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Dentistry & Otolaryngology



Minimal Invasive Techniques

Rehabilitation of Total Maxillectomy

Highlights

Potentially Malignant Disorders

Assessment of Chromosomal Damage

Discovering Thoughts, Inventing Future

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Assessment of Chromosomal Damage and Apoptosis in Exfoliated Buccal Cells of Potentially Malignant Disorders and Oral Cancer

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Abstract- *Aim:* To assess the chromosomal damage and apoptosis in exfoliated buccal cells of individuals with potentially malignant lesions and oral cancer.

Materials and methods: Our study included 90 subjects which were divided into three groups of 30 each, Group A-potentially malignant disorders, Group B-Oral cancer and Group C-control.

Results: A significant increase in the frequency of micronucleated cell from lesions than in cells from normal areas. We also observed a gradual decrease in apoptosis from normal mucosa to precancerous lesions to carcinoma.

Conclusion: Thus oral cancer is associated with a very high frequency of chromosomal damage and impaired apoptosis in the exfoliated buccal cells. Perhaps, beside the micronucleus assay, the inclusion of degenerative nuclear alteration indicative of apoptosis can be a useful tool for biomonitoring oral cancer patients.

Keywords: *exfoliative buccal cells, micronucleated cells, apoptosis, potentially malignant disorders, oral cancer.*

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Assessment of Chromosomal Damage and Apoptosis in Exfoliated Buccal Cells of Potentially Malignant Disorders and Oral Cancer

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Keywords: exfoliative buccal cells, micronucleated cells, apoptosis, potentially malignant disorders, oral cancer.

I. Introduction

Oral Cancer is one of the malignant neoplasia of highest incidence worldwide and is particularly common in developing countries.[1] Other potentially malignant lesions or conditions include erythroplakia, lichen planus, submucous fibrosis, and chronic immunosuppression.[2] Cytogenetic biomarkers are the most frequently used end points in human population studies. One of the cytogenetic biomarkers for predicting cancer risk in humans is the micronucleus (MN) test. The MN test in exfoliated buccal cells is an attractive candidate for the genotoxic biomonitoring of human populations and individuals, especially because of its non-invasive application nature. It is considered to be a useful biomarker of genetic damage caused by lifestyle habits, exposure to environmental pollutants, medical procedures and also inherited genetic defects in DNA repair [3-8]. Oral cancer results from alterations that includes point mutations and chromosomal abnormalities in genes that control the cell cycle or in genes that are involved in DNA repair. With the evidence of metastasis, cancer is also characterized by its loss of ability of the cells to evolve to death when genetic damage occurs (apoptosis)[9]. However, oral exfoliative cytology is a minimally invasive test for sampling tissues and does not cause undue stress to study subjects[10,11]. Thus, micronuclei (MNi) are suitable internal dosimeters for revealing tissue specific genotoxic damage in individuals exposed to carcinogens. Thus, this could be used as a biomarker for the detection of early oral mucosal malignant transformations[12].

II. Materials and Methods

The present study consisted a total of 90 subjects, with an age ranging from 20 to 60 years inclusive of both the genders. Relevant case history was recorded including their oral habits, frequency and duration. Detailed clinical examination was carried out. Subjects with oral lesions suspected to be Potentially Malignant Disorders and Oral cancer were included. Selected cases were confirmed with histopathological diagnosis. The study was approved by the Ethical Review Board of V S Dental College and Hospital, Bengaluru. Written informed consent from the selected patients were taken for the procedures to be carried out on them subsequently. The study samples were divided into three groups: Group A–30 cases of Potentially Malignant Disorders (PMD's) (Leukoplakia, Lichen Planus and Oral Submucous Fibrosis). Group B–30 cases of Oral Cancer (Oral Squamous Cell Carcinoma). Group C–30 cases of normal healthy subjects as Controls.

Sample collection and preparation: The sample for analysis was taken from the buccal mucosa without lesions in case and control groups; and from areas with lesion by gentle scraping of the epithelium using a cytobrush. From the collected sample smears were prepared on the clean slides onto which two drops of saline solution was placed priorly. The smears were fixed in a methanol/ acetic acid solution (3:1) and after 24hrs it was stained using the Schiff reagent and counterstained with 1% fast green.

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Cytological analysis: These slides were analysed and a minimum of 1000 cells presenting intact cytoplasm were counted. In which:

a. The number of pyknotic, condensed chromatin, karyorrhectic cells indicating apoptosis were counted.
b. The number of micronucleated cells indicating chromosomal damage were counted.

Criteria for inclusion of cell in the total cell count was based on Tolbert et al[49] and protocol by Thomas et al was followed for identification of micronucleated cell, condensed chromatin, pyknotic and karryohectic cells.



Fig. 1 : Smear from carcinoma of buccal mucosa

III. Results

Table 1 : Micronucleus analysis in group A

[LA] lesion area, [NA] normal area, [a] significant, [b] nonsignificant, N=sampe size

Group	N	MN	MN(%)Mean ± SE	Total cells	Comparison	X^2 (DF=1)
Case [LA]	30	112	2.07 ± 0.81	30,107	Case [LA] vs control	74.449(<0.001) [a]
Case [NA]	30	43	1.63 ± 0.31	36,420	Case [LA] vs case [NA]	61.362(<0.003)[a]
Control	30	28	0.36 ± 0.03	33,530	Case [NA] vs control	0.671(0.217) [b]

Table 2 : Micronucleus analysis in group B

[LA] lesion area, [NA] normal area, [a] significant, [b] nonsignificant, N=sampe size

Group	N	MN	MN(%)Mean± SE	Total cells	Comparison	X^2 (DF=1)
Case [LA]	30	277	8.16 ± 2.01	32,436	Case [LA] vs control	77.582(<0.0001) [a]
Case [NA]	30	107	3.11 ± 0.69	35,480	Case [LA] vs case [NA]	11.917(<0.009) [a]
Control	30	28	0.36± 0.03	33,530	Case [NA] vs control	1.67(0.321) [b]

Micronucleus Analysis: Micronucleus occurrence was significantly higher in smears obtained fromlesions in group A than that obtained from without lesins in group A and C(P <0.001). No significant difference was observed in cells obtained from the group C and from normal areas in group A (P = 0.217) as presented in Table 1. Micronuclei were significantly high in cells obtained from areas with lesions in the group B than in cells obtained from areas without lesions in both the group B and C(P <0.0001). A significant difference was noted in comparing cells from group C and from normal areas in the group B (P = 0.009) as presented in Table 2.

Apoptosis analysis: The occurrence of the cells representing apoptosis were significantly less in lesion areas than that obtained from group C (P < 0.0001). It was also less frequent in cells from normal areas in the group A than in normal areas in group C (P < 0.0001). There was no difference in apoptosis occurrence between the lesion areas and normal areas in group A(P = 0.957). Apoptosis occurred significantly less frequently in cells obtained from lesion areas than from group C (P < 0.0001). There was a significant difference in apoptosis occurrence between the lesion areas and the normal areas in the group B(P = 0.0001). And there was also a significant difference from normal areas in the group B than in normal areas in the control group C (P < 0.0001).

IV. Discussion

Genomic damage is one of the important cause of developmental and degenerative diseases. The genomic damage may be produced by certain genotoxins, various medical procedures that includes radiation & chemicals, micronutrient deficiency, lifestyle factors and genetic factors such as inherited defects in DNA metabolism or repair. To evaluate the genotoxic risks, DNA damage can be assessed by cytogenetic markers like chromosomal aberrations, sister chromatid exchanges and micronuclei. Epidemiological studies reveal a positive correlation between micronutrient deficiencies and development of cancer. Thus the measurement of frequency of micronuclei becomes a valuable tool to study the link between nutrition and DNA damage. This in turn will assist in stepping up implementation of public health strategies to reduce diseases of ageing and cancer.[13]

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The presence of Micronucleated cell (MNC) in exfoliated buccal cells reflects the carcinogenic exposure on the target tissue from which carcinoma arises .This increase in frequency may indicate that the individuals are at high risk of progressing to malignancy. Our results are similar to those conducted by Delfino V et al14, Kamboj M et al[15], Giovanini AF et al[16], Mahimkar MB et al[17], Grover et al[18]. They concluded that there is highly significant increase in the mean micronuclated cells in PMD as compared to their control group. High frequency of mean MNCs was found in OSCC patients. This reflects the there is genomic instability associated with malignant lesion. It could be considered as to continuous use of the habits with increased frequency and duration. It is apparent that buccal cells of OSCC patients possess higher degree of genetic damage manifested in the form of micronucleated cells. The multiple micronucleation in the target tissue indicates extensive genetic damage resulting in chromosomal instability which is a hallmark of human tumors. It seems likely that the genomic damage is directly proportional to its exposure to carcinogens. Thus the overall values of the mean MNCs obtained from the study groups reveal that there was an increase in MNCs from normal mucosa to PMDs and then to carcinoma suggesting a link of this biomarker with malignant neoplastic progression.

We also observed a gradual decrease in apoptotic cells from normal mucosa to PMDs and then to carcinoma. These results are in accordance with Jain et al[19], Macluskey *et al*[20] and Bentz *et al*[21]. Thus apoptosis may play a vital role in preventing the genetic abnormalities associated with cells progressing to neoplasia[22]. Tumor growth is a summation of mitosis or the cell production and cell loss or death.

V. Conclusion

The present study observed a stepwise increase in the frequency of MNCs from normal buccal mucosa to PMD and then to carcinoma and also a gradual decrease in apoptosis from normal to PMDs and then to carcinoma. Therefore, micronuclei assay holds a promising specific biomarker for exposure to various carcinogens, and can also be used as screening test in oral health centers. It is therefore a simple, reliable, technically easy with minimal expenditure test that aids in serving as a excellent tool for educating people regarding the ill effects of the habits and its consequences.

References Références Referencias

1. Dorea L T M, Meirles J R C, Lessa J P R, Oliveira M C, Pereira C A B, Campos A P et al. Chromosomal Damage and Apoptosis in Exfoliated Buccal Cells from Individuals with Oral Cancer. Int J Dent 2012; 1-6.
2. Halder A, Chakraborty T, Mandal K, Gure PK, Das S, Raychowdhury R, *et al*. Comparative Study of Exfoliated Oral Mucosal Cell Micronuclei Frequency in Normal, Precancerous and Malignant Epithelium. Int J Hum Genet 2004. p. 257-60.
3. Martins, R. A., Gomes, G. A., Aguiar, O., Jr and Ribeiro, D. A. (2009) Biomonitoring of oral epithelial cells in petrol station attendants: comparison between buccal mucosa and lateral border of the tongue. Environ. Int., 35, 1062–1065.
4. Holland, N., Bolognesi, C., Kirsch-Volders, M., Bonassi, S., Zeiger, E., Knasmueller, S. and Fenech, M. (2008) The micronucleus assay in human buccal cells as a tool for biomonitoring DNA damage: the HUMN project perspective on current status and knowledge gaps. Mutat. Res., 659, 93–108.
5. Nersesyan, A. K. and Adamyan, R. T. (2004) Micronuclei level in exfoliated buccal mucosa cells of patients with benign and malignant tumors of female reproductive organs and breast. Tsitol. Genet., 38, 72–75.
6. Celik, A., Cavasx, T. and Ergene-Go¨zu¨ kara, S. (2003) Cytogenetic biomonitoring in petrol station attendants: micronucleus test in exfoliated buccal cells. Mutagenesis, 18, 417 421.
7. Burgaz, S., Erdem, O., Cakmak, G., Erdem, N., Karakaya, A. And Karakaya, A. E. (2002) Cytogenetic analysis of buccal cells from shoeworkers and pathology and anatomy laboratory workers exposed to nhexane, toluene, methyl ethyl ketone and formaldehyde. Biomarkers, 7, 151–161 Erratum in: Biomarkers, (2006) 11(4): 383.
8. Burgaz, S., Karahalil, B., Bayrak, P., Tasxkin, L., Yavuzaslan, F., Bo¨kesoy, I., Anzion, R. B., Bos, R. P. and Platin, N. (1999) Urinary cyclophosphamide excretion and micronuclei frequencies in peripheral lymphocytes and in exfoliated buccal epithelial cells of nurses handling antineoplastics. Mutat. Res., 439, 97–104.
9. D. Hanahan and R. A. Weinberg, "The hallmarks of cancer,"*Cell*, vol. 100, no. 1, pp. 57–70, 2000.
10. Jois H S, Kale A D, Kumar K.P M. Micronucleus as Potential Biomarker of Oral Carcinogenesis. IJDA (2010); 2(2): 197-202.
11. Holland N, Bolognesi C,Volders M K , Bonassi S, Zeiger E, Knasmueller S et al. The micronucleus assay in human buccal cells as a tool for biomonitoring DNA damage: The HUMN project perspective on current status and knowledge gaps. Mutat Res 659 (2008) 93–108.
12. Samanta S, Dey P. Micronucleus and Its Applications. Diag Cytopathol (2010); 40(1):84-90.
13. Lal A, Ames BN. Association of chromosome damage detected as micronuclei with haemato-logical diseases and Micronutrient Status. Mutagenesis 2011; 26(1): 57-62.

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14. Delfino V, Casartelli G, Garzoglio B, Scala M, Mereu P, Bonatti S et al.Micronuclei and p53 accumulation in preneoplastic and malignant lesions in the head and neck. Mutagenesis (2002); 17(1): 73-77.
15. Kamboj M, Mahajan S. Micronucleus—an upcoming marker of genotoxic damage. Clin Oral Invest (2007) 11: 121–126.
16. Giovanini AF, Vieira DC, Franco LB, Zielak JC, Pizzatto E, Gonzaga CC. Analysis of micronuclei in exfoliation cytology of oral leukoplakia. Perspect. Oral Sci. (2009 ; 1(1): 19-23.
17. Mahimkar MB, Samant TA, Kannan S, Patil T. Influence of genetic polymorphisms on frequency of micronucleated buccal epithelial cells in leukoplakia patients. Oral Oncol 46 (2010) 761–766.
18. Grover et al ; Evaluation of diagnostic reliability of micronuclei in potentially malignant disorders of oral cavity;; Journal of Health and Research /Vol 1/Issue 1/Jan-Apr 2014.
19. Anshu Jain, Veena Maheshwari, Kiran Alam, Ghazala Mehdi, S. C. Sharma., Apoptosis in premalignant and malignant squamous cell lesions of the oral cavity: A light microscopic study; Indian journal of pathology and microbiology, april –june 2009 52(2).
20. Macluskey M, Chandrachud LM, Pazouki S, Green M, Chisholm DM, Ogden GR, *et al*. Apoptosis, proliferation and angiogenesis in oral tissues, possible relevance to tumor progression. J Pathol 2000; 199: 368-75.
21. Bentz BG, Chandra R, Haines GK, Robinson AM, Shah P, Radosevich JA. Nitric oxide and apoptosis during human head and neck squamous cell carcinoma development. Am J Otolaryngol 2002; 23: 4-11.
22. Langlois NE, Eremin O, Heys SD. Apoptosis and prognosis in cancer: Rationale and relevance. J R Coll Surg Edinb 2000; 45: 211-9.

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Rehabilitation of Total Maxillectomy with Magnet Retained Obturator- A Case Report

By Ashish Kalra, Gowda E Mahesh, Dua Parag, Kalra Shilpa & Verma Kamal

CMDC

Introduction- Prosthetic rehabilitation of patients who have undergone total maxillectomy has always been a challenging task for the Prosthodontist. Such a patient presents with unique combination of multiple problems.[1] In addition to the debilitation associated with surgery the patient has to continue nasogastric feeding till the maxillary defect is obturated prosthetically or by surgical reconstruction.[2] It is challenging for the treating prosthodontist to combine and achieve all the characteristics a maxillofacial prosthesis such as, light weight, retention, stability, and esthetics and being functionally adequate, in a compromised clinical situation as that of a total maxillectomy.[3] In the clinical situation described, clinician has used his ingenuinity in fabricating a light weight, 2-piece obturator with magnetic attachments. The final prosthesis was considerably retentive, stable and proved to be functionally efficient for the patient.

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Rehabilitation of Total Maxillectomy with Magnet Retained Obturator- A Case Report

Ashish Kalra [α], Gowda E Mahesh [σ], Dua Parag [ρ], Kalra Shilpa [ω] & Verma Kamal [¥]

Keywords: total maxillectomy, 2-piece obturator, magnets.

I. Introduction

Prosthetic rehabilitation of patients who have undergone total maxillectomy has always been a challenging task for the Prosthodontist. Such a patient presents with unique combination of multiple problems.[1] In addition to the debilitation associated with surgery the patient has to continue nasogastric feeding till the maxillary defect is obturated prosthetically or by surgical reconstruction.[2] It is challenging for the treating prosthodontist to combine and achieve all the characteristics a maxillofacial prosthesis such as, light weight, retention, stability, and esthetics and being functionally adequate, in a compromised clinical situation as that of a total maxillectomy.[3] In the clinical situation described, clinician has used his ingenuinity in fabricating a light weight, 2-piece obturator with magnetic attachments. The final prosthesis was considerably retentive, stable and proved to be functionally efficient for the patient.

II. Case Report

A 72 yrs old female patient reported to dental center complaining of a loose obturator. History revealed that she had undergone partial maxillectomy of right side 04 years back for Adenoid cystic carcinoma following which she was provided with an obturator.

A thorough intraoral examination revealed another diffuse swelling of palate on the left side. Biopsy confirmed the recurrence of the lesion on left side of palate. The total maxillectomy was planned by oncosurgeons. Pre-surgical impressions were made to fabricate a surgical obturator and the extent of resection was outlined by oncosurgeon on the maxillary cast. The surgical obturator was fabricated and secured intra orally using ligature wires and screws inserted bilaterally in the zygomatic arch (Fig 1). In the defect area, considerable portion of the nasal septum, part of the inferior nasal conchae, and the superior wall of maxillary sinuses on either side could be appreciated clinically (Fig 2). Treatment plan narrowed down to fabrication of an interim obturator followed by a 2 piece magnet retained hollow bulb definitive obturator to restore patient's oral functions, speech and to improve esthetics.

Surgical obturator was retrieved after 20 days and the clinical procedures for an interim obturator were initiated. Elastomeric impressions were made using a custom tray with medium body (Aquasil Monophase; Dentsply; Caulk, Germany). Jaw relations were recorded. Initially only anterior teeth were set in the interim obturator Fig 3). The improvement in esthetics and phonetics considerably motivated the patient to develop a more positive outlook towards her clinical condition. The interim obturator was relined intraorally with monomer free silicone soft liner (GC reline, GC Japan). The patient was kept on a strict and regular follow up and post insertion hygiene maintenance protocol. The patient was recalled after 03 months for the fabrication of definitive obturator.

Fabrication of Definitive Two Piece Magnet Retained Hollow Bulb Obturator. The definitive obturator comprised of an 'Antral' and an 'Oral' section. Both were fabricated in different phases as outlined below.

a) Antral section of obturator (hollow bulb)

The patient's interim obturator was customized to be used as an impression tray. Border molding was done with green stick compound and the final impression was made with medium body elastomeric impression material. Master cast was fabricated and duplicated. The undesirable tissue undercuts were blocked by equal mixture of plaster and pumice. A 2-mm thick baseplate wax was then adapted over the antral portion of the obturator and a flat wax lid was fabricated over it. The obturator was polymerized using heat cure polymerizing acrylic material (DPI, Mumbai, India), as per manufacturer's instructions. The acrylized antral part was separated from the cast and the plaster/pumice mix blocking the undercuts was removed. The superior surface of the antral part of the obturator, which was to come in contact with the tissues, was roughened with acrylic bur. Permanent silicone soft liner material (Permaflex, Kohler, Germany) was then mixed and placed into the mold space and the antral obturator placed over it. Curing was carried out as per manufacturer's recommendations.

The antral part of the obturator was then removed and cleaned (Fig 4). The flat lid was secured onto the antral portion with the help of self cure acrylic polymer resin. On the inferior surface of the antral section three triangular elevations, one in central and

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two in posterior areas were carved out with autopolymerizing resin. This would help to orient the oral part with the antral part of the obturator during all further clinical procedures. The antral part was tried in and corrected for any overextensions and sharp margins (Fig 5). The anatomical undercuts present in the maxillary tuberosity, sinus areas and the perioral musculature provided acceptable retention for the prosthesis.

b) Oral section of obturator

The antral section was re-positioned on the earlier duplicated master cast and wax occlusal rim was fabricated over it using hard modelling wax (Cavex, Netherland). Jaw relations were recorded. Anterior and posterior try in of teeth was done and patient's esthetics and phonetics were evaluated (Fig 6). To give the patient a feel of normal palatal contours and to improve the pronunciation of linguopalatal sounds, a thin layer of wax was adapted in the palatal region of the prosthesis (Fig 7). The prosthesis was then polymerized in heat cure acrylic resin. Trimming, finishing, and polishing procedures were completed, and the prosthesis was tried in the patient's mouth. Occlusal errors were checked and corrected, and an almost non functional occlusion with passive intercuspal contacts of the teeth was incorporated. Five pairs of commercially available magnets (cobalt-samarium, Ambica Corporation, New Delhi, India) were positioned in the prosthesis with the help of autopolymerizing acrylic resin (Fig 8) with the keeper in antral part and magnet in oral part. The completed prosthesis was inserted in the patient's mouth (Fig 9).

c) Insertion and Review

The prosthesis was evaluated for retention, stability, phonetics, esthetics and comfort. Patient was instructed to wear the antral portion first and once this was comfortably seated, the oral part was to be inserted. During removal, the patient was instructed to stabilize the posterior part of the antral part of the prosthesis with her left index finger and remove the oral part of the obturator with her right hand to avoid displacement of the antral part along with the oral part of the obturator. Patient was recalled after 24 hours for a review checkup. She was instructed to start consuming semisolid food. Periodical review follow-up was done upto 06 weeks during which the patient had no complaints. After a period of 3 months, the patient was found to be completely comfortable in handling and using the prosthesis to continue to use. She was also satisfied with her speech, esthetics and function.

III. Discussion

Obturator prosthesis is the treatment of choice for patients who have undergone maxillectomy.[1] It recreates a partition between the oral and nasal cavities, restores facial contour, improves mastication, articulation and speech intelligibility. Patients with a bilateral maxillary resection present a tough clinical situation for the prosthodontist. Support and retention of the prosthesis is often compromised due to the absence of palate and teeth, lack of favorable tissue undercuts, and presence of non keratinized nasal mucosa. The retention of the antral part of the obturator in such cases can be achieved from the available anatomy using resilient liners. The use of a resilient liner is a simplified treatment modality because it is modifiable and comparatively economical.[4,5] Magnets, on the other hand, are useful due to their small size and provide strong attractive forces. They can be placed within the prostheses without being obtrusive in the mouth.[6] Cobalt samarium magnets are rare earth magnets and have been used since 1960s for dental applications.[6] In the 1980s neodymium iron-boron magnets were introduced. Though these were efficient for dental applications, they presented a few limitations, such as brittle nature and low corrosion resistance. Long term use of this type of magnet is not indicated. To rectify these limitations, samarium-iron-nitride magnets are presently being researched for intraoral use.[6] Dental implants are generally ruled out in such cases due to non availability of adequate bone. Furthermore, due to inadequate zygomatic bone and the morbidity associated with the surgical procedures, the modality of implant anchorage from the zygomatic arch was totally ruled out for this patient.

IV. Summary

This technique offers a practical means of rehabilitating a patient who has undergone total maxillectomy. The majority of maxillary defects can be ideally reconstructed with a simple obturator. However, the insertion and removal of a large prosthesis used for the rehabilitation of midfacial defects requires adequate neuromotor coordination. A 2 piece sectional obturator with antral and oral sections retained with magnets provides a suitable, economical and functional means of rehabilitation for total maxillectomy patient. The outcome was very rewarding and motivating for the patient.

References Références Referencias

1. Minsley GE, Warren DW, Hinton V. Physiologic responses to maxillary resection and subsequent obturation. J Prosthet Dent 1987; 57: 338-44.
2. Oh W, Roumanas ED. Optimization of maxillary obturator thickness using a double-processing technique. J Prosthodont 2008; 17: 60-63.
3. Antoniou DV, Toljanic JA, Graham L. Obturator prosthesis retention for edentulous patients with large palatal defects: A clinical report. J Prosthet Dent 1996; 76: 227-29.
4. Desjardins RP. Obturator prosthesis design for acquired maxillary defects. J Prosthet Dent 1978; 39: 424-35.

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5. Murray CG. A resilient lining material for the retention of maxillofacial prostheses. J Prosthet Dent 1979; 4: 53-57.

6. Riley MA, Walmsley AD, Harris IR. Magnets in prosthetic dentistry. J Prosthet Dent 2001; 86: 137-42.















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Chronic Inflammation Induced Immunosuppression in Tumor Microenvironment of Oral Cancer

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Abstract- Oral Cancer is a wound that do not heal is a complex disease consists of heterogeneous tissue in their tumor microenvironment. Oral cancer accounts eighth most Common Cancer worldwide. Chronic inflammatory mediators released from immune cells in tumor microenvironment of oral cancer such as macrophages, T lymphocytes, dendritic cells, Natural killer cells release cytokines, Chemokine's and growth factors helps in generation of myeloid derived suppressor cells. Myeloid derived suppressor cells are derived from myeloid progenitor cells of bone marrow secretes inflammatory mediators iNOS, arginase-1, PGE2,IL-10 and IL-4 suppresses adaptive and innate immunity by interacting with macrophages, T-cells, Natural killer cells and dendritic cells favours pro-tumoral activity by activating transcriptional factors (NF-KB,STAT -3,HIF) further progress in to oral cancer. Myeloid derived suppressor cells reduces T cell activation and function by Arginase-1, iNOS, peroxynitrate over expression and cysteine depletion.

Keywords: *myeloid derived suppressor cells, chronic inflammation, oral cancer, granulocytic monocytic colony stimulating factor, natural killer cells, transforming growth factor- beta, vascular endothelial growth factor, prostaglandin E2, hypoxic inducible factor, toll like receptor, lipopolysaccharide, cytokines, chemokines, growth factors.*

GJMR-J Classification: *NLMC Code: WU 158*



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Chronic Inflammation Induced Immunosuppression in Tumor Microenvironment of Oral Cancer

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Abstract- Oral Cancer is a wound that do not heal is a complex disease consists of heterogeneous tissue in their tumor microenvironment. Oral cancer accounts eighth most Common Cancer worldwide. Chronic inflammatory mediators released from immune cells in tumor microenvironment of oral cancer such as macrophages, T lymphocytes, dendritic cells ,Natural killer cells release cytokines, Chemokine's and growth factors helps in generation of myeloid derived suppressor cells. Myeloid derived suppressor cells are derived from myeloid progenitor cells of bone marrow secretes inflammatory mediators iNOS, arginase-1, PGE2,IL-10 and IL-4 suppresses adaptive and innate immunity by interacting with macrophages ,T-cells, Natural killer cells and dendritic cells favours pro-tumoral activity by activating transcriptional factors (NF-KB,STAT -3,HIF) further progress in to oral cancer. Myeloid derived suppressor cells reduces T cell activation and function by Arginase-1, iNOS, peroxynitrate over expression and cysteine depletion. This article describes mainly about immune cells in tumor microenvironment especially macrophages, T lymphocytes, dendritic cells, Natural killer cells their interactions with myeloid derived suppressor cells.

Keywords: myeloid derived suppressor cells, chronic inflammation, oral cancer, granulocytic monocytic colony stimulating factor, natural killer cells, transforming growth factor- beta, vascular endothelial growth factor, prostaglandin E2, hypoxic inducible factor, toll like receptor, lipopolysaccharide, cytokines, chemokines, growth factors.

I. Introduction

Inflammation is the body response to any type of injury, in which various mediators are released in surrounding environment. Recent debated topic is inflammation associated onco -promotion in tumor microenvironment. Inflammatory mediators in oraltumor micro-environment consists of mediators of inflame-mation are Neutrophils, lymphocytes, macrophages, Natural killer cells, Dendritic cells secreting cytokines. Which can induce Immuno-modulation by myeloid derived suppressor cells (MDSC) results in Oral tumor promotion, progression, and metastasis(1).

Immune cells has an important role in preventing or promoting cancer through immune surveivellance of tumor by mechanism of immune-editing, immuneprocessing and immuneevasion. Immunoevasion is one of the hallmark of tumor in order to progress. Immunoevasion mechanism involves the production of cytokines, which are immunosuppressive, T cell apoptosis or loss of HLA class1 and costimulatory molecules. In Immunoediting high immunogenicity tumorseliminate tumor by NK cells, macrophages,T cells. Reduced tumor cell variant immunogenicity favour tumor progression by immunosuppression or resistant to immune attack. Immuno processing stage genetic instability and heterogeneity of cancer cells favour promotion of tumor which, are poorly recognized by immune system or immunosuppression.

Immunoescape stage altered by expression of MHC1 and 11 and costimulatory molecules, antigen processing dysregulation antigen processing, expression of low levels tumor antigen, other mechanisms of immunosuppression are T cell tolerance to tumor antigen and immunosuppressive cytokines IL-10,TGF-Beta or T regulatory cells (Treg). (48)

Oral cancer is an eighth most common cancer in the worldwide. Every year nearly 300,400 new cases have been reporting worldwide and costs 145,400 lives a year. Squamous cell carcinoma involves 90% of head and neck region especially from mucosal epithelium linked to various adverse habits such as smoking form of tobacco, smokeless tobacco, alcohol drinking and also human papilloma virus.

Advance oral cancer locally, management has been a challenging issue involving multidisciplinary approach of surgery, chemotherapy and radiotherapy. Despite recent improvement in management of oral cancer still the prognosis is grave with five year survival rate nearly 50%.

Early stage of inflammation neutrophils are predominant leucocyte and first cell to migrate are regulated by macrophages and mast cells in tissue. As inflammation proceeds various types of leucocytes majority of them are lymphocytes gets activated and recruited to the inflammatory site by a signalling network involving chemokines, cytokines, growth factors for defense against infection. Shifting of antimicrobial tissue damage to tissue repair occurs mediated by PGE2, TGF-Beta and reactive oxygen and nitrogen inter-mediates having dual role in both aggravating and suppressing inflammation. Resolution of inflammation requires macrophages, dendritic cells and phagocytes by apoptosis and phagocytosis, which promote an anti-

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inflammatory response. If inflammation is dysregulated, aggravating to chronic inflammatory cellular respose causing immunosuppression, tissue and DNA damage by cytokines, growth factors, reactive oxygen and nitrogen species released from macrophages and lymphocytes(1,2).

II. Factors Affecting Inflammation Induced Immunosuppression in Tumor Microenvironment of Oral Cancer

Oral tumor microenvironment consists of various heterogeneous inflammatory mediators such as neutrophils, natural killer cells, T and B lymphocytes, mast cells, and antigen presenting cells(APC) such as macrophages, Dendritic cells and other distinct cell types including fibroblasts, Carcinoma associated fibroblast, smooth musclecells, myo-fibroblast, endothelial cells and their precursors, pericytes. Recent data have demonstrated a role of these individual components, in particular carcinoma associated fibroblasts, macrophages and endothelial cells, in promoting tumor growth and progression (1-2). The tumorstroma has an indispensable role in acquiring hallmark capabilities. The stroma provides support with growth factors (GM-CSF,G-CSF,M-CSF; VEGF; TGF), cytokines (IL-1,IL-4,IL-5,IL-6,IL-10,IL-13, TNF-Alfa, Interferon –Gamma), chemokines (CCL2,CCL4,CCL5, CXCL1, CXCL12 and CXCL8) along with COX2 which, secrete prostaglandin E2,promotes the generation of Myeloid derived suppressor cells.

III. Role of mdsc in Immunosuppression

These are immature heterogeneous myeloid cells that fail to terminally differentiate in to granulocytes, dendritic cells or macrophages on chronic inflammatory conditions and exhibit immunosuppressive function by multiple mechanism. Their broadly distinct phenotypical characteristics, Among human MDSCs, the two subsets can be distinguished as Granulocytic and Monocytic(3). which, is responsible for immuno-modulatory activity in tumor microenvironment by evading active immune system by various factors by potent inhibitors of both antigenic –specific and non-specific T-cell activation. These factors are arginase, nitric oxide, Reactive oxygen species (ROS), PGE2, Cystein, peroxynitrate. An important mutagenic factor frequently abundant in an inflammatory microenvironment is ROS (eg. Oxygen ions and peroxides) results from oxidative stress induced by phagocytic cells.ROS are highly reactive, unstable molecules that damage DNA increases the cell mutation rate, thus favouring the appearance of clones with oncogenic properties. Potential key mechanism of MDSC –induced CD8+ T-cell immunosuppression in tumor bearing hosts by increased NADPH oxidase, NOX_2 activity (4-5). Nitric oxide is produced by MDSC by utilising L-arginine as substrate for nitric oxide synthase (6,7). Which, suppresses T-cell activation, adhesion, proliferation and migration (8-13).It also suppresses T-cell function, particularly CD8+ T cells by blocking the activation of signalling molecules in T cells, including JAK1(Janus activated kinase 1), STAT5, ERK and Akt (8,11). It has also been shown to inhibit MHC class 2 expression and promote CD8 T-cell apoptosis (14,15). Other important moderator synthesize by MDSC is Arginase. L- Arginine is a conditionally essential aminoacid and metabolized by arginases and nitric oxide synthases to produce either L- ornithine and urea (16,17,18). L- arginine is an amino acid required for T-cell function and proliferation. L-arginine deprivation has been reported to induce T-cell dysfunction and suppression of T-cell function (19,20,21).These mechanisms seem to contribute to the protumoral function of MDSC(22). MDSC are copious producers of peroxynitrate and increased levels are associated with tumor progression by inhibiting antigen specific, cytotoxic T-cell responses (23). Cysteineis an essential amino acid required for T-cell activation, differentiation and proliferation (24). MDSC mediated cysteine depletion, block activation of T-cell from the local microenvironment results in the inhibition of T-cell activation and function (25). PGE2 is an eicosanoids synthesise by COX2produced and secreted by MDSC, mediated over expression of arginase, Corelated with their pro-inflammatory and immunosuppressive properties, further inhibiting the activity of CD8+ T cells. MDSCs immunosuppressive function, activation and proliferation is activated by IFN-gamma, TLR ligands, IL-13, IL-4, and TGF –beta, which trigger STAT3and NF-kb signalling pathways(26,27,28). These various factors are produced during the course of inflammation following cellular stresses, in response to hormones, growth factors, endotoxin and inflammatory cytokines or by growing tumors which induces angiogenesis, apoptosis, chronic inflammation and immunosuppression(28,29).

IV. Interaction of mdsc with other Immunecells

MDSCs communication network between macrophages and DCs that promotes and maintains an immunosuppressive microenvironment. This communication is mainly mediated by inflammatory mediators IL-1beta, IL-6, IL-10, PGE-2, and TGF – beta (30,31). The activating NK receptors inhibited by IDO (Indoleamine 23-dioxygenase) andPGE2 are counteracted by NKG2A an inhibitory receptor utilized by both T and NK cells (32). An early response of damaged tissue is production of IL-8 by the epithelial cell itself, which together with macrophages and mast cells secrete TNF- alfa and histamine allows neutrophil extravasion to injure site initiating inflammation. Chemokines secreted by

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endothelial cells and macrophages brings inflammatory and immune cells to the site of inflammation(33). Among inflammatory factors promoting proliferation are TGF-beta, fibroblast growth factor, epithelial growth factor, TGF-beta synthesized by mast cells, macrophages and lymphocytes as an inactive precursor in inflammatory microenvironment activated by proteases. TGF-beta promotes mesenchymal Cell proliferation and immuno - modulation by promoting N2 neutrophils and M2 macrophages, facilitates tumor invasion and metastasis (34,35). LPS is a known activator of macrophage cross talk with MDSC in the presence of LPS. Later LPS binds to LPS binding protein. Which helps in transfer ofLPS to the membrane bound receptor CD14 through TLR4signalling pathway. TLR4 signalling pathway gets activated by CD14 binds with TLR4 further downstream activation of NF-kb driving MDSC production of IL-10 resulting in immunosuppression and immune evasion by promoting M2 polarization of macrophages(36). Alternatively activated macrophages(M2 type) are an important source of both Fibroblast growth factors, and Endothelial growth factors activated by cytokines such as IL-4, IL-5, IL-6, IL-9, IL-13, IL-17 and TGF-beta acts as a immunosuppressor towards Treg (Regulatory T cell) cells maintain immunosuppressive microenvironment (37,38). Tumor stromacan also suppress immune effector function. Extra cellular accumulation of lactate, adenosine, VEGF under hypoxic condition activated by hypoxia inducible transcriptional factor (HIF) further induces angiogenesis. Cross talk between MDSC and dendritic cells in presence of cytokines such as IL-4, GM-CSF and PGE2 results in decrease in production of mature dendritic cells , blocking T-cell production of IFN-gammaand dendritic cells production of Pro-inflammatory cytokine IL-23driving the proliferation and inflammatory function of Th17 cells. Which suppresses both adaptive and innate immunity, due to immunosuppressive network, the immature dendritic cell fail to activate to become mature dendritic cell on antigenic presentation. So, the activation ofCD4+ and CD8+ T cells don't take place. All together co-operate to inhibit Dendritic cell antigen- processing, presenting activity and dendritic cell tolerance (39-47).All these factors contribute to pro-tumoral activity, tumor progression, invasion and metastasis. Inflammation is considered to be a' Seventh hallmark' of cancer (4).

Myeloid derived suppressor cells are immature myeloid cells of myeloid progenitor cells upon chronic inflammation. They are of two types Monocystic-MDSC and Granulocytic-MDSC. Myeloid derived suppressor cells induce immunosuppression by various mechanisms suppresses both innate and adaptive immunity, it also possess plasticity and the type of MDSC in tumor microenvironment determines the immunesuppression. Complex interactions between MDSC and immune cells and their role in immune-suppression need to be studied. Understanding of MDSC biology, chronic inflammatory mediators, which helps in MDSC recruitment, generation, activation and their role in immunosuppression must be revealed for therapeutic strategy and its role in tumor prognosis.

V. Conclusion

Thorough understanding of immune cells of Oral tumor microenvironment , role of immune cells such as Macrophages, T lymphocytes and natural killer cells which, drive towards tumorigenesis. Role of Inflammatory cells and their mediators such as cytokines, their interactions with myeloid derived suppressor cells are major immunosuppressor and immune evasion cells. Phonotypical and functional role of myeloid derived suppressor cells in oral tumor microenvironment linking between inflammation and oral cancer. Hence, modulating targeted or combined immune cells in oral tumor microenvironment, could possibly hold a future therapeutic opportunity with better survival rate and less possible complications.

Abbreviations

HGF, Hepatic growth factor,
VEGF, Vascular endothelial growth factor,
MMP-9, Matrix mettaloproteinases-9,
COX2, Cyclo-oxygenase2,
INOS, Inducible nitric oxide synthase,
ROS, Reactive oxygen species,
PDGF, Platelet derived growth factor,
EGF, Epidermal growth factor,
FGF, Fibroblast growth factor,
TNF-Alfa, Tumour necrosis factor-Alfa,
IFN-Beta, Interferon Beta,
IL-10, Interleukin 10,
TGF-Beta, Transforming growth factor- Beta,
CCL17, CC Chemokine ligand 17,
CCL18, CC Chemokine ligand 18,
CCL22, CC chemokine ligand 22,
PGE2, Prostaglandin E2,
IDO, Indoleamine 2,3 –dioxygenase,
UPA, Urokinase plasminogen activator,
IL-2, Interleukin 2,
IL-4, Interleukin 4,
IL-6, Interleukin -6,
IFN-Gamma, Interferon Gamma,
COX-1, Cyclo-oxygenase 1,
COX2, Cyclo-oxygenase 2,
NF-KB, Nuclear factor KB,
MCP-1, Macrophage/Monocyte chemoattractant protein-1,
M-CSF, Macrophage colony stimulating factor,
IL-17, Interleukin 17,
CD4+ Th17, CD4+ T helper lymphocyte17,
MDSC, Myeloid derived suppressor cells,
SR-A, The class A macrophage scavenger receptor msr1,

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GM-CSF, Granulocyte Macrophage- Colony stimulating factor,
G-CSF, Granulocyte colony stimulating factor,
STAT3, Signal transducer and activator of transcription 3,
bFGF- basic fibroblast growth factor,
MMPS, Matrix metallo proteinases,
HIF-1 Alfa, Hypoxia- Inducible factor Alfa. T reg cell, T regulatory cell, T h1, T helper1, Th2, T helper 2,
TAM, Tumor associated macrophages,
TLR, Toll like receptor,
DC, Dendritic cells,
NK cells, Natural killer cells,
HLA, Human leucocyte antigen,
MHC 1, Major histocompatibility antigen 1,
Akt, Protein kinase B,
ERK, Extracellular signal-regulated kinase.

References Références Referencias

1. Pietras k, Ostman A. Hallmarks of cancer; Interactions with the tumorstroma. *Exp cell Res,* 2010; 316: 1324-1331.
2. Condamine T, Ramachandran I, Youn JI, Gabrilovich DI. Regulation of tumor metastasis by myeloid-derived suppressor cells.Annual review of medicine. 2015; 66: 97-110.
3. Peranzoni E, Zilio S, Marigo I, Dolcetti L, Zanovello P, Mandruzzato S, Bronte V. Myeloid-derived suppressor cell heterogeneity and subset definition. Curr OpinImmunol 2010; 22: 238-244.
4. Colotta F, Allavena P, Sica A, Garlanda C, and Mantovani A. Cancer –related inflammation, the seventh hallmark of cancer; links to genetic instability. Carcinogenesis 2009; 30: 1073-1081.
5. Fiaschi T and Chiarugi P. Oxidative stress, tumor microenvironment, and metabolic reprogramming: a diabolic liaison. International Journal of Cell Biology 2012; 20: 80-88.
6. Bauer H, Jung T, Tsikas D, Stichtenoth DO, Frolich JC, Neumann C. Nitric oxide inhibits the secretion of T-helper 1- and T-helper 2-associated cytokines in activated human T cells. Immunology 1997; 90: 205-211.
7. Sosroseno W, Bird PS, and Seymour G J. Effect of exogenous nitric oxide on murine splenic immune response induced by Aggregatibacter actinomy-cetemcomitans lipopolysaccharide. Anaerobe 2009; 15: 95-98.
8. Bingisser RM, Tilbrook PA, Holt PG, and Kees U R. Macrophage-derived nitric oxide regulates T cell activation via reversible disruption of the Jak3/ STAT5 signaling pathway. J Immunol 1998; 160: 5729-5734.
9. Edgington-Mitchell, Laura E., and Belinda S. Parker. Disparate functions of myeloid-derived suppressor cells in cancer metastasis. Cancer Forum 2014; 38: 38-77.
10. Lejeune P, Lagadec P, Onier N, Pinard D, Ohshima H, Jeannin, JF . Nitric oxide involvement in tumor-induced immunosuppression. J Immunol 1994; 152: 5077- 5083.
11. Mazzoni A, Bronte V, Visintin A, Spitzer J H, Apolloni E, Serafini P, Zanovello P, Segal DM. Myeloid suppressor lines inhibit T cell responses by an NO-dependent mechanism. J Immunol 2002; 168: 689-695.
12. Medot-Pirenne M, Heilman M J, Saxena M, McDermott P E, Mills C D. Augmentation of an antitumor CTL response In vivo by inhibition of suppressor macrophage nitric oxide. J Immunol 1999; 163: 5877-5882.
13. Sato K, Ozaki K, Oh I, Meguro A, Hatanaka K, Nagai T, Muroi K, and Ozawa K. Nitric oxide plays a critical role in suppression of T-cell proliferation by mesenchymal stem cells. Blood 2007; 109: 228-234.
14. Harari O, Liao JK. Inhibition of MHC II gene transcription by nitric oxide and antioxidants. Curr Pharm Des 2004; 10: 893-898.
15. Rivoltini L, Carrabba M, Huber V, Castelli C, Novellino L, Dalerba P, et al. Immunity to cancer: attack and escape in T lymphocyte-tumor cell interaction. Immunol Rev 2002; 188: 97-113.
16. Bogdan C. Nitric oxide and the immune response. Nat Immunol 2001; 2: 907-916.
17. Morris, S.M., Jr. Regulation of enzymes of the urea cycle and arginine metabolism. Annu Rev Nutr 2002; 22: 87-105.
18. Zhao W, Xu Y, Xu J, Wu D, Zhao B, Yin Z, Wang X. Subsets of myeloid-derived suppressor cells in hepatocellular carcinoma express chemokines and chemokine receptors differentially. International immunopharmacology. 2015; 26(2): 314-21.
19. Bronte V, Serafini P, De Santo C, Marigo I, Tosello V, Mazzoni A, *et a*. IL-4-induced arginase 1 suppresses alloreactive T cells in tumor-bearing mice. J Immunol 2003; 170: 270-278.
20. Medina-Echeverz J, Aranda F, Berraondo P. Myeloid-derived cells are key targets of tumor immunotherapy. Oncoimmunology. 2014; 3(4): 28-37.
21. Rodriguez PC, Ochoa AC. Arginine regulation by myeloid derived suppressor cells and tolerance in cancer: mechanisms and therapeutic perspectives. Immunol Rev 2008; 222: 180-191.
22. Parker KH, Beury DW, Ostrand-Rosenberg S. Myeloid-Derived Suppressor Cells: Critical Cells Driving Immune Suppression in the Tumor Microenvironment. Advances in Cancer Research. 2015; 12: 25-32.
23. Nagaraj S, Gupta K, Pisarev V, Kinarsky L, Sherman S, Kang L, Herber DL, Schneck J, Gabrilovich DI. Altered recognition of antigen is a mechanism of

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CD8+ T cell tolerance in cancer. Nat Med 2007; 13: 828-835.
24. Jiang J, Guo W, Liang X. Phenotypes, accumulation, and functions of myeloid-derived suppressor cells and associated treatment strategies in cancer patients. Human immunology. 2014; 75(11): 1128-37
25. Srivastava MK, Sinha P, Clements VK, Rodriguez P, Ostrand-Rosenberg S. Myeloid-derived suppressor cells inhibit T-cell activation by depleting cystine and cysteine. Cancer Res 2010; 70: 68-77.
26. Keskinov AA, Shurin MR. Myeloid regulatory cells in tumor spreading and metastasis. Immunobiology. 2015; 220(2): 236-42.
27. Ostrand –Rosenberg S and Sinha P. Myeloid –derived suppressor cells: linking inflammation and cancer. Journal of immunology 2009; 188(8): 4499-4506.
28. Eruslanov E, Daurkin I, Ortiz J, Vieweg J, Kusmartsev S. Pivotal advance; Tumor –mediated induction of myeloid –derived suppressor cells and M2- polarized macrophages by altering intracellular PGE2 catabolism in myeloid cells. J. Leukol. Biol 2010; 88: 839-848.
29. Legler DF, Bruckner M, Vetz-Von Allmen E , Krause P. Prostaglandin E2 at new glance; Novel insights in functional diversity offer therapeutic chances. International. Journal of Biochem cell Biol 2010; 42: 198-201.
30. Ostrand –Rosenberg S, Sinha P, Beury DW and Clements V.K. Cross-talk between myeloid – derived suppressor cells (MDSC), macrophages, and dendritic cells enhances tumor – induced immune suppression. Seminars in cancer biology 2012; 22(4): 275-281.
31. Dilek N, Vuillefroy d silly R, Blancho G, and Vanhove B. Myeloid –derived suppressor cells: mechanisms of action and recent advances in their role in transplant tolerance. Frontiers in immunology 2012; 3: 208-218.
32. LO Manaco E, Tremante E, Cerboni C, Melluci E, Sibilio L, Zingoni A et al . Human Leukocyte antigen E contributes to protect tumor cells from lysis by natural killer cells. Neoplasia 2011; 13: 822-830.
33. Harda A, Sekido N, Akahoshi T, Wada T, Mukaida N, Matsushima K. Essential involvement of interleukin -8 (IL-8) in acute inflammation. Journal of leukocyte biology 1994; 56: 559-564.
34. Xu Q, Wang L, Li H. Mesenchymal stem cells play a potential role in regulating the establishment and maintenance of epithelial –mesenchymal transition in MCF7 human breast cancer cells by paracrine and induced autocrine TGF-beta. International journal of oncology 2012; 41:46-58.
35. Wang H, Wu J, Zhang Y .Transforming growth factor beta – induced epithelial –mesenchymal transition increases cancer stem –like cells in the PANC-1 cell line. Oncology letters2012; 3: 229-233.
36. Jiang Q, Akashi S, Miyake K, Petty HR. Lipopolysaccharide induces physical proximity between CD14 and toll-like receptor 4 (TLR4) prior to nuclear translocation of NF-kappa B. J Immunol 2000; 165: 3541–3544.
37. Wang Y, Li L, Guo X. Interleukin -6(IL-6) signaling regulates anchorage independent growth, proliferation, adhesion and invasion in human ovarian cancer cells. Cytokine 2012; 59: 228-236.
38. Tindall EA, Severi G, Hoang N. Interleukin -6 promoter variants, prostate cancer risk and survival. The prostate 2012; 72: 1701-1707.
39. Mancino A, Schioppa T, Larghi P. Divergent effects of hypoxia on dendritic cell functions. Blood 2008; 112: 3723-3734.
40. Elia AR, Cappello P, Puppo M. Human dendritic cells differentiated in hypoxia down modulate antigen uptake and change their chemokine expression profile. Journal of leukocyte biology 2010; 84: 165-171.
41. Yang M, Ma C, Liu S. HIF-dependent induction of adenosine receptor A2b skews human dendritic cells to a Th2 –stimulating phenotype under hypoxia. Immunology and cell biology 2010; 88: 165-171.
42. Douglas M, Dmitry I. Gabrilovich. Myeloid derived suppressor cells in the tumor microenvironment; Expect the unexpected. The journal of Clinical investigation 2015; 7: 1125-1135.
43. Poschke I, Mao Y, Adamson L, Salazar-Onfray F, Masucci G, Kiessling R. Myeloid-derived suppressor cells impair the quality of dendritic cell vaccines. Cancer Immunol Immunother2011; 8: 210-213.
44. McKenzie BS, Kastelein RA, Cua DJ. Understanding the IL-23-IL-17 immune pathway. Trends Immunol 2006; 27: 17–23.
45. Raffaghello L, Bianchi G. Myeloid-Derived Suppressor Cells and Tumor Growth. In Interaction of Immune and Cancer Cells. Journal of cancer 2014; 91-109.
46. Diaz-Montero CM, Finke J, Montero AJ. Myeloid-derived suppressor cells in cancer: therapeutic, predictive, and prognostic implications. Seminars in oncology 2014; 41: 174-184.
47. Teng MW, Andrews DM, McLaughlin N, von Scheidt B, Ngiow SF, Moller A, et al. IL-23 suppresses innate immune response independently of IL-17A during carcinogenesis and metastasis. Proc Natl Acad Sci 2010; 107: 8328–8333.
48. Sosroseno, W. *et al*. (2009) Effect of exogenous nitric oxide on murine splenic immune response induced by Aggregatibacteractinomycetemcomitans lipopolysaccharide. *Anaerobe,* 15, 95-98.
49. Bingisser, R. M. *et al*. (1998) Macrophage-derivednitric oxide regulates T cell activation via

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reversible disruption of the Jak3/STAT5signaling pathway. *J Immunol*, 160, 5729-5734.
50. Bobe, P.*et al*. (1999) Nitric oxide mediation of active immunosuppression associated with graft-versus hostreaction. *Blood*, 94, 1028-1037.
51. Lejeune, P. *et al*. (1994) Nitricoxide involvement in tumor-induced immunosuppression. *J Immunol*, *152*, 5077- 5083.
52. Mazzoni, A. *et al*. (2002) Myeloid suppressor lines inhibit T cell responses by an NO-dependent mechanism. *J Immunol*, *168*, 689-695.
53. Medot-Pirenne, M.*et al*. (1999) Augmentation of an antitumor CTL response in vivo by inhibition of suppressor macrophage nitric oxide. *J Immunol*, 163, 5877-5882.
54. Sato, K. *et al*. (2007) Nitric oxide plays a critical role in suppression of T-cell proliferation by mesenchymal stem cells. *Blood*, 109, 228-234.
55. Harari, O. *et al*. (2012) Inhibition of MHC II gene transcription by nitric oxide and antioxidants. *Curr Pharm Des*, 10, 893-898.
56. Rivoltini, L. *et al*. (2013) Immunity to cancer: attack and escape in T lymphocyte-tumor cell interaction. *Immunol Rev*, 188, 97-113.
57. Bogdan, C. *et al*. (2011) Nitric oxide and the immune response. *Nat Immunol*, 2, 907-916.
58. Morris, S.M. *et al*. (2002). Regulation of enzymes of the urea cycle and arginine metabolism. *Annu Rev Nutr*, 22, 87-105.
59. Wu, G.*et al*. (1998) Arginine metabolism: nitric oxide and beyond. *Biochem J*, 336, 1-17.
60. Bronte, V. *et al.* (2003) IL-4-induced arginase 1 suppresses alloreactive T cells in tumor-bearing mice. *J Immunol*, 170, 270-278.
61. Bronte, V. *et al.* (2005) Regulation of immune responses by L-arginine metabolism. *Nat Rev Immunol*, *5*, 641-654.
62. 21. Rodriguez, P.C. *et al*. (2008) Arginine regulation by myeloid derived suppressor cells and tolerance in cancer: mechanisms and therapeutic perspectives. Immunol Rev, 222, 180-191.
63. Rodriguez, P.C. *et al*. (2004) Arginase -1 production in the tumor microenvironment by mature myeloid cells inhibits T-cell receptor expression and antigen-specific T-cell responses. *Cancer Res*, 64, 5839-5849.
64. Nagaraj, S. *et al*. (2007) Altered recognition of antigen is a mechanism of CD8+ T cell tolerance in cancer. *Nat Med*, 13, 828-835.
65. Gout, P.W.*et al*. (2011) A potent suppressor of lymphoma growth by inhibition of the x(c)- cystine transporter: anew action for an old drug, *oncogene*, 15, 1633-1640.
66. Srivastava, M.K.*et al.* (2010) Myeloid-derived suppressor cells inhibit T-cell activation by depletingcystine and cysteine. *Cancer Res*, 70, 68-77.
67. Keskinov AA, Shurin MR. Myeloid regulatory cells in tumor spreading and metastasis. Immunobiology. 2015 Feb 28; 220(2): 236-42.
68. Ostrand –Rosenberg, S. *et al*. (2009) Myeloid –derived suppressor cells: linking inflammation and cancer. *Journal of immunology*, 188, 4499-4506.
69. Eruslanov, E.*et al*. (2010) Pivotal advance ; Tumor –mediated induction of myeloid –derived suppressor cells and M2- polarized macrophages by altering intracellular PGE2 catabolism in myeloid cells. *J. Leukol. Biol*, 88, 839-848.
70. Legler, D.F. *et al*. (2010). Prostaglandin E2 at new glance; Novel insights in functional diversity offer therapeutic chances. International. *Journal of Biochem cell Biol*, 42, 198-201.
71. Ostrand –Rosenberg, S. *et al*. (2012) Cross-talk between myeloid – derived suppressor cells (MDSC), macrophages, and dendritic cells enhances tumor – induced immune suppression. *Seminars in cancer biology*, 22, 275-281.
72. Dilek, N. *et al*. (2014) Myeloid –derived suppressor cells: mechanisms of action and recent advances in their role in transplant tolerance. *Frontiers in immunology*, 3, 208-14.
73. LO Manaco, E. *et al*. (2011) Human Leukocyte antigen E contributes to protect tumor cells from lysis by natural killer cells. *Neoplasia*, 13, 822-830.
74. Harda, A. *et al*. (1994) Essential involvement of interleukin -8 (IL-8) in acute inflammation. *Journal of leukocyte biology*, 56, 559-564.
75. Xu, Q. *et al*. (2012) Mesenchymal stem cells play a potential role in regulating the establishment and maintenance of epithelial –mesenchymal transition in MCF7 human breast cancer cells by paracrine and induced autocrine TGF-beta. *International journal of oncology*, 41, 46-58.
76. Wang, H.*et al*. (2012) Transforming growth factor beta – induced epithelial –mesenchymal transition increases cancer stem –like cells in the PANC-1 cell line. *Oncology letters*, 3, 229-233.
77. Jiang, Q.*et al*. (2000) Lipopolysaccharide induces physical proximity between CD14 and toll-like receptor 4 (TLR4) prior to nuclear translocation of NF-kappa B. *J Immunol*, 165, 3541–3544.
78. Wang, Y. *et al*. (2012) Interleukin -6(IL-6) signaling regulates anchorage independent growth, proliferation, adhesion and invasion in human ovarian cancer cells. *Cytokine*, 59, 228-236.
79. Tindall, E. A. *et al*. (2012) Interleukin -6 promoter variants, prostate cancer risk and survival. *The prostate*, 72, 1701-1707.
80. Mancino, A. *et al*. (2008) Divergent effects of hypoxia on dendritic cell functions. *Blood*, 112, 3723-3734.
81. Elia, A.R. *et al*. (2010) Human dendritic cells differentiated in hypoxia down modulate antigen

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uptake and change their chemokine expression profile. *Journal of leukocyte biology*, 84, 165-171.
82. Yang, M. *et al*. (2010) HIF-dependent induction of adenosine receptor A2b skews human dendritic cells to a Th2 –stimulating phenotype under hypoxia. *Immunology and cell biology*, 88, 165-171.
83. Gabrilovich, D. *et al*. (2014) Mechanisms and functional significance of tumour-induced dendritic-cell defects. *Nat Rev Immunol*, 4, 941–952.
84. Poschke, I. *et al*. (2011) Myeloid-derived suppressor cells impair the quality of dendritic cell vaccines. *Cancer Immunol Immunother*, 8, 210-213.
85. McKenzie, B.S. *et al*. (2006). Understanding the IL-23-IL-17 immune pathway. *Trends Immunol*, 27, 17–23.
86. Langrish, C.L. *et al*. (2005) IL-23 drives a pathogenic T cell population that induces autoimmune inflammation. *J Exp Med*, 201, 233–240.
87. Langowski, J.L. *et al*. (2006) IL-23 promotes tumour incidence and growth. *Nature*, 442, 461–465.
88. Teng, M.W. *et al*. (2010) IL-23 suppresses innate immune response independently of IL-17A during carcinogenesis and metastasis. *Proc Natl Acad Sci*, 107, 8328–8333.
89. Mittal, D. *et al*. (2014) New insights into cancer immunoediting and its three component phases-elimination, equilibrium and escape. *Curr opin immunol*, 27, 16-25.

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Minimal Invasive Techniques in Caries Detection, Diagnosis and Mangagement - A Clinical Study

By Lt Col Sonali Sharma, Prof Dr. Mithra N Hegde, Dr. Vandana Sadananda & Dr. Blessen Matthews

Abstract- *Background:* Laser fluorescence for caries detection, caries detecting dyes and air abrasion, as an exploratory tool, aid in practicing minimal invasive dentistry.

AIM: To clinically assess newer method of caries detection of non cavitated lesions and to contrast and correlate with the traditional methods

Materials and Methods: 200 patients fulfilling the inclusion criteria in first and or second mandibular molar were included in the study. Depending on the laser fluorescence values, visual and radiographic scoring the selected patients were designated to the following groups:

Group I: 0-14 DIAGNOdent reading, Ekstrand criteria scoring- 0 in both clinical and radiographic evaluation. No caries- No active treatment (Control)

Keywords: *laser fluorescence, air abrasion, minimal invasive dentistry.*

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Minimal Invasive Techniques in Caries Detection, Diagnosis and Mangagement - A Clinical Study

Lt Col Sonali Sharma [α], Prof Dr. Mithra N Hegde [σ], Dr. Vandana Sadananda [ρ] & Dr. Blessen Matthews [ω]

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Group I: 0-14 DIAGNOdent reading, Ekstrand criteria scoring- 0 in both clinical and radiographic evaluation. No caries- No active treatment (Control)

Group II: 15- 25 DIAGNOdent reading, Ekstrand criteria scoring- 0, 1 in both clinical and radiographic evaluation. Remineralized by CPP ACP F paste.

Group III: > 25 DIAGNOdent reading, Ekstrand criteria scoring- 0, 1, 2, in both clinical and radiographic evaluation. Enamel biopsy was done by Air Abrasion.

Statistical Analysis: The statistical analysis was done by Chi square test of significance for proportion analysis.

Result: Of 200 teeth which were evaluated, it was found that 153 patients had caries, but it was correctly detected in 150 patients by laser fluorescence, in 83 patients by visual method and in 50 patients by radiographic method.

Conclusion:

1. Laser fluoresce method of caries detection is a valuable adjunct in caries detection.
2. Air abrasion can be used as an exploratory tool to confirm hidden caries.

Keywords: laser fluorescence, air abrasion, minimal invasive dentistry.

I. Introduction

The management strategies of dental caries are dependent on the stage at which caries is detected. The incipient carious lesions are characterized by subsurface dissolution due to more fluoride ions in the 50-100 microns of the tooth's outer surface and less fluoride in subsurface region. Sub surface, non cavitated lesions are amenable to remineralization, thus early detection and diagnosis is of prime importance. [1-3]

Traditionally diagnosis of dental caries was based on visual detection. In addition, the diagnosis of early noncavitated carious lesion also requires detection and diagnostic aids which are more valid and reliable. There is a plethora of such devices flooding the market. One such valid and reliable method is laser based fluorescence caries detection method.[4] It is a noninvasive method for caries detection of hidden caries. It emits 655nm of infrared rays that is absorbed by organic and inorganic tooth structure and the remitted fluorescence shows various scales between 0-99.It is postulated that bacterial products like porphyrins fluorescence when they irradiated with infra-red light.[5-7]

Histopathologically, carious dentin is divided into two layers, outer layer called infected dentin, which is soft and cannot be remineralized and the inner decalcified affected dentin, which is hard and can be remineralized. Caries detecting dyes are used as a clinical guide for complete removal of the outer carious zone in dentinal caries, as it contains denatured collagen which is stained, making caries excavation minimal.[9,10]

Today in dentistry there is a paradigm shift from the old G.V. Black principles of extension for prevention, to preservation of tooth structure by ultraconservative techniques of minimal invasive dentistry also known as microdentistry. Compared with principles of traditional operative dentistry the modalities of microdentistry are centred on early detection and diagnosis, prevention and minimal intervention. Air abrasion is a treatment modality,which preserves the structural integrity of the sound tooth structure remaining around a cariouslesion. The abrasive particles strike the tooth at high speeds and removes carious tooth structure preferentially. [11-14]

As an adjunct to traditional methods of caries detection, laser fluorescence method can detect and diagnose early carious lesion, which depending on the stage of carious can be managed with minimal intervention.

II. Material & Method

Adult patients between 18 – 25 years of age, reporting to the department of Conservative Dentistry and Endodontics, were screened with laser fluorescence device (Diagnodent pen 2190, KAVO, Birbech Germany) to determine any suspected or hidden initial pit and fissure caries on their first or second mandibular molars. The indices used for case selection and segregation clinically and radiographically, was Ekstrand criteria of severity index for occlusal fissure carious lesions. Laser fluorescence scoring was based on Lussi Criteria for

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measuring the severity of carious lesion. The total number of patients which were screened was 200 and segregated as follows:

Group I: 0-14 Laser fluorescence reading, Ekstrand criteria score - 0 for both clinical and radiographic evaluation. No caries, No active treatment (Control)

Group II: 15- 25 Laser fluorescence reading, Ekstrand criteria score - 0, 1 for both clinical and radiographic evaluation. Incipient caries which can be remineralized by CPP ACP F paste.

Group III: > 25 Laser fluorescence reading, Ekstrand criteria score - 0, 1, 2, in both clinical and radiographic evaluation. Confirmed by exploratory cavity preparation by Air Abrasion.

III. Procedure

Group I: Laser fluorescence values were less than 15. As per Ekstrand clinical criteria it showed that there was no or minimal changes on air drying and radiological also did show any radiolucency denoting a carious lesion. Hence this group was reassessed at the end of 12 months by laser fluorescence and radiographically. Sample size was 41.

Group II: Laser fluorescence values were 15-25. Clinically there was no opacity, or opacity (white) hardly visible on the wet surface, but distinctly visible after air-drying (5 second). Radiographically there was no lesion or there was minimal involvement of enamel. Remineralizing paste containing casein phospho peptide amorphous calcium phosphate with fluoride (CPP-ACP- F) was applied for 4 minutes and repeated at an interval of one week for one month. The evaluation by laser fluorescence was done at the interval of 3 months, 6 months, 9 months and 12 months. Sample size was 87

Group III: Laser fluorescence values > 25. Clinically there was no opacity or opacity (white) hardly visible on the wet surface, but distinctly visible after air-drying (5 second) or opacity distinctly visible without air-drying. Radiographically a lesion may not be detected or seen involving enamel only or outer half of dentin. Sample size was 72. The selected teeth were isolated with rubber dam. Exploratory cavity preparation was done with air abrasion unit. The settings were 60 psi-80 psi, with 27-micron particles. The recommended movements of the tip were short controlled bursts kept at 1mm from the tooth surface at an angle of 45-60 degree, designed to trace out and identify the pits and fissures and incipient caries while following path of least resistance. Restoration was done with flowable composite or posterior composite as per depth of the cavity.

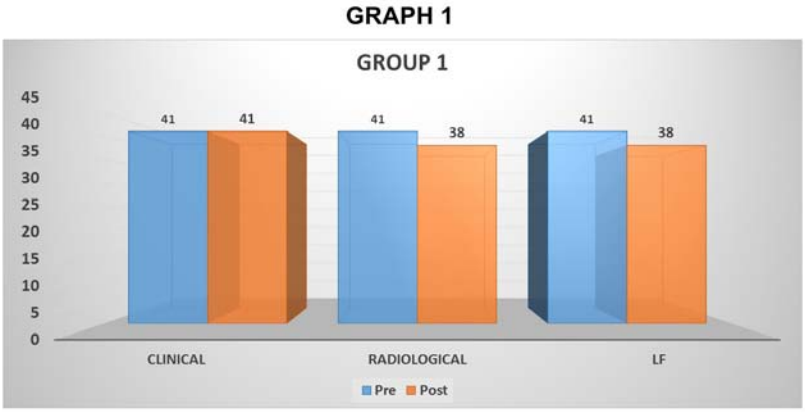
IV. Result

The Excel and SPSS 17 software packages were used for data entry and analysis. The statistical analysis was done by Chi square test of significance for proportion analysis.

Table : Comparison of Diagnostic Ability of all Methods

	Clinical	Radiographic	Lf	Sample Size	Pearson Chi-square value	p-value	Overall actual caries present
Caries Detected	83	50	150	200	143.6	<0.001	76.5%
Caries Not Detected	70	103	3				

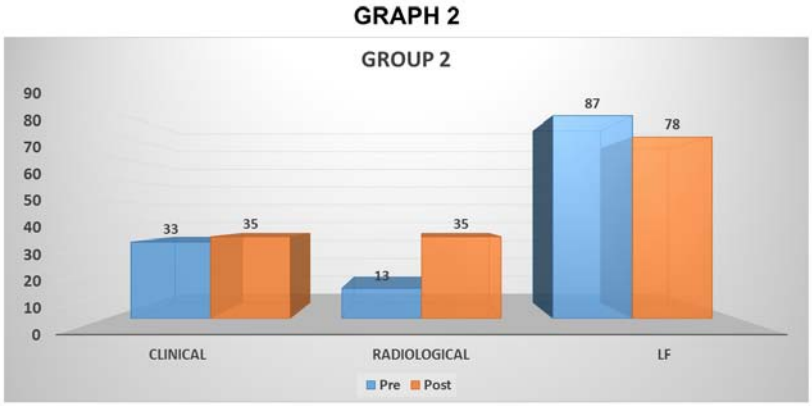
Of 200 teeth which were scanned, it was found that 76.5 % cases had caries i.e 153 patients, but it was correctly detected in 150 patients by laser fluorescence whereas visual method detected caries in 83 patients and radiographic method detected caries in 50 patients.



Graph 1 : Comparison of the Diagnostic Methods for Group 1

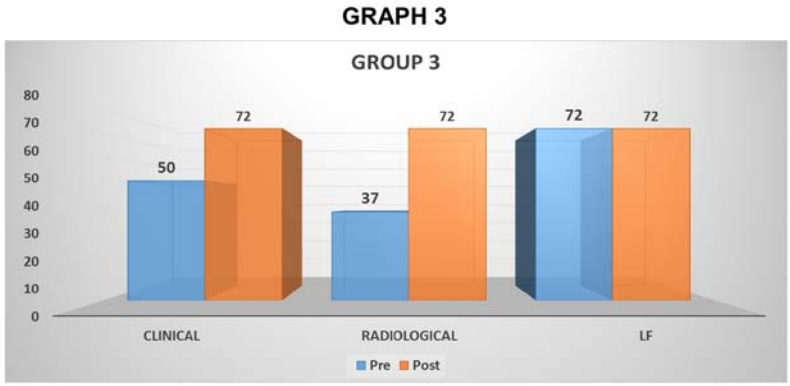
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There is no caries detected by all methods initially. But at 3 months, caries was detected in 3 patients by laser fluorescence which was not detected by visual method and detected by radiographic method at 12 months.



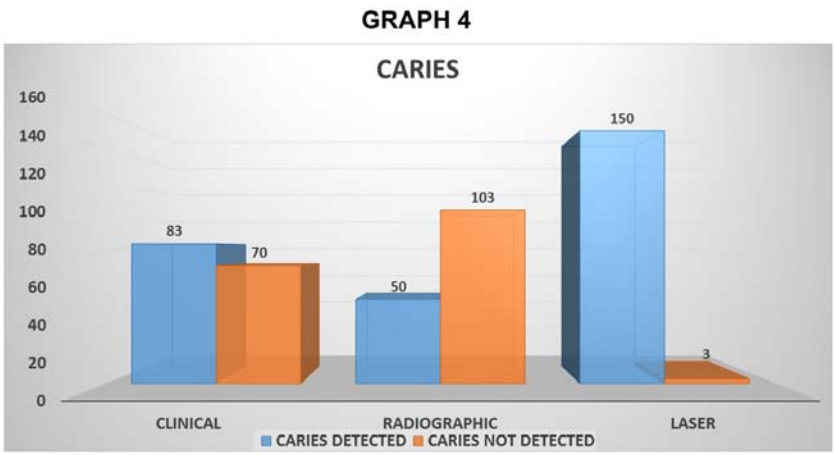
Graph 2 : Comparison of the Diagnostic Methods for Group 2

In 54 patients the caries visually was not detected when it was detected by LF. In 74 patient caries was not detected radiographically when it was detected by LF



Graph 3 : Comparison of the Diagnostic Methods for Group 3

In 22 cases visual method did not detect caries when it is present. which is confirmed when cavity preparation is done. In 35 cases radiological method does not detect caries but it confirmed when cavity preparation is done by air abrasion.



Graph 4 : Comparison of Caries Detection in all Groups by all Diagnostic Methods

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Of 200 teeth which were scanned, it was found that 76.5 % cases had caries i.e 153 patients, but it was correctly detected in 150 patients by laser fluorescence whereas visual method detected caries in 83 patients and radiographic method detected caries in in 50 patients.

V. Discussion

Dental caries is one of the most prevalent oral diseases of the world. It is the result of localized chemical dissolution of a tooth surface resulting from metabolic events in a biofilm.[1-3] There is no global consensus or construct on the criteria for detection of carious lesions.[13]

The initiation of carious lesion begins with subsurface dissolution; this is due to the fact that 50-100microns of surface layer is resistant to decay as a result of the increased concentration of fluoride ions. Subsurface dissolution can be remineralized.[1-3] Fluoride is a gold standard in caries prevention. Newer remineralization paste like CPP ACP have been used alone or in combination with fluoride with varying degree of success. The changes have been evaluated by diagnodent and scanning electron microscopy. Due to inclusion of NaF in CPP ACP F, it showed better remineralizing potential than CPP ACP alone.[14-16] Thus in our study we used CPP ACP F as a remineralizing paste. The decrease in laser fluorescence values as compared to baseline in Group II showed that the 71teeth were in state of remineralization. (Graph 2) In Group I we haven't used any preventive protocol hence the laser fluorescence value remains constant in 38 patients (Graph 1)

To harness the phase of remineralization it is important that caries be detected before cavitation. There are various diagnostic aids available for the clinician with varying degree of sensitivity and specificity. Lussi et al in an invitro study evaluated the new laser fluorescence device – Diagnodent pen with older version of diagnodent. The clinical finding were correlated with the histogical reading. The authors found that diagnodent was more sensitive a tool than specific. Based on past invivo and invitro studies[5-7, 17-18] laser fluorescence method of caries detection was considered in the study. It served as a caries detecting tool and also monitoring the progression of caries and remineralization. (Table, Graph 1-4) There are three essential tools that the microdentist relies when performing minimal invasive method in restorative dentistry. First is good diagnostic aid for early caries detection. Hence we have used laser fluorescence method. The next is caries-detection dye, which is used to follow the progress of the caries-removal process. Third, is an air-abrasion unit that is reasonably adjustable and responsive.[11,12] Magnification and visualization is enhanced by use of loupes in this study.

Minimal clinical cavity access is defined as the least amount of enamel removal to enable adequate access for visualization and removal of the infected dentine leaving behind the affected dentin which has then the potential to form secondary dentin. Caries detecting dye serves as a diagnostic aid for occlusal caries as well as for residual caries and works by bonding to denatured collagen[9-10]. In this study caries detecting dye is used in diagnostic, intraoperative as well as postoperative phase to detect any residual caries thus making the cavity preparation very conservative.

For over a century cavity preparation is done by the conventional method of using bur and air rotor, which tends to remove tooth structure indiscriminately by lateral application of force. Unlike rotary cutting instruments; the principle action of air-abrasion has been demonstrated as end cutting. Hence making cavity preparation in incipient lesions extremely ultraconservative. In our study, the subsurface carious lesions which were detected by laser fluorescence but not detected by radiographic and visual methods and they were confirmed by ultra conservative exploratory cavity preparation by air abrasion.[11-13, 19-20] (Table, Graph 3,4)

Thus the laser caries detection can detect hidden caries or incipient lesion which may not be detected by visual and radiographic methods. In our study out of 200 teeth which were evaluated, it was found that 76.5 % cases had caries i.e 153 patients, but it was correctly detected in 150 patients by laser fluorescence whereas visual method detected caries correctly in 83 patients and radiographic method detected caries correctly in 50 patients.

VI. Conclusion

1. Laser fluoresce method of caries detection is a valuable adjunct in caries detection along with traditional method of caries diagnosis.
2. Air abrasion can be used as an exploratory tool to confirm hidden caries the preparation is ultra-conservative.

References Références Referencias

1. Fejerskov O, Nyvad B, Kidd E. Dental caries: The disease and its clinical management. Edn 2015. Wiley Blackwell.
2. Featherstone JDB. Dental caries: a dynamic disease process. Australian Dental Journal 2008; 53: 286–291.
3. J Hicks, FG Godoy, C Flaitz. Biological factors in dental caries enamel structure and the caries process in the dynamic process of demineralization and remineralization (part 2) J Clin Pediatr Dent. 2004; 28(2): 119-124.

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4. Moriyama CM, Rodrigues JA, Lussi A & Diniz MB. Effectiveness of Fluorescence-Based Methods to Detect in situ Demineralization and Remineralization on Smooth Surfaces. Caries Res 2014; 48:507–5.
5. Lussi A, Hellwig E. Performance of a new laser fluorescence device for the detection of occlusal caries in vitro: J Dent. 2006 Aug; 34(7): 467-71.
6. Patricias M de Freitas Lasers in Dentistry. Guide for Clinical Practice. 2015.
7. Convissar RA Principle and Practice of Laser Dentistry. 2011.
8. Fung L, Smales R, Ngo H and Mount G. Diagnostic comparison of three groups of examiners using visual and laser fluorescence methods to detect occlusal caries *in vitro.* Australian Dental Journal. 2004; 499 (2): 67–71.
9. Mcomb D.Caries – Detector Dyes- How Accurate and Useful are they? J Can Dent Assoc 2000; 66: 195-8.
10. Neves et al. Current Concepts and Techniques for Caries Excavation and Adhesion to Residual Dentin. J Adhes Dent. 2011; 13; 7-22.
11. Rainey J T. Air abrasion: an emerging standard of care in conservative operative dentistry. Dent Clin N Am. 2002; 46: 185–209.
12. Hegde VS, Khavatkar R A. A new dimension to conservative dentistry: Air abrasion: J Conserv Dent. 2010; 13(1): 4–8.
13. Mount G J. Minimal intervention dentistry: cavity classification & preparation. International Dentistry Sa. 2010; 12(3): 54-61.
14. Peters M C Strategies for Noninvasive Demineralized Tissue Repair. Dent Clin N Am.2010; 54: 507–525.
15. Jayarajan J, Janardhanam P, Jayakumar P, Deepika. Efficacy of CPP-ACP and CPP-ACPF on enamel remineralization – An *in vitro* study using scanning electron microscope and DIAGNO dent. Indian Journal of Dental Research, 2011; 22(1): 77-82.
16. Yengopal V, Mickenautsch S. Caries preventive effect of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP): a meta-analysis. Acta Odontol Scand 2009; 67: 321-32.
17. Bamzahim M, Shi XQ, Angmar & Mansson B. Occlusal caries detection and quantification by DIAGNOdent and Electronic Caries Monitor: in vitro comparison. Acta Odonto Scand. 2002 Dec; 60(6): 360-4.
18. Kuhnisch J, Ziehe A, Brandstadt A, Heinrich & Weitzien R. An in vitro study of the reliability of DIAGNOdent measurements. J Oral Rehabil. 2004; 31(9): 895-9.
19. Watson. Operative Dentistry and the Abuse of Dental Hard Tissues: Confocal Microscopical Imaging of Cutting. Oper Dent. 2008; 33-2: 15-224.
20. Lívia Azeredo Alves et al. Effectiveness of high speed instrument and air abrasion on different dental substrates. Brazilian oral research. 2008; 22(3): 235-4.

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Comparative Evaluation of Upper Airway Dimensions and Oxygen Saturation in Completely Edentulous Patients with and without Dentures

By Brig E Mahesh Gowda, Maj Gen NK Sahoo, Lt col Guruprasada, Wg Cdr Naveen KS & Maj Kamal Verma

CMDC

Abstract- *Background:* Majority of the elderly people complain of difficulty in sleeping. Although the causes for the sleep disturbances may be multifactorial in nature, the sleep disordered breathing (SDB) is one of the primary disorder. The study was undertaken to study the effect of Complete Denture rehabilitation which could have profound impact on rehabilitation protocol on complete edentulous patients.

Aim: The aim of this study is to Cephalometrically evaluate the effect of complete denture rehabilitation on upper airway dimensions and position of hyoid bone and also to examine if complete denture rehabilitation influences oxygen saturation and degree of sleepiness by overcoming upper airway collapsibility.

Keywords: *sleep disordered breathing, obstructive sleep apnea, epworth sleepiness scale.*

GJMR-J Classification: *NLMC Code: WU 515*



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Comparative Evaluation of Upper Airway Dimensions and Oxygen Saturation in Completely Edentulous Patients with and without Dentures

Brig E Mahesh Gowda [α], Maj Gen NK Sahoo [σ], Lt col Guruprasada [ρ], Wg Cdr Naveen KS [ω] & Maj Kamal Verma [¥]

Abstract- Background: Majority of the elderly people complain of difficulty in sleeping. Although the causes for the sleep disturbances may be multifactorial in nature, the sleep disordered breathing (SDB) is one of the primary disorder. The study was undertaken to study the effect of Complete Denture rehabilitation which could have profound impact on rehabilitation protocol on complete edentulous patients.

Aim: The aim of this study is to Cephalometrically evaluate the effect of complete denture rehabilitation on upper airway dimensions and position of hyoid bone and also to examine if complete denture rehabilitation influences oxygen saturation and degree of sleepiness by overcoming upper airway collapsibility.

Material and Method: 30 edentulous patients who complained of snoring during sleep were selected for the study. The baseline lateral cephalogram of all the patients were taken by asking the patient to attain the natural head position.MAS (Minimal Airway Space), PAS (Posterior Airway Space), SAS (Superior Airway Space), MP-H (Perpendicular distance from hyoid bone to mandibular plane) were also recorded. The patients were also subjected to pulse oximetry test to assess the oxygen saturation and ESS (Epworth Sleepiness Scale) to assess the day time sleepiness. All these subjects were rehabilitated using conventional complete denture fabricated using standard prosthodontic protocol and after 6-8 weeks they were subjected to same tests again with dentures in situ.

Results: The results of this study showed no statistically significant difference on MAS (Minimal Airway Space), PAS (Posterior Airway Space), SAS (Superior Airway Space), MP-H (Perpendicular distance from hyoid bone to mandibular plane), ESS (Epworth Sleepiness Scale) and Oxygen saturation.

Conclusion: Wearing the Complete Denture during night does not improve the airway space, oxygen saturation and day time sleepiness significantly when compared with edentulous patients.

Keywords: sleep disordered breathing, obstructive sleep apnea, epworth sleepiness scale.

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I. Introduction

Disturbed sleep is a common source of disgruntlement among elderly people. It is estimated that up to 50% of elderly adults complain of difficulty in sleeping, further aggravating the risks of morbidity in the ageing population [1]. It has been described that 43% of those over the age of 65 have difficulty in the onset and maintenance of sleep, while 25% report daily drowsiness [2]. Many authors in 1970 delineated the causes of upper airway sleep disorders and in 1980 they described the oral appliances as pivotal treatment modality. Drowsiness and symptoms of sleep disturbance have been associated with declining cognitive capacity, depression, falls and mortalities. Sleep disturbances are multifactorial in nature and could be impacted by alterations of the circadian rhythm, neuropsychological impairment, use of medications and some medical conditions. In most of the cases disturbed sleep is constantly associated with sleep-disordered breathing (SDB) which can range from the cessation of respiration lasting for at least 10 seconds (apneas) and or partial or reduced respiration (hypopne as) during sleep [3].

One of the exacerbating factors that were recommended to allay SDB is edentulism. Complete tooth loss sequels in anatomical changes that may sway upper airway dimensions and pass out by influencing the postural rest position of the mandible, muscle tone and tongue posture during sleep. A decrease in retropharyngeal space and or the hypotonicity of the pharyngeal musculaturein edentulous people have been recommended to increase the collapsibility of airways [4]. Using supine lateral cephalometric studies in complete denture wearers, Bucca et al, substantiated decreased in retropharyngeal space and anteroposterior oropharyngeal distance in the absence of dentures. They found that there may be perpetuation of OSA (Obstructive Sleep Apnea) and lower arterial hemoglobin oxygen saturation in patients following the removal of dentures. Thus, they collectively assign edentulism as a reason for exacerbation of OSA [5]

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There are very few studies to analyze the role of complete denture rehabilitation on the upper air way dimension and its influence on oxygen saturation to analyze and assess whether edentulism favors the occurrence or alleviating of OSA which would have intense effect on rehabilitation protocol in complete edentulous patients with SDB.

II. Materials and Method

The samples were taken from the completely edentulous patients visiting our institution seeking complete dentures. All patients were informed of the modalities and purpose of the study before obtaining consent to participate. The inclusion criteria for the study were first time complete edentulous patients with well-formed residual ridges in class I relation, presence of snoring or known case of obstructive sleep apnea, age group of between 50-70 years, clinically stable with no systemic involvement especially respiratory disease and infections. The exclusion criteria included any metabolic or craniofacial syndrome, BMI>3, nasal obstruction, pharyngeal tumours, history of tongue, palate or upper airway surgery, skeletal class III relationship, grossly resorbed residual alveolar ridges and musculo skeletal disorders.

All complete dentures were made and assessed by the same clinician at all stages and were fabricated by the same technician in accordance with the standard prosthodontic treatment and laboratory protocol.

The sample consisted of 30 edentulous patients who complained of snoring. Out of which 14 were males and 16 were females with mean age of 63.15 Yrs. Baseline lateral cephalograms were recorded at the end expiration, palate not involved in deglutition and jaws in physiologic rest position by asking the patients to attain natural head position (NHP) Fig 1 and Fig 2. To attain NHP, patients were made to stand without head fixation in cephalost at, after moving head forward and backward 3 times, swallowing and lips at rest. Exposure time and other parameters were kept constant and radiographs were made with a film object distance of 180 cm and film to median plane distance of 10 cm which was constant for both pre and post cephalometric radiographs.

All the patients were also subjected to overnight pulse oximetry test to assess oxygen saturation and ESS (Epworth Sleepiness Scale) to assess day time sleepiness Fig 3 and Fig 4.

All the 30 study subjects were rehabilitated with conventional polymethyl methacrylate complete dentures (CD) using standard prosthodontic fabrication protocols. After 6-8 weeks, following the use of CD and having observed the compliance of use, they were subjected to lateral cephalograms with CD in situ as per standardised protocol followed during pre-treatment cephalometry using the same cephalometric machine. All the rehabilitated study subjects were also subjected to overnight pulse oximetry with wearing CD to assess oxygen saturation and ESS scores were evaluated. The data recordings of sleep duration lasting for more than 4 hrs were considered as acceptable for the purpose of our study.

Based on the outer border of the radiograph, vertical and horizontal lines were traced perpendicular to each other. These two lines acted as references to calculate the angles between the head and neck on the cephalograms and the measurements for Posterior Airway Space (PAS), Minimal Airway Space (MAS), Superior Airway Space (SAS) and Perpendicular distance from hyoid bone to mandibular plane (M-PH). (Fig 5 and Table 1)

III. Results

The mean SAS without dentures was 8.96mm (±1.84) and with denture wear was 8.90 mm(±1.79) with difference in mean of 0.06 (±0.52). The comparison of means was done using paired T test, wherein P value was of 0.48 indicating no statistically significant difference in SAS, between with and without denture wearers (Table 2). The mean MAS without dentures was 7.00 mm (±1.59) and with denture wear was 7.30 mm (±1.46) with difference in mean of 0.30 (±0.53). The P value was of 0.005 indicates statistically significant difference in MAS, between with and without denture wearers (Table 3).The mean PAS without dentures was 11.76 mm (±1.83) and with denture wear was 11.93 mm (±2.08) with difference in mean of 0.16 (± 0.53). The P value of 0.096 indicates no statistically significant difference in PAS, between with and without denture wearers (Table 4).The mean H- distance without denture was 11.73 mm (± 1.7) and with denture wear was 11.7 mm (±2.08) with difference in mean was 0.03(± 0.85). The P value of 0.83 indicates no statistically significant difference in H- Distance to the mandibular plane, between with and without denture wearers (Table 5).The ESS score without denture was 8.83 (± 1.64) and with denture wear was8.83(± 1.81) with difference in mean of 0.00 (± 0.74). The P value of 1.00 indicating no statistically significant difference in ESS between with and without denture wearers (Table 6).The Oxygen saturation percentage score without dentures was 93.30 (±1.74) and with denture wear was 93.20 (±1.58) with difference in mean of 0.10 (± 0.88). The P value of 0.54 indicates no statistically significant difference in Oxygen Saturation percentage between with and without denture wearers (Table 7).

IV. Discussion

From a methodical viewpoint, sleep is defined on the basis of both the behavior of the person while asleep and related physiological changes that occur to

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the alert brain's electrical rhythms in sleep [6]. The behavioral criteria consist of a complete lack of mobility or slight mobility, sluggish eye movements, peculiar sleeping posture, decreased response to external stimulation, increased reaction time and arousal threshold, an impaired cognitive function and a reversible unconscious state. The physiological parameters are based on the findings of EEG, electro-oculography (EOG) and electromyography (EMG).

Sleep Apnea, based on the denotation, should have at least five apneas or hypopne as per hour of sleep accompanied by Excessive Daytime Sleepiness (EDS). The manifestations of OSAS can be divided into two groups; those occurring during sleep and those occurring during awake. Nocturnal symptoms includes choking during sleep. habitual loud snoring and halting of breathing and abnormal motor activities during sleep, severe sleep disruption, heartburn as a result of gastro esophageal reflux, nocturnal enuresis which is seen mostly in children and profuse sweating at night. The daytime symptoms includes sleep attacks lasting 0.5 to 2 h and occurring mostly when the patient is relaxing i.e. sitting down or watching television.

Increased pharyngeal collapsibility is a frequent cause of obstructive sleep apnea (OSA) [5] which results from the combination of anatomical abnormalities of the upper airway with changes in neural activation mechanisms. Innumerable structural changes in facial morphology have been associated with OSA pathogenesis like retrognathic mandibles, posteriorly placed pharyngeal walls, large tongues and soft palate. Missing teeth produces prominent anatomical changes that may influence upper airway size and function, such as decreased vertical dimension of occlusion, reduction of the lower third facial height and mandible rotation correlating its role in the pathogenisis of OSA [7].

Bucca et al [5][8] confirmed that removal of dentures significantly decreases the retropharyngeal space and sleeping without dentures is associated with significant decrease in Apnea – Hypopnea Index (AHI) and decrease in mean arterial hemoglobin saturation. The authors stressed the fact of wearing complete dentures during night will negate the effects of OSA. Their results were in contrast to our study results, wherein there was no significant difference in cephalometric findings in Superior Airway Space (SAS) (Table 2) and Posterior Airway Space (PAS) (Table 4) whereas there was a significant difference in Minimal Airway Space (MAS) (Table 3) between patients with and without complete dentures. This could be because our study sample was of non-confirmed cases of OSA with only snoring as an inclusion criteria.

Ergovini et al [9] described the effect of removal of dentures and modifications of prosthesis on pharyngeal collapse and showed statistically significant reduction in PAS. They concluded that wearing denture induces modifications in the position of tongue, the jaw and the pharyngeal air way space which was not in accordance with our study. This may be because of the selection of sample size of 27 subjects with reduced vertical dimension compared to our study sample of ideal jaw relations.

Gupta et al [4] evaluated completely edentulous patients cephalometrically with increasing vertical jaw relation using an acrylic jig of 2 – 3 mm and revealed that there was a statistically significant correlation between PAS and retropharyngeal space between edentulous and patients with complete dentures and they concluded that increasing vertical dimension of occlusion within acceptable limits is beneficial to patients with OSA.

Navone PS [10] and Ariska et al [11] had evaluated the risk for OSA in completely edentulous patients with and without complete dentures respectively and concluded that the episode of AHI increases along with reduction in oxygen saturation and retropharyngeal space without dentures indicating worsening of the OSA among subjects. But although there was a definite improvement of AHI among all denture wearers, the oxygen saturation level was recorded at 95.4 ± 2.4 without dentures and 95.6 ± 1.6 with dentures indicating no statistically significant difference. This result is in concurrence to our study wherein the oxygen saturation level was recorded at 93.30 ± 1.74 without dentures and 93.20 ± 1.58 reveling no statistically significant difference.

In a study by Tsuda et al [12], they demonstrated that edentulism favors upper airway obstruction during sleep. In fact, both AHI and mean SaO2 were significantly worse in the patients who slept without dentures than in the patients slept with dentures. Almeida analysed completely edentulous patients with OSA and contrary to other study findings concluded that dentures substantially increases AHI especially in supine position. They had the mean oxygen saturation percentage value of 94.2 ± 1.57, almost similar to our study findings 93.25 ± 1.31(Table 7), which is almost nearer to the proved normal basal oxygen saturation of 95.5 %. The findings may be attributed due to the recordings taken only during sleep and supine position and not compared with patients when awake. This can be attributed due to interruption of elevator muscles due to the denture wear during sleep leading to the more collapsibility of the airway thus leading to reduced oxygen saturation. The day time sleepiness measured using Epworth Sleepiness Scale score was 10.2 ± 4.4 compared to our results of 8.83 ± 1.72,(Table 6), indicating there was no EDS compared between patients with or without complete dentures. The variation between the results may be attributed to the selection of subjects with Non confirmed OSA subjects selected by us.

Our study results showed no correlation between oxygen saturation and hyoid bone distance to

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mandibular plane. The antero posterior measurement of retro pharyngeal space on cephalograms at three areas of SAS, PAS and MAS, revealed only MAS significant when compared between completely edentulous patients wearing with and without complete denture.

V. Conclusion

Within the limitation of the study it is concluded that: Denture wearing at night in healthy completely edentulous patients will not significantly improve quality and quantity of sleep as determined by oxygen saturation levels and ESS scoring. There is no significant increase in airway space and oxygen saturation levels are not affected with the use of complete dentures during sleep.It is recommended that further studies involving large sample size with OSAS may be required to be studied to conclusively prove the hypothesis of wearing denture at night improves the air way space and reduces the symptoms of OSAS.Further studies with confirmed OSA patients and varying the prosthesis vertical dimension of occlusion and MRI study with 3-D measurements may give definite insight on understanding their effect on sleep parameters and on airway changes.

References Références Referencias

1. Foley DJ, Monjan A, Simonsick EM, Wallace RB, Blazer DG. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. Sleep 1999; 22: 366–72.
2. VazFragoso CA, Gill TM. Sleep complaints in community- living older persons: a multifactorial geriatric syndrome. Journal of the American Geriatrics Society 2007 Nov; 5(11): 1853–66.
3. Ivanhoe JR, Cibirka RM, Lefebvre CA, Parr GR. Dental considerations in upper airway sleep disorders: a review of the literature. J Prosthet Dent 1999 Dec; 82(6): 685–98.
4. Gupta P, Thombare R, Pakhan AJ, Singhal S. Cephalometric evaluation of the effect of complete dentures on retropharyngeal space and its effect on spirometric values in altered vertical dimension. ISRN Dent 2011; 51: 69.
5. Bucca C, Carossa S, Pivetti S, Gai V, Rolla G, Preti G. Edentulism and worsening of obstructive sleep apnea. Lancet 1999 Jan; 353(9143): 121–2.
6. Chokroverty S. An overview of normal sleep. Sleep disorders medicine: Basic science, technical-considerations and clinical aspects, 3rd ed. Philadelphia: Elsevier/Butterworth; 2009.
7. Morelli DL, Jackson N, Gislason T, Arnardottir ES et al. The Effect Of Edentulism On Ahi, Odi, And Tongue Morphology In Iceland Sleep Apnea Cohort (ISAC). Am J RespirCrit Care Med 183; 2011: 3676.
8. Arisaka H, Sakuraba S, Tamaki K, Watanabe T, Takeda J, Yoshida K. Effect of wearing complete dentures during sleep on the apnea-hypopnea index. Int J Prosthodont2009 Mar - Apr; 22(2):173-7.
9. Bucca C, Cicolin A, Brussino L et al. Tooth loss and obstructive sleep apnea. Respir Res. 2006 Jan 17; 7:8.
10. Carossa S, Bucca C, De Lillo A, Corsalini M, Rizzatti A, Lombardo S, Pera P. Correlation between edentulism, sleep disorders and arterial hypertension. Preliminary research. Minerva Stomatol. 2000 Sep; 49(9): 399-404.
11. Gupta P, Thombare R, Singhal S, Pakhan AJ. Obstructive sleep apnea and edentulism-role of complete dentures/oral appliance from prosthodontic respective: a review. Indian J Sleep Med 2010; 5: 116–119.
12. Tsuda H, Almeida FR, Walton JN, Lowe AA. Questionnaire-based study on sleep-disordered breathing among edentulous subjects in a university oral health center. Int J Prosthodont. 2010 Nov-Dec; 23(6): 503-6.

Tables

Table 1 : Definitions of various cephalometric measurements

S No	Cephalometric variables	Definition
1)	Superior airway space (SAS)	A horizontal distance from the tip of the soft palate to pharyngeal wall.
2)	Posterior airway space (PAS)	Horizontal distance from the posterior margin of the tongue to pharyngeal wall measured on the B- Go line.
3)	Minimum airway space (MAS)	Minimum horizontal distance between the anterior and posterior wall of pharynx in the oropharyngeal region or horizontal distance between the anterior and posterior wall at the narrowest part of oropharynx
4)	Hyoid distance (H- MP)	A perpendicular distance between the superior most point on the body of hyoid bone and the mandibular plane

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Table 2 : Effect of wearing complete denture on SAS

Variable	Pre treatment		Post treatment		Mean of Diff	P value
	Mean	SD	Mean	SD		
SAS	8.96	1.84	8.90	1.79	0.066	0.489

Table 3 : Effect of wearing complete denture on MAS

Variable	Pre treatment		Post treatment		Mean of Diff	P value
	Mean	SD	Mean	SD		
MAS	7.00	1.59	7.30	1.46	0.30	0.005

Table 4 : Effect of wearing complete denture on PAS

Variable	Pre treatment		Post treatment		Mean of Diff	P value
	Mean	SD	Mean	SD		
PAS	11.76	1.83	11.93	2.08	0.16	0.096

Table 5 : Effect of wearing complete denture on H- Distance

Variable	Pre treatment		Post treatment		Mean of Diff	P value
	Mean	SD	Mean	SD		
H - Distance	11.73	1.70	11.70	2.08	0.03	0.831

Table 6 : Effect of wearing complete denture on ESS

Variable	Pre treatment		Post treatment		Mean of Diff	P value
	Mean	SD	Mean	SD		
ESS	8.83	1.64	8.83	1.81	0.00	1.000

Table 7 : Effect of wearing complete denture on Oxygen Saturation

Variable	Pre treatment		Post treatment		Mean of Diff	P value
	Mean	SD	Mean	SD		
Oxy Sat	93.30	1.74	93.20	1.58	0.10	0.541

Figures



Figure 1 : Pre-insertion Cephalogram



Figure 2 : Post-insertion Cephalogram

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Figure 3 : Sleep Study Being Carried out



Figure 4 : Electrodes Attached while doing Sleep Study

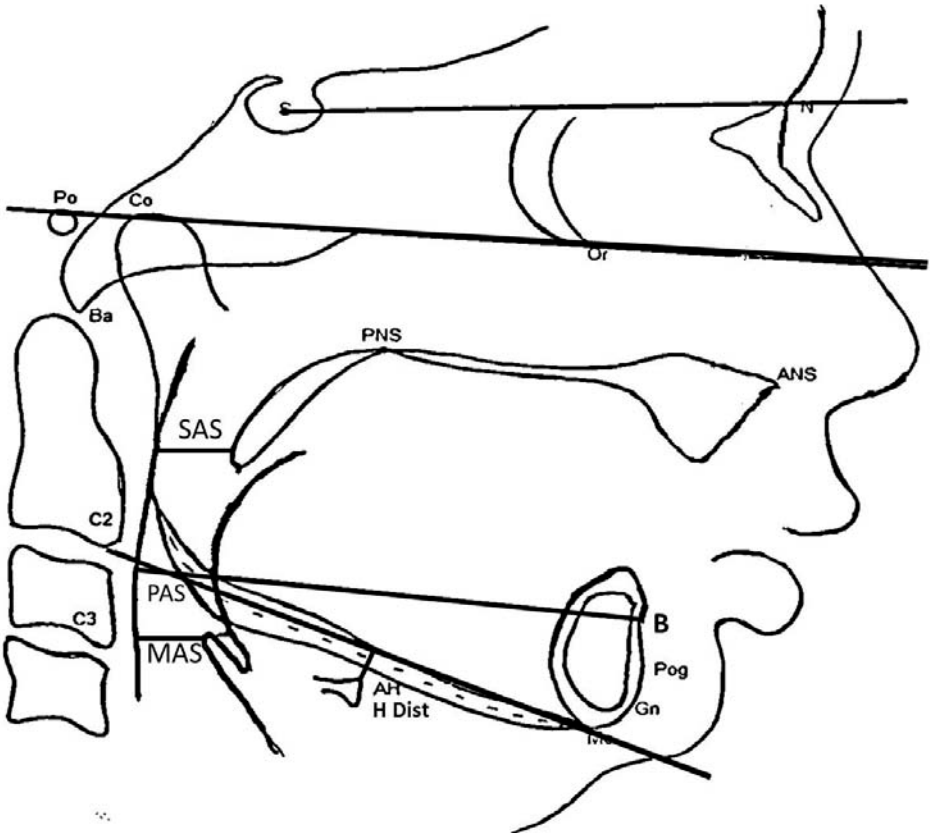


Figure 5 : Cephalometric Landmarks and Cephalometric Measurements

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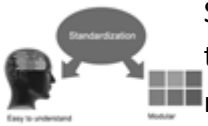


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References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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