipids and nucleic acids giving rise to giving rise to AGEs , thereby altering their functions. Thus binding of glucose to hemoglobin, collagen or albumin produces complications in the respective organs where the AGEs are deposited (nervous system, kidney, retina or blood vessels)

Periodontal diseases are multifactorial , bacterial diseases , which affect the tooth supporting tissues.The 1999 American Association of
Periodontology (AAP) classification, currently the most widely used, identifies six categories: gingival disease, chronic periodontitis, aggressive periodontitis, periodontitis as manifestation of systemic disease, necrotizing periodontal disease, and periodontal abscess [6].

According to current concepts of the multifactorial etiology of periodontal disease, it is caused by the interaction among single or multiple microbial agents (necessary but not sufficient primary etiologic factors), a host with some degree of susceptibility, and environmental factors with influence on both. Bacteria appear to act directly during the first moments of infection. However, most of their activity is indirect, via cell and humoral components of specific and non-specific host responses to protect the biofilm [4].

Diabetes as a risk factor for periodontal disease

Many authors have described diabetes as a risk factor for periodontal disease. Hence, Mealey concluded that diabetic patients had a three-fold higher risk of periodontal disease compared with non-diabetic patients after controlling for age, sex, and other confounding factors [5].

For diabetes to be acknowledged as a risk factor it must meet the risk analysis criteria set out by Johnson & Hill, especially the two following conditions [6]:

1) Biological plausibility that the factor can cause a given disease by a known action mechanism, and
2) Demonstration in prospective studies that the factor chronologically precedes the disease.

Genetic factors evidently play a major role in susceptibility to these diseases. However, the complex interactions in periodontal disease between host response
mechanisms and the action of pathogenic microorganisms hamper clarification of the role of genetic factors [7]. Nevertheless, an association has been observed
between both diseases and an HLA genotype. The HLA molecule (human major histocompatibility locus molecule) is genetically determined on chromosome 6, and disorders in this chromosome appear to predispose the host to both diabetes and periodontitis by altering antigen presentation to T cells and therefore the specific immune response of the patient. However, more studies are required in this area before conclusions can be drawn.

The role of the immune system in the etiopathogeny of diabetes and periodontal disease is well documented [7].

The following are the sequential steps to how diabetes leads to periodontal destruction

AGEs
MACROPHAGES (AGE-RAGE)
SYNTHESIS/RELEASE OF TNFĮ, IL-1ù
DEGRADATION CASCADE
HYDROLASE, MMP, COLLAGENASES
DESTRUCTION OF CONNECTIVE TISSUE

The above model depicts how diabetes mellitus could contribute to the development of periodontal disease. The binding of AGEs to their receptors triggers a cascade of events that produce the destruction of connective tissue.

AGE= advanced glycation end product, RAGE= receptor for AGE,
TNFα = tumor necrosis factor alpha, IL-1β = interleukin-1 beta, MMP = matrix metalloproteinase.

Patients with diabetes type-1 or -2 or periodontal disease show an imbalance or hyper-release of soluble cytokines against the attack of coadjuvant factors. In response to the presence of these modifying factors, cells of both diabetic and periodontal patients release

an increased amount of certain cytoactive chemicals e.g., prostaglandin E2 (PGE2), interleukin 1 (IL-1), and tumor necrosis factoralpha (TNF-α).

This up-regulation of immune response mediators has been demonstrated in vitro and in comparisons between diseased animals and healthy controls and may represent another possible explanation for the association between the two diseases[5]. AGEs may be deposited on mononuclear or polymorphonuclear cells, inhibiting their chemotactic and phagocytic capacities and permitting the advance of gram-negative anaerobic bacteria, which would explain the higher prevalence and severity of periodontal disease in diabetic patients[4]. According to this theory, AGE-stimulated macrophages and polymorphonuclear cells show a hyper-response to the progression of bacterial biofilm, releasing a larger amount of cytokines and soluble mediators.

To summarize, it has been shown, in a biologically plausible manner, how the host defense capacity can be altered in diabetes. The bacterial species in the periodontium are the same in diabetic and non-diabetic patients, suggesting that the increased periodontal disease risk in diabetic patients derives from an AGE-generating immunologic disorder[2]. In turn, periodontal pathogens cause the up-regulation of cytokines and tissue degrading enzymes, which may also have systemic consequences[8].

Periodontal disease might increase the already elevated cytokine levels in diabetic patients and thereby contribute to systemic inflammation.Excessive formation and accumulation of AGEs in tissues is the most common cause of diabetic complications. The binding of these molecules to neutrophils produces a hyperinflammatory state that amplifies the response to cytokines. These previously activated neutrophils also show a heightened response on making contact with LPS of gram-negative bacteria (e.g., P.g.) in the subgingival biofilm, and the consequent triggering of the inflammatory cascade increases the destruction of periodontal connective tissue and the severity of diabetes.[9].

Conclusion

Given the interrelationship between diabetes and periodontal disease, it is important to establish a good communication between the specialist responsible for a diabetic patient and the patient's dentist. Although the association between these diseases is now accepted as a reality, the clinical implications need to be adequately investigated. Importantly, the possibility of the simultaneous presence of the two diseases should be borne in mind to ensure their early diagnosis.

In view of the very high prevalence of both diseases and their potentially severe repercussions, the medical specialist should play a leading role in encouraging diabetic patients to visit their dentists regularly to control detrimental factors, such as the sustained presence of bacterial plaque in the periodontal pocket. Likewise, oral health personnel should bear in mind that impaired sugar metabolism and diabetes can affect the outcome and severity of periodontal disease

References

1. Mealy .B.L, Oats .T.W ; American Academy of Periodontology. Diabetes mellitus and periodontal diseases. J Periodontol, 2006; 77 : 1289- 303.

2. Mealy .B.L. Diabetes and Periodontal diseases, two sides of a coin. Compend Contin Educ Dent. 2000 ; 943 -6, 948, 950.

3. Grossi.SG, Genco. R J, Periodontal diseases and Diabetes mellitus: a two way relationship. Ann Periodontol. 1998; 51 – 61

4. Liljenberg.B, Lindhe.J; Some microbiological, histopathological, immunohistochemical charectaristics of progressive periodontal disease. J Clinical Periodontol. 1994; 21 : 720-7

5. Soskolne.W A; Epidemiological and clinical aspects of periodontal diseases in diabetics. Ann Periodontol. 1998 ; 3 : 3-12.

6. Pihlstrom B L , Periodontal risk assessment, diagnosis and treatment planning. Periodontol 2000; 2001: 25 : 37 – 58.

7. Emrich.LJ, Sclossman M, Knowler WC, Genco RJ, Periodontal disease in non-insulin dependent diabetes mellitus. J Periodontol . 1991, 62: 123-31.

8. Janket SJ, Van Dyke TE, Does periodontal treatment improve glycemic control in diabetic patients ? A meta-analysis of intervention studies. J Dent Res 2005 ; 84. 1154 -9.

9. Serrano-Rios M, Corbaton A, Diabetes mellitus, Heart failure and mortality. Med Clin (Barc), 2005, 125, 182-3.

Source of Support: Nill Conflict of Interest: None declared

IJWDC : Vol2 issue 1 Jan-June 2014

Original Research

FORENSIC APPLICATION OF PALATAL RUGAE PATTERN AS AN ADJUVANT FOR GENDER DETERMINATION

Dr. Divya Raj**** Dr. Rathy R.* Dr. Anil.G* Dr. Ajith*** Dr. Sunil S.** Dr. Sruthi A.K.**** Dr. Rekha V.R.****
Dept of Oral & Maxillofacial Pathology, Dept. of orthodontics
Azeezia College of Dental Science & Research, Meeyannoor, Kerala State, India

ADDRESS FOR CORRESPONDENCE

Dr. DIVYA RAJ, BDS
Post Graduate Student
Dept of Oral and Maxillofacial Pathology,
Azeezia College of Dental Science & Research,
Diamond Hills, Meeyannoor, Kollam,
Kerala State – 691537,
E-mail:

Abstract

The Palatal Rugae are considered relevant for human identification due to its stability .Several studies done in the past have revealed that the rugae patterns are highly individualistic and there are differences between gender.The aim of the study was to determine the different biometric characteristics of palatal rugae and to determine the common pattern in male and female

.Materials and methods

The study sample consisted of 300 preorthodontic dental castsof 150 males and females of age group 15-30 yrs. The method of identification of palatal rugae pattern was based on classification of Thomas etal. Other parameters evaluated in this study are shape of the incisive papillae, length of Median Palatine Raphae and Palatal length

.**Results**

Discriminant analysis was done using statistically significant variables shape of rugae and length of median palatal raphae for gender determination. Low medium palatine raphae was the strongest predictor of gender followed by shape of the rugae. Equation for gender determination obtained was 61% accurate. Logistic regression analysis was also done to check the reliability of shape of palatal rugae and length of median palatine raphe for gender determination. LRA was found to be good fit for the model and got an accuracy of 61%. **Conclusion:**Shape of palatal rugae showed significant difference in gender in Kerala population and there is significant association between length of median palatine raphe and gender.

Forensic odontology is that branch of dentistry which deals with the appropriate handling and examination of dental evidence , and with proper evaluation and presentation of dental findings in the interest of justice.[1] Here dentist play a role in supporting legal and criminal issues. Most commonly used scientific methods for forensic identification are DNA finger print and dental record comparisons. Identification of sex is of significance when bodies are damaged beyond recognition in case of major disasters[2]. Odontometrical analysis , finger prints and DNA comparisons cannot be applied in certain cases in such situations palatal rugoscopy is used for personal identification[3].

Irregular mucosal elevations present in the anterior third of the palate are known as palatal rugae or transverse palatine. Palatoscopy is the study of palatal rugae. Palatoscopy was first proposed by Trobo Hermosa in 1932.Palatal rugae are similar to finger prints and are unique to an individual [4]. Palatoscopy was first suggested as method of identification in 1889 by Allen.[5]In mass disasters and in case of mutilated bodies beyond recognition personal identification forms an important part of forensic science. Palatal rugae are relevant for human identification due to its internal position stability and perinnity.Rugae patterns are specific to racial groups so it facilitates population identification[6].

Theory of discriminant analysis was developed by Fisher. This technique is used to classify individuals on the basis of set of measurements.In the

*Professor & Head **Professor ***Reader****Post Graduate Student

present study discriminent analysis was used for gender determination.

Studies done in the past statistically proved that rugae patterns are highly individualistic and there are differences between genders. Studies have demonstrated uniqueness of rugae pattern and that the characterstic rugae pattern of palate does not change as a result of growth. But most of the previous studies are done using limited sample size. The purpose of the present study is to assess the rugae pattern in males and females of this part of the country using a larger sample size. The aim of the study was to determine the different biometric characteristics of palatal rugae ,determine the common pattern in male and female and application of discriminant function analysis and logistic regression analysis in gender determination

MATERIALS AND METHODS

The study sample consisted of 300 preorthodontic dental cast of 150 males and 150 females of age group 15-30 yrs which were collected randomly. Casts with full complement of tooth except third molars were included in the study. Casts with severe malocclusion and palatal asymmetries and those with voids and air bubbles were excluded. Rugae patterns on the study model were delineated using HB graphite pencil under adequate light. Brass wire was adapted over the rugae and the length was measured using caliper.

The method of identification of palatal rugae pattern was based on classification of Thomas etal[7]. Rugae are classified depending on length as Primary (>5mm),Secondary (3 to 5mm) and Fragmentary(< 3mm). Rugae less than 2mm were disregarded. Ruga's length are determined by measuring its greatest dimension regardless of its shape.According to the shape rugae are classified as Curved (They had a crescent shape and curved gently) Wavy (a slight curve at the origin or termination of the ruga) Straight **(** run directly from their origin to termination) Circular **(**Rugae that form a definite continuous ring) The direction of the rugae are determined by measuring the angle formed by the line joining its origin and termination and the line perpendicular to the median raphe. Forwardly directed rugae are with positive angles. Backwardly directed rugae are with negative angles.Perpendicular rugae with zero angles.In case of unification two rugae with the same origin from the midline but immediately branched was considered diverging and rugae with different origins from midline, but which joined on their lateral portions are considered converging

Other parameters evaluated in this study are shape of the incisive papillae , length of Median Palatine Raphae and Palatal length. According to the shape incisive papillae are classified as elliptical ,triangular (triangle shape with vertex directed towards the incisors), or thin (thin and narrow)[8]

The Median Palatine Raphae were classified according to the size as short, medium, long as follows. Short raphe reaches at a virtual line touching the distal aspect of right and left canines. The medium raphe crosses the virtual line distal to the canine and reaches a virtual line touching the distal aspect of right and left second premolar. Long raphe crosses this virtual line and reaches the first molar[8]. Palatal length are measured from the centre of incisive papilla to the point on a horizontal line drawn along the distal margins of first permanent molars[9].

STATISTICAL ANALYSIS

Chisquare test was done for comparison of relationship between the attributes. Association of shape of palatal rugae and length of median palatine raphae in sex determination were tested using discriminant analysis and logistic regression analysis using SPSS 20 version.

RESULTS

In the distribution of length of rugae primary rugae was the predominant one in the sample.(68%) curved and wavy rugae were more in case of shape(87%).In unification diverging pattern was the predominant (67%). In length of median palatine raphae medium was 69%, long 29%, and short 0.3%.

Elliptical shaped incisive papillae was the predominant one in the whole sample (44%).

In the gender wise comparison (Table 1) it was found

that males have more primary rugae.Wavy pattern was predominant one in males . other patterns which were more in males were converging type , triangular shaped incisive papillae and long median palatine raphae.

Palatal length was between 3-4 cm in both males and females.

Statistically significant variables in the gender wise comparison were shape of rugae with P value 0.003(Table 2) and length of median palatine raphae with P value 0.007(Table 3)

Discriminant analysis was done using statistically significant variables shape of the rugae and length of median palatine raphae and the equation constructed was

Gender = -0.073x curved + 0.124x wavy+ 0.585x straight+ 1.31 x circular +- 1.635 x length of Median palatine raphae+ 2.749

Executing the above equation with new data sex determination was done with help of adjusted canonical centroids of –0.264 to 0.264. if the product obtained is close to -0.264 then the proposed gender is male and if it is close to 0.264 then the gender is female. 61% of the respondence could be classified correctly in to male or female group. Correlation between original gender and gender that was determined by discriminant function was a positive correlation with P value 0.00 . it was found to be highly significant.paired T test had been conducted between original gender and discriminant and was found to be significant. (P= 0.05)

Logistic regression analysis was done using gender as dependent variable and rugae shape and length of medial palatine raphe as independent variable. The model fit was significant where the chisquare value was 41.196, P< 0.001 which indicated that full model predicts accurately the null model . In goodness of fit table (Table 4) for both pearson and deviance the significant value was greater than 0.05 and was found to be good fit.

Pseudo Rsquare table (Table 5) represents the amount of variable in the outcome variable. Higher value indicates better fit. In the present study R square values were comparatively less.

In the Likelihood ratio test shape of rugae and length of median palatine raphe were good predictors to the null model.

Parameter estimate classification table shows how well our full model correctly classified. The overall percentage which showed full model was 61% accurate which was good.

Table 1

PARAMETERS	MALES	FEMALES
LENGTH OF RUGAE	PRIMARY	PRIMARY& SECONDARY
SHAPE OF RUGAE	WAVY	CURVED &WAVY
DIRECTION	FORWARD& BACKWARD	FORWARD, BACKWARD& PERPENDICULAR
UNIFICATION	CONVERGING	DIVERGING
INCISIVE PAPILLAE	TRIANGULAR	ELLIPTICAL
MEDIAN PALATAL RAPHAE	LONG	MEDIUM

PALATAL LENGTH IS BETWEEN 3-4CM IN BOTH MALES AND FEMALES

SHAPE OF RUGAE Fig 1

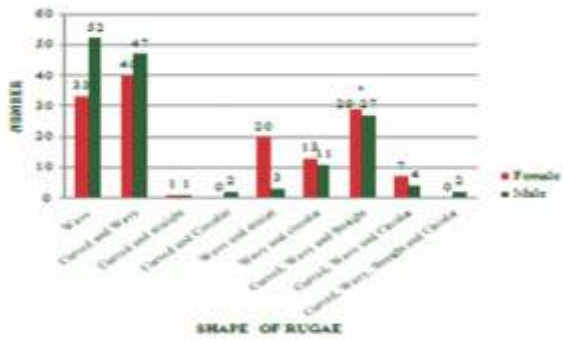


Table 2

	Value	df	sig
Pearson chisqure	26.432	10	0.003

LENGTH OF MEDIAN PALATINE RAPHE Fig 2

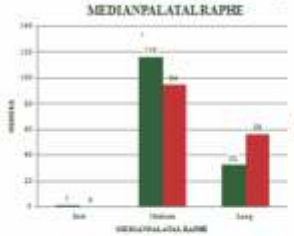


Table 3

	Value	df	sig
Pearson chi square	10.05	2	0.007

Table 4 Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	7.422	8	.492
Deviance	8.812	8	.358

Pseudo R-Square

Cox and Snell	.128
Nagelkerke	.171
McFadden	.099

Likelihood Ratio Tests

Effect	Model Fitting Criteria			Likelihood Ratio Tests		
	AIC of Reduced Model	BIC of Reduced Model	-2 Log Likelihood of Reduced Model	Chi-Square	df	Sig.
Intercept	72.905	120.684	46.905[a]	.000	0	.
ShapeofRugae	83.174	94.285	77.174	30.669	10	.001
medianpalatalraphe	78.624	119.366	56.624	10.119	2	.006

DISCUSSION

Numerous scientific principles and methods are used for human identification. In some forensic situations there are limitations in using finger prints dental records and DNA for identification. In such cases palatoscopy is used to establish person's identity. Palatal rugae are relatively stable and resist decomposition for up to 7 days after death[10]. Glycosaminoglycans which are the structural element of rugae contributes to the maintenance of shape of rugae throughout life .

The present study is crossectional in nature and assessed the difference in palatal rugae pattern, shape of incisive papilla, length of median palatine raphe and palatal length between males and females. In the present study dental casts were used for analysis because of advantages of simple analysis, reduced cost and easy availability.

Numerous classification system was developed by different authors for the classification of palatal rugae pattern. Some of which are classification systems by Silva, Carrea, Lysell , Thomas and Kotze. The method of classification used in the present study is that of Thomas etal which was found to be practical and easy method compared to others.

In the present study in length of rugae primary rugae were the predominant one followed by Secondary and fragmentary in the whole sample. This finding was consistant with the study done by chopra etal [10]. In gender wise comparison primary rugae were more in males compared to females which was not statistically significant. In the study done by Kapali etal there was no significant difference in number of primary rugae between aboriginal males and females [11]. Study done by saraf etal also did not show any significant difference in the number of rugae between Indian males and females[1].

In shape of rugae curved and wavy pattern was predominant in the whole sample. In study done by Surekha etal[6] and Paliwal etal[12] predominant rugae shape in Kerala population was wavy pattern followed by curved. But in the study done by shetty et al in malayalee populations of south India wavy and straight were the predominant shapes[13]. Males had more wavy rugae in the present study and shape of rugae was found to be statistically significant variable P value 0.009. This finding was consistent with study done by Manjunath etal in Indians at Manipal [14]and study done by M.Shetty etal in student population in Manglore[15].

In the unification diverging was predominant in the whole sample. Males had more converging rugae than females which was not statistically significant. This finding is in contrast with the findings of saraf etal[1]. And consistent with the study done by chopra etal[10].Madhankumar etal studied rugae pattern in student population, Chennai got a statistical difference in the number of unification type of rugae among males and females[16].

Length of medium palatine raphae medium was more in whole sample. Males had long medium palatine raphe and females had medium. This was statistically significant variable with P value 0.007. Study done by martin etal long median palatine raphe was the predominant one[8]. Studies on length of medium palatine raphe for sex determination were scanty on the literature.

In case of incisive papillae triangular shaped incisive papillae was more in males.In both males and females palatal length showed no statistically

significant difference.

Discriminant analysis was done using statistically significant variables shape of rugae and length of median palatal raphae for gender determination. Low medium palatine raphae was the strongest predictor of gender followed by shape of the rugae. Equation for gender determination obtained was 61% accurate. Study done by Sreenivas etal association between rugae length and shape with sex determination was computed using discriminant analysis and got an accuracy of 73% [2].

Logistic regression analysis was also done to check the ability of shape of palatal rugae and length of median palatine raphe for gender determination. LRA was found to be good fit for the model and got an accuracy of 61%. Acharya etal in odontometric sex assessment proved the use of LRA as a better alternative to Discriminant function analysis[15].But in the present study we got almost equal accuracy for both discriminant analysis and LRA for gender determination.

CONCLUSION

Shape of palatal rugae showed significant difference in gender in Kerala population and there is significant association between length of median palatine raphe and gender. Length of median palatine raphae can be used for gender determination along with palatal rugae pattern. Discriminant analysis and logistic regression analysis can be applied for gender determination and both had almost equal accuracy.Palatal rugae can be used as an adjuvant for gender determination. Further studies has to be done for comparison between populations.

REFERENCES

1. A. Saraf, S. Bedia, A. Indurkar et al . Rugae patterns as an adjunct to sex differentiation in forensic identification. Journalofforensic odontostomatol 2011; 29: 14-19
2. Sreenivas T Bharath, G R Kumar, R Dhanpal. Sex determination by discriminent function analysis of palatal rugae from a population of coastal Andhra. Journal of forensic dental sciences 2011;vol 3(2):58-62
3. Sankar shanmugham, Krishnamurthy et al . Palatal rugae in population differention between south and north Indians : a discriminent funcyion analysis . journal of forensic dental sciences 2012; vol 4(2):75-79
4. Preethi Nayak, Acharya et al. Differences in the palatal rugae in two populations of india. Archives of oral biology 2007;52(10):977-982
5. Indira AP ,Gupta et al. Palatal rugae pattern for establishing individuality. Journal of forensic dental sciences 2012;Vol4(1):2-5
6. Surekha R,Reddy et al. Assessment of alatal rugae patterns in Manipuri and kerala population. journal of forensic dental sciences 2012 ; vol 4(2):93-96
7. Thomas C J,Kotze etal .The palatal rugae pattern a new classification. Jdent assoc Afr 1983; 38:153-157
8. Martins filho, Peres etal. Palatal rugae patterns as bioindicators of identification in forensic dentistry. RFO; Vol 3:227-233
9. Hassanali J, J W Odhiambo. Analysis of dental casts of 6-8 and 12 year old Keneyan children. European journal of orthodontics 2000;22:135-142
10. Amandeep chopra , N C Rao etal . Palatal rugae and arch length a tool in gender determination. universal research journal of dentistry 2013; vol 3(2)
11. Kapali S, Townsend G etal . Palatal rugae pattern in Australian aborigines and Caucasians. Aust dent J 1997; 42: 129-33
12. A. Paliwali,S.Wanjari etal . Palatal rugoscopy establishing identity.J forensic dent science 2010;2(1): 27-31
13. D.K. Shetty, P.S. Machale etal. Comparison of palatal rugae patterns in Kodava and Malayalee

populations of south India. journal of forensic dental sciences 201;5(2): 85-89

14. Manjunath , sankar etal .Palatal rugae patterns among the Indians at Manipal ,India. Journal of pharmaceutical and biomedical sciences 2012; 20(10)
15. M.Shetty ,K. Premalatha etal. Study of palatal rugae pattern among the student population in Mangalore. J Indian acad forensic med 2011; vol 33(2)
16. S.Madhankumar,S.Natarajan.Palatal rugae pattern for gender identification among selected student population in Chennai,India. Journal of scientific research and reports 2013;2 (2): 491-496
17. Acharya A, Prabhu et al.Odontometric sex assessment from logistic regression analysis.Int J legal med 2011;125(2):199-204

Source of Support: Nill Conflict of Interest: None declared

Case Report

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA : CASE SERIES WITH REVIEW OF LITERATURE

DR.RATHY R.*, DR. VISHNUMOHAN, DR . SUNIL S***, DR. NIVIA M.****, DR. SRUTHI A.K.*****

Dept of Oral & Maxillofacial Pathology, Dept of Oral & Maxillofacial Surgery
Azeezia College of Dental Science & Research, Meeyannoor, Kerala State, India

ADDRESS FOR CORRESPONDENCE

Dr. RATHY R. MDS.
Professor and HOD,
Dept of Oral and Maxillofacial Pathology,
Azeezia College of Dental Science & Research,
Diamond Hills, Meeyannoor, Kollam,
Kerala State – 691537,
E-mail:rathyravindran27@gmail.com

Abstract:

Proliferative verrucous leukoplakia (PVL) is an aggressive form of oral leukoplakia that is persistent, often multifocal and refractory to treatment with high risk of malignant transformation. The term proliferative verrucous leukoplakia was assigned by Hansen et al in 1985. It encompasses a spectrum of clinical and histopathological stages prone to exhibit recurrences. PVL exhibits progressive histopathological features observed in single biopsy, multiple biopsies at same or over a period of time. The etiology remains unknown. The mean malignant transformation rate is 6.08 years. Hence its recognition at an early stage is beneficial. Here we report 2 cases of PVL, one of which had undergone malignant transformation over a short period of 1.2 years. The literature reviewed with emphasis on diagnostic criteria and management.

Keywords: Proliferative verrucous leukoplakia, Multifocal, Progressive

Introduction

Leukoplakia was described by WHO as a precancerous lesion. The prevalence of white lesion in oral cavity is approximately 24.8% according to Axell[1]. Recently following the latest workshop on oral precancer organized in 2005 by WHO collaborating centre for oral cancer, the term premalignant and precancerous was substituted for and all premalignant lesion and condition grouped under potentially malignant disorders[2].

Barely a few decades ago a rare aggressive form of oral leukoplakia known as proliferative verrucous leukoplakia (PVL) was reported.PVL is an aggressive form of oral leukoplakia that is persistent , often multifocal and refractory to treatment with highrisk of recurrence and malignant transformation. Its malignant transformation varies from 0.1 to 17.5%.

Shear and pind borg coined the term verrucous hyperplasia in 1980. Silverman et al documented high rate of malignant transformation in a sub set of study patients with verrucous leukoplakia . In 1985 Hansen assigned the term PVL. It encompasses a spectrum of clinical and histopathological stages prove to exhibit recurrence which develops critically as white plaque of hyperkeratosis that eventually becomes multifocal disease with confluent exophytic and proliferative features progressive to verrucous carcinomas or squamous cell carcinoma. They are slow growing

*Professor & Head **Reader ***Professor****Postgraduate student

persistent, irreversible and resistant to all forms of treatment with high recurrence rate

The etiology of PVL is unknown without a widely accepted diagnostic and treatment criteria. Here we report 2 cases of PVL, one of which had undergone malignant transformation over a short period of 14 months. The litenature reviewed with emphasis on diagnostic criteria & management.

CASE REPORT

CASE 1

A 62 year old male patient reported to dental OPD with a chief complaint of whitish discoloration in the mouth. The patient gave history of tobacco smoking since 52 years.

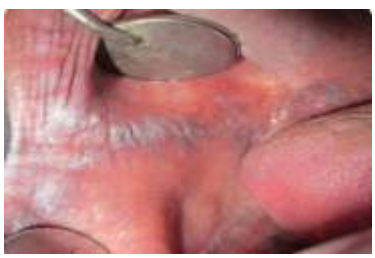


Figure 1: White plaque like lesion on buccal mucosa

Figure 2: White lesion on labial mucosa

Intra oral examination revealed white non scrappable patch on both buccal mucosa, labial mucosa, palate, upper and lower alveolar ridge and ventral surface of tongue(figure 1,2,3,4). On both buccal mucosa the surface of lesion was almost smooth with few fissures measuring approximately 5x1 cm. On the Upper and lower labial mucosa it extended from left to right commisures of size 3 X 1.5 cm. The lesion on the lower ridge and labial vestibule extended from canine to canine region and of size 2 X 1.5 cm. On the floor of the mouth in the midline near the lingual frenum, non scrapable white patch of size 0.5 X 0.5 cm was seen . Based on the history and clinical examination, a provisional clinical diagnosis of Proliferrative Verrucous Leukoplakia was made. Biopsy revealed Epithelial hyperplasia with mild dysplasia(figure 5).

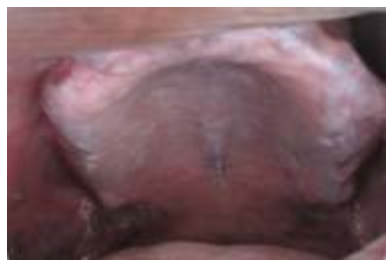


Figure 3: White patch on hard palate and alveolar ridge.

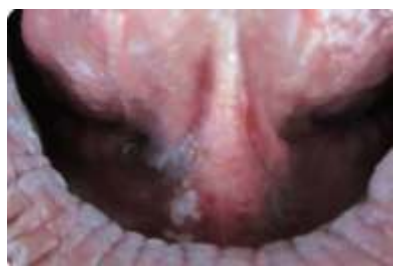


Figure 4: White papillary lesion on the floor of the mouth

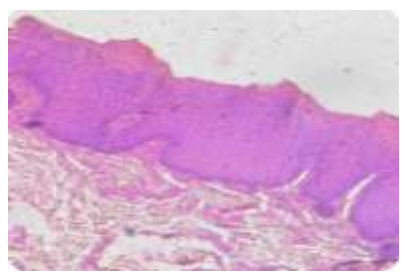


Figure 5: Epithelial hyperplasia with mild dysplasia. (H&E 10X)

CASE 2:

A 65 year male patient reported with a chief complaint of white patch in mouth. Patient gave a history revealed of an incisional biopsy taken for a white patch on the cheek 8 months back and the reported

to be epithelial hyperplasia with mild dysplasia.The lesion continued to progress over time. He is a smoker since 35 years.

Figure 6: Thick white plaque with wrinkled surface extending from angle of mouth to retromolar area on right buccal mucosa

.

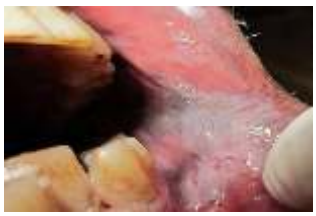


Figure 7: Non scrappable white thick plaque like lesion on left buccal mucosa

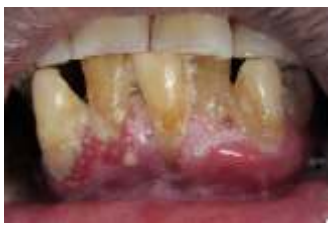


Figure 8: White lesion speckled with red areas on lower anterior gingiva

Intra oral examination revealed nonscrappable thick white plaque with wrinkled surface on right & left buccal mucosa extending from near angle of mouth posteriorly towards retromolar region , speckled red and white lesion on lower labial gingiva(6,7,8). Based on the history and clinical examination, a provisional clinical diagnosis of Proliferative Verrucous Leukoplakia was made. Biopsy revealed epithelial hyperplasia with mild dysplasia(figure 9). Patient reported with malignant transformation after six months and was referred to regional cancer centre for further treatment.

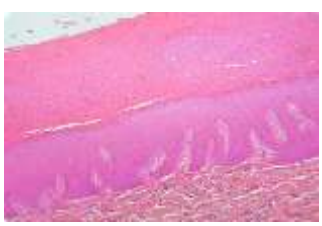


Figure 9: Epithelial hyperplasia with mild dysplasia . (H&E 10X)

The overall clinical and histopathological findings of all the above cases were considered diagnostic for Proliferative verrucous leukoplakia based on multifocal involvement ,progressive nature and malignant transformation over short period of 14 months

Disscussion

Cabay etal (2007) defined PVL as a distinct clinical form of oral leukoplakia which inturn is defined by its progressive clinical course, changing clinical and histopathological features and potential to develop into cancer One of the hallmarks of PVL is its variable and progressive clinical presentation. PVL shows an aggressive behavior, multifocal involvement, refractory to treatments and tendency to recur with rate of malignant transformation higher than 70%.[3]. 74.62%of the published cases, reported a mean malignant transformation rate of 6.08yrs.Hence an early diagnosis can be beneficial in the prognosis of patients. Women are more commonly affected (4:1 ratio) and age at time of diagnosis slightly over 60yrs[3,4,7].

The buccal mucosa and tongue most common sites in the report by Reichart and philipsen, 2003. Other have reported gingival and tongue to be frequently affected (Silverman and Gorsky1997). Bagan etal series showed 87% cases occurred on the gingival [5]. In the series reported by Gandolfo et al 2009 PVL most frequently observed on alveolar crest (87.2%) with gingiva in46.8% cases.

PVL exhibits progressive histopathological features observed in single biopsy, multiple biopsies at same time or over a period of time. Often an interface lymphocytic in filtration in superficial lamina propria similar to and often mistaken for Lichen plans. Apoptotic cells, eosinophilic ovoid (civatte, colloid, cytoid, hyalinse) bodies may be occasionally identified. With time shows increased keratosis with verruciform surface, enhanced acantnosis, basilar hyperplasia with or without dysplasia. In advanced cases, deeply folded

tissues may erode and infiltrate underlying bone forming pseudocysts mistaken for odontogenic cysts[4].

PVL grows slowly and can take up to 7-8yrs for malignant transformation. Bagan et al reported an average period of 4-7yrs for malignant transformation whereas Hansen et al reported 6 1yrs. Silverman and Gorsky reported longerduration of 11 6yrs[6,8,9].

The present case showed malignant transformation over a period of 1.2yrs.

Hansen et al proposed microscopic grading of PVL on a scale from 0 to 10 denoting continuum of severty that included histologically normaloral mucosa, clinically hormogenousleukoplkia, verrucous hyperplasia, verrucous carcinoma, papillary squamous cell carcinoma, less differentiated squamous cell carcinoma and intermediates.

Batsakis et al suggested histological staging of PVL that included four phases clinically flat leukoplakia, verrucous leukoplakia, verrucous hyperplasia, verrucous hyperplasia, verrucous carcinoma, squamous cell carcinoma with intermediates[4] Ghazali et al established the following criteria for PVL

1. Lesion starts an homogenous leukoplakia with evidence of dysplasia.
2. With time some areas of the leukoplakia become verrucous
3. Disease progress to multiple lesions at same or different time.
4. With time diseases progresses into different histological stage.
5. Appearance of new lesion after treatment
6. Clearly histologically PVL after followup period of no less than one year

Gandolto Set al established the following criteria

1 Homogenous plaque that progresses over time to exophytic, diffuse, multifocal lesion with the verrucous epithelial growth pattern

2 Histopatnologically changes from simple hyperkeratosis without dysplasia to verrucous hyperplasia verrucous carcinoma or oral squamous cell carcinoma

Recently Bagan et al (2010) proposed a set of diagnostic criteria. This includes 5 major criteria and 4 minor criteria

Major criteria

1 A leukoplakic lesion with more than two different oral sites which is most frequently in the gingival, alveolar processes and palate

2 The existence of verrucous area

3 That the lesion have spread or engrossed during development of disease

4 That there has been recurrence in a previously treated area.

5 Histopataologically, there can be from simple epithetial hyperkeratosis to verrucous hyperplasia, verrucous cercinoma or oral squamous cell carcinoma, whether in situ or in filtrating

Minor criteria

1. An oral leukoplakia lesion that occupies at least 3cm when adding all affected areas.
2. That the patient be female

3. That patient be a nonsmoker

4. A disease evolution higher than 5 year

In order to make a diagnosis it was suggested that one of two following combination should be met

1. Three major criteria (5 being among them)

2. Two major criteria (5 being among them) & minor criteria[4]

The etiology of PVL remains unclear. The predilection for elderly women in a ratio of 4:1. The reason for potential gender difference not clear but gender and age related effects on immune competence have been postulated. PVL and its progession to cancer not linked to tobacco use, known risk for squamous cell carcinoma[4,10] .Other cofactors postulated include HPV or candida fection. Silverman et at reported 68% of PVL to be positive for candida albicans but did not find fungal infection linked to PVL occurrence and progression to carcinomia. Several studies investigated role of HPV in verrucous lesion reporting between 0% to 89% of PVL lesion to be HPV positive[10]

Management

PVL is resistant to available treatment modalities. The primary objectives of leukoplakia therapy should be prevention of malignant transformation.

Surgical treatment via scalpel or laser therapy. Surgical shave followed by cryotherapy and photodynamic therapy been suggested.

Non surgical therapeutic approaches for PVL such as externalbeam radiotherapy, and topical vitamin, therapy but none proven to be beneficial[1,4,11].

In future anti.HPV, anti – TGF and propoptic management strategies considered. The challenge is to administer aggressive therapy consistent with clinical progression of lesion depite benign histological findings. Poor outcomes with high risk of progression to cancer may be reflective of under treatment and lack of effective therapies for PVL if molecular markess of PVL and associated progression to cancer are found, identification of more effective therapies than those available may be facilitated.

Conclusion

PVL is highly aggressive lesion which shows tendency for recurrence and is refractory to treatment. The mean malignant transformation rate is 6.08yrs. Hence its recognition at an early stage is beneficial. The diagnostic criteria has been reviewed with emphasis in early diagnosis for creating clinical awareness on the part of clinician . There is lack of a successful treatment and number of recurrences reported after management.

References

1 Kharma my Tarakji B current evidence in diagnosis and treatment of proliferative verrucous leukoplakia. Ann Saudi med 2012, 32 (4) : 412-414

2 Warnakulasuriya s, Johson Nw, Vanderwaal I Nomenclature and classification of potentally malignant disorder of oral mucosa. J oral path of med 2007, 36 575 – 580

3 Bagan JV, Lapie dra Rc, Martinez DB Lopez LM, Gomez GE. Proliferative verrucous leukoplakia. A proposal for diagnostic criteria. Med oral path of oral cir Buccal. 2010 Nov 1, 15(6) : e 839 – 45

4 Robert JC, Thomas HM, Joel BE, proliferative verrucous leukoplakia and its progression to oral carcinoma : a review of literature. Joral pathol med 2007, 36 : 255 – 261

5 Bagan J, Scully C, Jimenez, Martorell prolifeative verrucous leukoplakia a concise update oral diseases 2010, 16:328 332

6 Ge L, Wu Y, Wu LY, Zhong L Xie B, Zeng X, Lin M, Zhou H case report of rapidly progressive proliferative verrucom leukoplakia

and a proposal for actiology is mainland china. World Jouranl of surgical oncology 2011, 9:26

7 Mete O, Kesikia Y, Matiz G, Kayhen K Unur M oral proloferative verrucous leukoplekia : unduediagnosed oral precussor lesion. Dermatology online Journal 16(5):6

8 Roda Rp, Bagan JV, Soriano YJ, Fernandex JMD, Esteve Cg. Retinods nd proliferative verrucus leukoplekia. A prelimenray study. Med oral parrot oral cir Bucal. 2010. Jan 1; 15(1): e 3-9.

9 Began JV, Jimenez-sorianoo Y, Diaz-Fernandez JM, Murillo-cortez J, Sanchin-Bielsa HM, Poveda-Roda R, Bagan.L. Malignent transformation of proliferative verrucan lukoplakia to oral squemous cell carcinoma: a series qe 55 cases. Oral oncol 200 Aug; 47(8) : 732-5.

10 Kreastly LA, Mallery SR, Knobloch T Jetal Frequent Altterctions of P16 INK 49 and P14 ARE is oral proliferative verrucan lukoplokia. Cancer Epidomiol Biomarkers prev 2008; 17 : 3179 – 3187.

11 Singh A P, Chaitra T K, Kulkarni A U, Jathar P N. Idiopathic proliferative verrucam leukoplakia: report of a clinical caring. BMJ care reports. 2012; 10.

Source of Support: Nill Conflict of Interest: None declared

Case Report

Inverted Impacted Mandibular Third molar associated with Dentigerous Cyst

Dr. Prasanth P.*, Dr. Anjana. G**

ConsultantMaxillofacial surgeon, Amritha Multispecialty and Pediatric Dental Clinic, Kadavanthra, Kochi
Department of Pediatric Dentistry, Royal Dental college

ADDRESS FOR CORRESPONDENCE

Dr. Anjana G. MDS
Prof. & HOD,
Department of Pediatric Dentistry,
Royal Dental college,
Kerala State, India

Abstract:

Though mandibular third molar impactions are very common, inverted mandibular third molar impaction associated with a Dentigerous cyst is not a common occurrence. This case report discusses such a rare occurrence, possible etiology and the surgical management.

Key words: Impacted inverted third molar, Dentigerous cyst, Enucleation

Introduction

When a tooth is prevented from its normal path of eruption due to deficient space in the dental arch or any obstruction in its path of eruption it is called an impacted tooth. The cause of mandibular third molar impaction is said to be inadequate space between distal of the second mandibular molar and the anterior border of the ascending ramus[1]. Though the third molar is the most common impacted tooth, the numbers of cases reported in literature about inverted and impacted mandibular third molars are few[2]. Moreover, inverted impacted mandibular third molar associated with a Dentigerous cyst is not reported. A rare case of a unilateral inverted and impacted mandibular third molar associated with a Dentigerous cyst and its management is reported.

Case report

A 23 year old male patient reported to our private dental practice with pain and mobility of the right mandibular lower molar teeth (47) since 2 months. On examination, evident root stumps of 46 and carious 47 associated with grade II mobility were present. However, an IOPA radiograph confirmed no pulpal involvement in relation to 47.

The Orthopantomograph (Fig. 1) revealed an inverted impacted 48 associated with a cyst like radioluscency which was extending till the mental foramen with a

* *ConsultantMaxillofacial surgeon, Amritha Multispecialty and Pediatric Dental Clinic, Kadavanthra, Kochi*
** *Prof. & HOD, Department of Pediatric Dentistry, Royal Dental college*

possible involvement of the mandibular canal. Necessary investigations were done to rule out systemic illnesses. It was decided to do a cyst enucleation along with the involved 48 as well as the extraction of 46 and 47. Patient was explained about the possible risk factors like parasthesia in the distribution of mandibular nerve. The entire cyst with the impacted 48 was removed along with the extraction of 47 and root stumps of 46 under sedation and local anaesthesia.

Figure 1

An incision was placed over the anterior border of the ramus. Sulcular incision was extended anteriorly upto the canine with a releasing incision into the buccal sulcus. Buccal mucoperiosteal flap was raised. Anterior boder of the ramus was exposed. Overlying bone was removed using a surgical drill to expose the tooth. The tooth was sectioned and removed and the cyst was enucleated. The cyst cavity was irrigated and the soft tissues sutured.

Patient cooperated well during the surgical procedure and the recovery was uneventful with no parasthesia or any other complications. Histopathology report confirmed the diagnosis of a Dentigerous cyst. After initial healing, the patient was given a removable prosthesis till the bone healing was complete and a fixed prosthesis can be considered.

Discussion

The frequency of occurrence of Dentigerous cyst increases sharply in the second decade of life, reaches its peak in the third decade after which there is a gradual decline[2]. The inverted impaction with the crown pointing downwards and root apex towards the alveolar crest is called complicated impaction.[4,5,6]

The mandibular third molars and maxillary canines are the most frequently associated teeth in Dentigerous cysts. In the mandible, the most common site of impaction is the ascending ramus[4,5]. Systemic factors like Cleidocranial dysplasia, endocrine deficiency, irradiation, febrile disease, Down's syndrome etc or local factors like malposed tooth germs, arch length deficiency, supernumerary teeth, odontogenic tumors, myxofibrous hyperplasia or ameloblastic fibroma causing mechanical obstruction in the eruption pathway or abnormal eruption pathway may cause the impaction of third molar teeth[2,6]. The primary failure of a well formed tooth to erupt may have a strong genetic component or can be acquired due to a temporary alteration of nerve activity in the region, which in turn has an influence on the eruption process[7].

Literature on inverted impacted third molar has reported only five cases [2,5,6,8,9] and the surgical management was successfully done only in two cases, but they were not associated with Dentigerous cyst as seen in the present case.

When surgical removal is planned, especially in a case like this, the risk factors that are associated with the surgical procedure should be explained to the patient, since removal of an inverted molar can be more complicated than a normal impaction owing to the presence of the cyst, its deeper position and the difficulty in accessing it [2,6]. The area of largest circumference of the tooth is deep inside the bone owing to its inverted position.

In the present case, the inverted impacted 48 was associated with a dentigerous cyst, in close proximity to the roots of 47, causing mobility of 47. Hence, the decision to extract all the three molars and cyst enucleation was successful in achieving a very good prognosis.

Conclusion

The removal of impacted inverted mandibular third molar itself can be quite a challenging task for the surgeon and when it is associated with a cyst, the procedure becomes more complicated.

The risk factors and complications should be carefully analysed and anticipated by the surgeon and should be

discussed with the patient prior to surgery.

References

1. O Breik, D Grubor, The incidence of mandibular third molar impactions in different skeletal face types.Australian Dental Journal, 2008,53:320-324.
2. Yuvaraj, Agarwal.G.D, Inverted Maxillary Third Molar Impaction- A case Report People's Journal of Scientific Research, 2011; 4(1):57-58.
3. Shear.M, Speight.M.P, Cysts of the Oral and Maxillofacial Regions, 4th ed.2007, Blackwell publishing Ltd.
4. Shafer.W.G,Hine.M.K,Levy.B.M, Textbook of Oral Pathology ,5th ed.2006, Elsivier.
5. Pai V, Kundabala M, Sequeira S P, Rao A, Inverted and Impacted maxillary and mandibular third molars- A very rare case, J Oral Health Comm Dent 2008;2(1): 8-9.
6. Chandra R, Kaushal A, Inverted Impacted third Molar, J Oral Health Comm Dent, 2011; 5(2) 56-7.
7. Kapur A,Goyal A, Jaffri S: Management of Inverted Impacted primary Incisors. Journal of Indian society of Pedodontics and Preventive Dentistry.2008; 26(1):26-8.
8. Alshamrani.M.S,Inverted and impacted maxillary third molars: Report of 2 cases, Odonto Stomologie Tropicale 2001 N°94, 15-7.
9. Gold J, Demby N, Rare inverted maxillary third molar impaction- Report of case, JADA, 1973; 87: 186-8.

Source of Support: Nill Conflict of Interest: None declared

GUIDELINES FOR AUTHORS

Manuscripts Preparation Manuscripts should be sent to be Editor, in original & two complete copies, including illustrations. The manuscript should also be sent in two floppies/Cd and pictures be sent in original for better reproduction. The author's name is to be written only on the original copy, and not on the Xerox copies. The manuscripts should be type written, double-spaced on one side of the paper. With at least one inch margin on all sides. All pages shou be numbered sequentially.

Title Page Title page should include the title of the article and the name, degrees, position, professional affiliation of each author. The corresponding author's fax, telephone, email address and complete mailing address must be provided.

Abstract/ Key Words Page 2 should include a maximum of 200 words abstract with abbreviated title for the page head use. The abstract should state the purpose of the study/ investigations, basic procedures, main findings and the principal conclusions. Emphasize new and important aspects of the study/ observations. Only approved abbreviations are to be used.

Clinical Relevance Statement

experimental investigations should include a brief statement of the clinical relevance of the paper.

Text: The text of articles should be divided into sections with the headings introduction, Material & Methods, Results and Discussions.

Indtroduction Summarise the purpose and rationale of the study. Give only pertinent references & do not extensively review the subject Clearly state the working hypothesis.

Material & Methods To allow confirmation of the observations, present the material & methods in sufficient detail. Published methods should be referred to & discussed briefly. Only if modifications have been made, provide details.

Results Present results in a logical sequence in the text, tables & illustrations. Do not repeat the text all the data in the tables, summarise only important observations.

Discussions Emphasize the new & important aspects of the study and the conclusions that follow them. Do not repeat the observations to other relevant studies. Relate observations to other relevant studies & point out the implications of the findings & their limitations. Avoid unqualified statements & conclusions not completely supported by your data. Recommendations, when appropriate, may be included.

Acknowledgements Acknowledge only persons who have made significant contributions to the study. Authors are responsible for obtaining written permission from persons acknowledged by the name because readers may infer their endorsement of the data & conclusions.

References Authors are responsible for the accuracy of the references. The reference list should be double spaced at the end of the article in numeric sequence.

All references given must be cited in the text, numbered in order of appearance. Use the style which are based on the formats used by index Copernicus™ Journals master list. Do not include unpublished data or personal communications in the reference list. Cite such references in parenthesis in the text & include a date. Avoid using abstracts as references. Provide complete information for each reference, including names of all authors. If the references is to a part of a book, also include the title of the chapter & names of the book's editor(s). Journal references should included author's name, article title, abbreviated (as per standards) journal name, volume number, page number & year. References must be verified by the author(s) against documents.

Illustrations All illustrations must be numbered and cited in the text in order of appearance. On the back of each illustration, place a label with the article title & figure number only Do not include author names. Indicate on the top edge lightly in pencil. Do not bend, fold or use, paper clips.

Instead of original drawings, roentgenograms & other material, send sharp, glossy colour, black and white photographic prints, usually 127 by 173 mm

(5 by 7 inch) but not larger than 203 by 254mm (8 by 10 inches). Letters, numbers and symbols should be clear and of sufficient size.
For illustrations in colour, supply colour positive transparencies and when necessary accompanying drawing marked to indicate the region to be reproduced.
Photographs of X-rays should be sent and not the original X-rays. If photographs of persons are used either the subjects must not be identifiable or the pictures must be photograph.

Labels Each table should be logically organized on a separate sheet & numbered consecutively. The title & footnotes should be included with the table

Copy right To ensure maximum dissemination and copyright protection of material published in the journal, copyright must be explicitly transferred from the author to the Indian Dental Association. Submission of manuscripts implies that the work described has not been published before (except in the form of an abstract or as part of published lecture, review or thesis) that is not under consideration for publication elsewhere, & if accepted, it will not be published elsewhere in the same form in either the same or another language without the consent of copyright holders. The copyright covers the exclusive rights of photographic reprints, video cassettes and such similar things. Certificate signed by author/s to this effect be submitted with the manuscript.
The editors & publishers accept no legal responsibility for any errors, omissions or opinion expressed by authors. The publisher makes no warranty for expressions implied with respect to the materials contained therein.
The journal is edited & published under the directions of the journal committee, which reserves the right to reject any material without giving explanations.
All communication should be addressed to the Editor. Request for change of address should be referred to Hon. Secy. General. No responsibility will be taken for undelivered issue due to circumstances beyond the control of the publisher.

Photographs Author's photograph-stamp size, glossy. Diagrams 8 cm (width)x4 cm(length)or larger.

Letters to the Editor Letters to the Editor are encouraged to stimulate a healthy dialogue relating to the specialty.

Books for Review Books and monographs will be reviewed based on their relevance to IJWDC readers. Books should be sent to the Editor and will become the property of IJWDC.

Subscription for Hard Copy: Rs : 2000 per b/w copy

Rs : 3000 per color copy

Edited By: **Dr. R. Rathy**
Designed By: **Koppara Enterprises**, Kollam
Published By: **Womens Dental Council**, WDC 2014, Kerala State Branch

****

WOMEN'S DENTAL CONCIL IDA KERALA STATE AND WOMEN'S DENTAL CONCIL IDA ERNAD BRANCH
CDE PROGRAMME: PULP THERAPY PRIMARY TEETH

WOMEN'S DENTAL CONCIL IDA KERALA STATE AND WOMEN'S DENTAL CONCIL IDA NORTH MALABAR BRANCH
SECOND CDE PROGRAMME

CONTENTS

Printed & Designed by: **KOPPARA**, Kollam - Tel. (0474) 2733169
Editor : **Dr. R. Rathy**