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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

By Shaik Begum Khalida, Manjunath M & Siddhartha Biswas

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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

Shaik Begum Khalida [α], Manjunath M [σ] & Siddhartha Biswas [ρ]

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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.

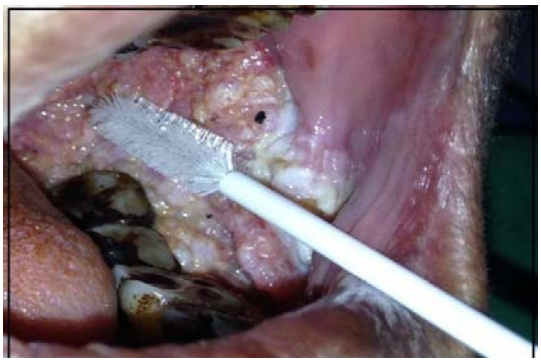

Fig. 1 : Smear from carcinoma of buccal mucosa

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]

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.

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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

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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.

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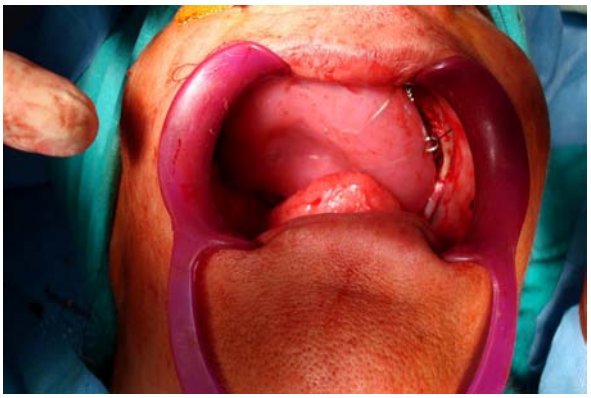

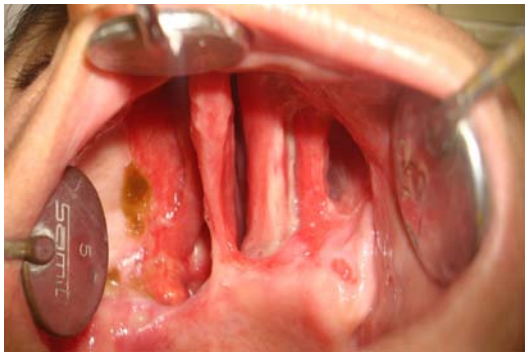

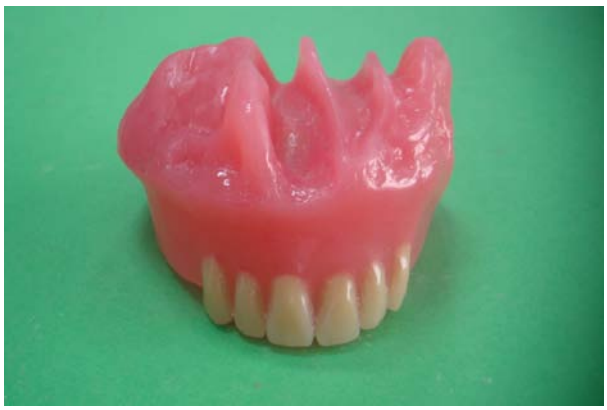

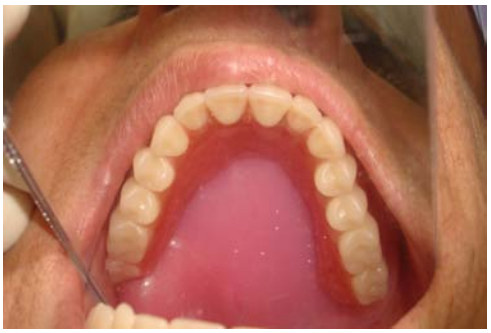

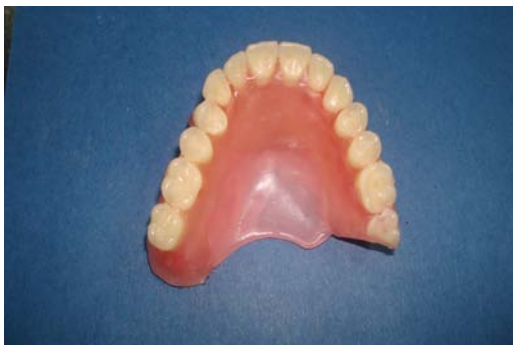

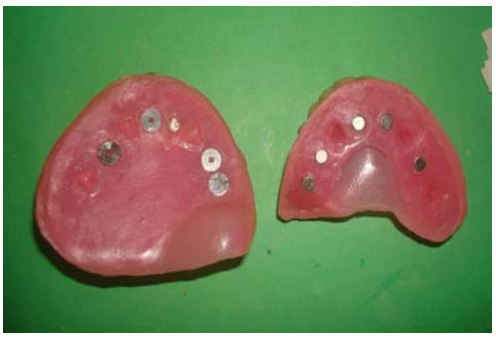

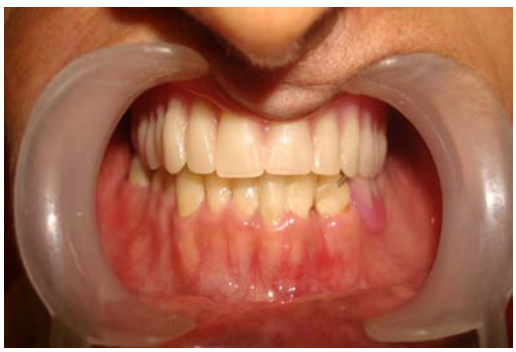

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Chronic Inflammation Induced Immunosuppression in Tumor Microenvironment of Oral Cancer

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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.*

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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

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,

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.

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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.*

GJMR-J Classification: *NLMC Code: WU 150*

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

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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)

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.

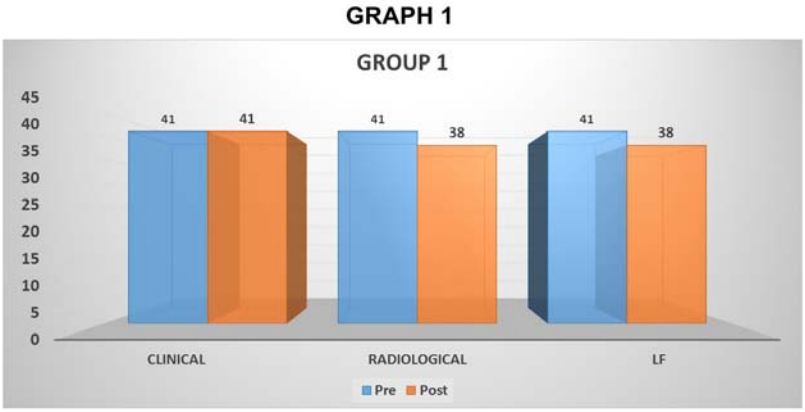
IV. Result

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

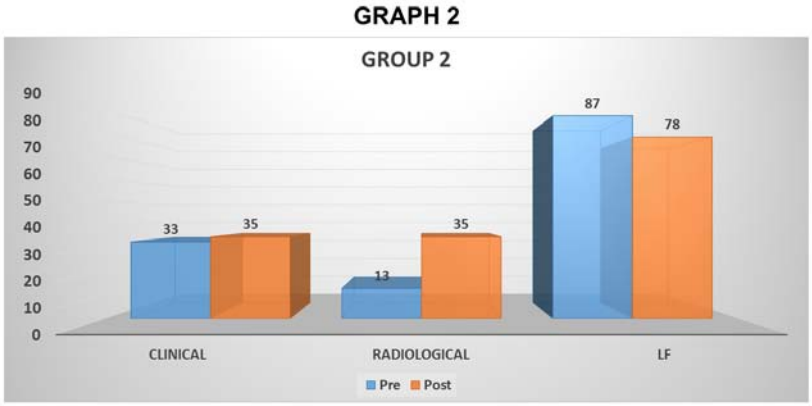
	Clinical	Radiographic	Lf	Sample Size	Pearson Chi-square value	p-value	Overall actual caries present
Caries Detected	83	50	150	200	143.6	<0.001	76.5%
Caries Not Detected	70	103	3				

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.



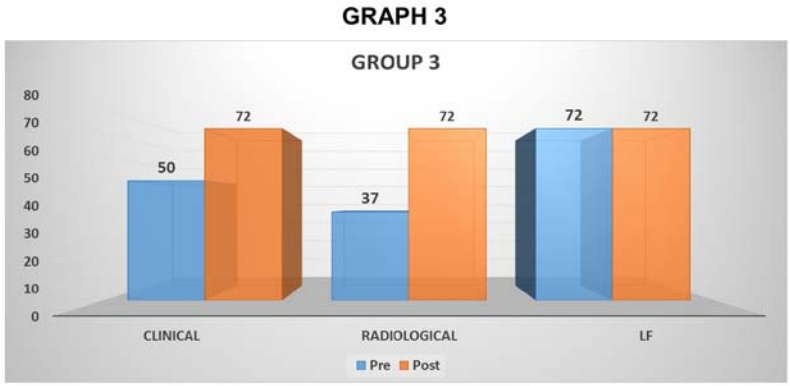
Graph 1 : Comparison of the Diagnostic Methods for Group 1

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.



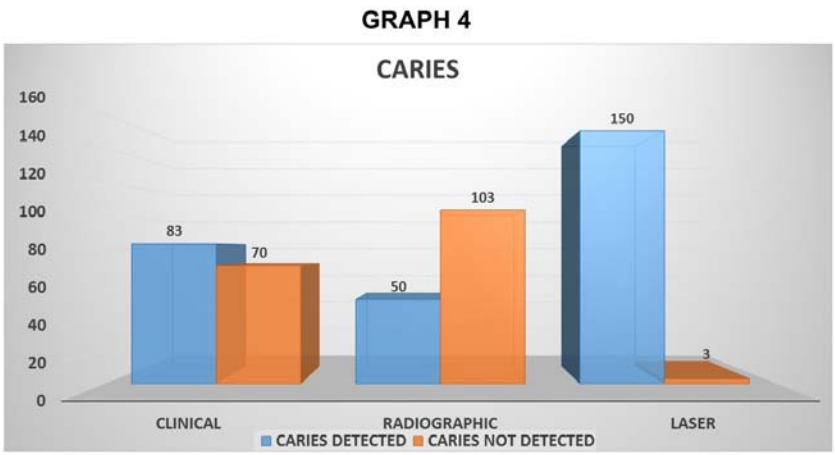
Graph 2 : Comparison of the Diagnostic Methods for Group 2

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

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.

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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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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]

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

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

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.

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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

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

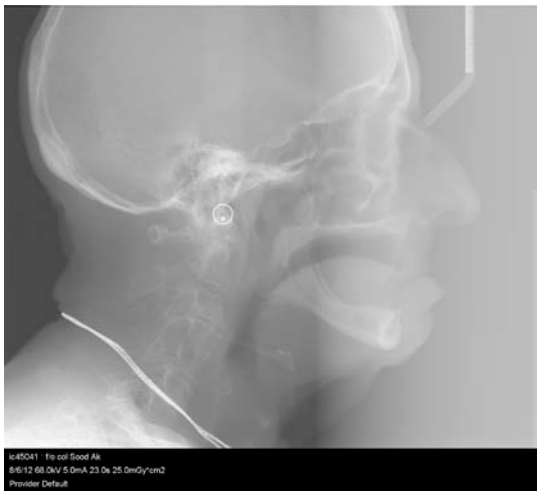

Figure 1 : Pre-insertion Cephalogram

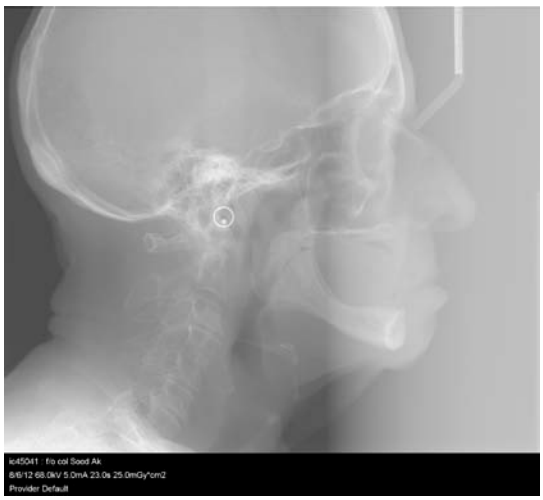

Figure 2 : Post-insertion Cephalogram

Figure 3 : Sleep Study Being Carried out

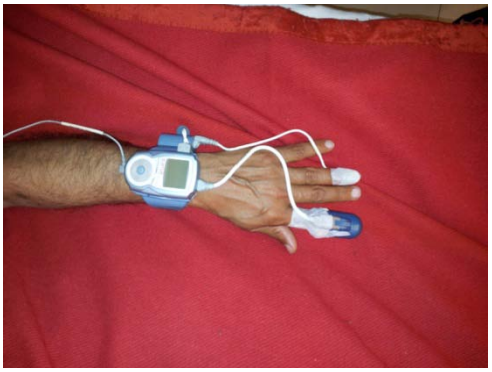

Figure 4 : Electrodes Attached while doing Sleep Study

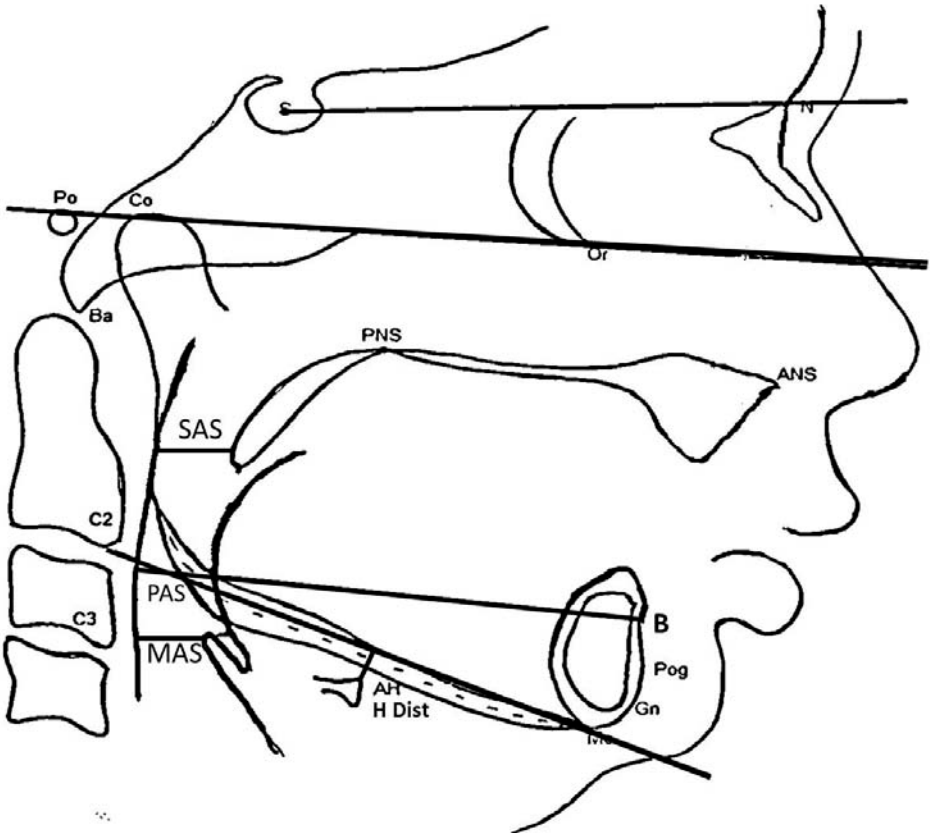

Figure 5 : Cephalometric Landmarks and Cephalometric Measurements

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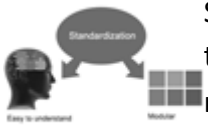

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The Area or field of specialization may or may not be of any category as mentioned in 'Scope of Journal' menu of the GlobalJournals.org website. There are 37 Research Journal categorized with Six parental Journals GJCST, GJMR, GJRE, GJMBR, GJSFR, GJHSS. For Authors should prefer the mentioned categories. There are three widely used systems UDC, DDC and LCC. The details are available as 'Knowledge Abstract' at Home page. The major advantage of this coding is that, the research work will be exposed to and shared with all over the world as we are being abstracted and indexed worldwide.

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- Author Name in Font Size of 11 with one column as of Title.
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- Two Column with Equal Column with of 3.38 and Gaping of .2
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- Paragraph before Spacing of 1 pt and After of 0 pt.
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You can use your own standard format also.
Author Guidelines:

1. General,

2. Ethical Guidelines,

3. Submission of Manuscripts,

4. Manuscript's Category,

5. Structure and Format of Manuscript,

6. After Acceptance.

1. GENERAL

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Complete support for both authors and co-author is provided.

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Original research paper: Such papers are reports of high-level significant original research work.

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Research articles: These are handled with small investigation and applications

Research letters: The letters are small and concise comments on previously published matters.

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The recommended size of original research paper is less than seven thousand words, review papers fewer than seven thousands words also.Preparation of research paper or how to write research paper, are major hurdle, while writing manuscript. The research articles and research letters should be fewer than three thousand words, the structure original research paper; sometime review paper should be as follows:

Papers: These are reports of significant research (typically less than 7000 words equivalent, including tables, figures, references), and comprise:

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(c) Up to ten keywords, that precisely identifies the paper's subject, purpose, and focus.

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(e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition; sources of information must be given and numerical methods must be specified by reference, unless non-standard.

(f) Results should be presented concisely, by well-designed tables and/or figures; the same data may not be used in both; suitable statistical data should be given. All data must be obtained with attention to numerical detail in the planning stage. As reproduced design has been recognized to be important to experiments for a considerable time, the Editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned un-refereed;

(g) Discussion should cover the implications and consequences, not just recapitulating the results; conclusions should be summarizing.

(h) Brief Acknowledgements.

(i) References in the proper form.

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A major linchpin in research work for the writing research paper is the keyword search, which one will employ to find both library and Internet resources.

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Search engines for most searches, use Boolean searching, which is somewhat different from Internet searches. The Boolean search uses "operators," words (and, or, not, and near) that enable you to expand or narrow your affords. Tips for research paper while preparing research paper are very helpful guideline of research paper.

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References

References follow the Harvard scheme of referencing. References in the text should cite the authors' names followed by the time of their publication, unless there are three or more authors when simply the first author's name is quoted followed by et al. unpublished work has to only be cited where necessary, and only in the text. Copies of references in press in other journals have to be supplied with submitted typescripts. It is necessary that all citations and references be carefully checked before submission, as mistakes or omissions will cause delays.

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TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

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7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

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22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

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34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

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To make a paper clear

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- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
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In every sections of your document

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· Present your points in sound order

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· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

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The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

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- Reason of the study - theory, overall issue, purpose
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- To the point depiction of the research
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- Significant conclusions or questions that track from the research(es)

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- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
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Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.

- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

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	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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