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Comparison of Epidermal Gingival Crevicular Fluid

Highlights

Zygomatic-Alveolar Crest Congenital Lobular Capillary

Discovering Thoughts, Inventing Future

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"Requirement of 1st Oral Analgesic Dose after Tonsillectomy by Various Method"

By Shamendra Kumar Meena, Rajkumar Jain, Vijay Kumar Meena, Ramraj Meena & Muniram Meena

R.U.H.S., India

Introduction & History- Pain is a highly unpleasant sensory and emotional experience and postoperative pain control in children is a big challenge for their inability to express and react. In the past two decades, there has been a considerable progress in the understanding of children's perception of pain and responses to pain and various pharmacological agents and analgesic delivery to avoid under treatment of pain in children. A parallel noteworthy advancement has occurred in the knowledge of anatomy, physiology and pharmacology of regional anesthetic techniques. Some of these techniques are now an integral part of perioperative and procedure-related pain management in all ages, in part because of a greater concern about postoperative pain management in patients and in part because of technical advances in equipment to perform the blocks.

Thus the present prospective comparative study is designed to evaluate the post operative analgesic efficacy of pre-incisional peritonsillar infiltration using tramadol, ketamine alone and combine with bupivacaine, xylocaine & normal saline.

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Strictly as per the compliance and regulations of:

"Requirement of 1st Oral Analgesic Dose after Tonsillectomy by Various Method"

Shamendra Kumar Meena [α], Rajkumar Jain [σ], Vijay Kumar Meena [ρ], Ramraj Meena [ω] & Muniram Meena [¥]

I. Introduction & History

Pain is a highly unpleasant sensory and emotional experience and postoperative pain control in children is a big challenge for their inability to express and react. In the past two decades, there has been a considerable progress in the understanding of children's perception of pain and responses to pain and various pharmacological agents and analgesic delivery to avoid under treatment of pain in children. A parallel noteworthy advancement has occurred in the knowledge of anatomy, physiology and pharmacology of regional anesthetic techniques. Some of these techniques are now an integral part of perioperative and procedure- related pain management in all ages, in part because of a greater concern about postoperative pain management in patients and in part because of technical advances in equipment to perform the blocks.

Thus the present prospective comparative study is designed to evaluate the post operative analgesic efficacy of pre-incisional peritonsillar infiltration using tramadol, ketamine alone and combine with bupivacaine, xylocaine & normal saline.

II. Aims & Objectives

1. To Provide Post Tonsillectomy Analgesia to patients.
2. To evaluate the post operative analgesic efficacy of pre incisional peritonsillar (PT) infiltration using various agents.
3. To evaluate the effect of various agents infiltration on start of oral intake and discharge from the hospital after tonsillectomy.
4. To investigate the possibility of any complication in relation to drugs infiltration into the peritonsillar Fossa.

III. Anatomy and Physiology

a) Embryology

Pharyngeal Grooves and Pouches and Their Derivatives. The lateral walls and floor of the cranial part of the early foregut become much altered by the development of the pharyngeal pouches in this region. These pouches first appear as grooves which extend ventrally across, or towards, the middle line. In their later development, however, they become greatly modified to give origin to a number of diverse structures. These include the tympanic (middle ear) cavity, the parathyroid glands, tonsils and the thymus.

i. *Preoperative Assessment*

Preoperative assessment in patients undergoing adenotonsillectomy is crucial and may reveal potential problems that may complicate either surgery or the patient's postoperative course. It is crucial to elicit the existence of any coagulation abnormalities. A family history of coagulation disorders or easy bruising may be a warning sign of an underlying bleeding disorder warranting further hematologic evaluation. Routine evaluation of coagulation studies before surgery in patients undergoing adenotonsillectomy is controversial. Manning and others determined that evidence of coagulation disorders in patients with no clinical history of or examination consistent with a hematologic disorder was extremely low, thereby not justifying routine preoperative coagulation studies

ii. *Analgesia*

Adequate analgesia is important in the immediate postoperative phase. Narcotics have a potent emetic effect and should be used with caution if at all. A single dose of narcotic may be administered in the recovery phase and codeine may be used in the early postoperative period, but subsequent to this, paracetamole is the drug of choice on the grounds of safety and efficacy. For some children this may not be adequate and a non-steroidal anti-inflammatory drug (NSAID) may be needed. There were concerns that the effect of these drugs on platelet adhesion might increase bleeding from the tonsil bed, but a recent meta-analysis found no such risk and a significant reduction in postoperative nausea and vomiting when compared with other analgesics notably narcotics. Aspirin should not be used in children because of the risk of Reye syndrome.

IV. Indications and Contraindications

a) Indications

i. *Absolute Indications*

.Respiratory obstruction

.Huge hypertrophy causing difficulty in feeding

.Sleep apnea syndrome

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ii. *Relative Indication*

.Peritonsillar abscess
.Chronic tonsillitis

- failure of medical treatment to reduce the size
- more than 3-4 acute episodes in per year
- Acting aseptic focus for rheumatic heart disease, glomerulonephritis, arthritis etc.

.Primary tuberculosis of the tonsil
.Diphtheria carrier
.Tumor of tonsils
.Tonsillar cyst, tonsillolith, embedded FB in tonsils etc.
Surgical approaches
.Elongated styloid process
.Glossopharyngeal neurectomy
.As a part of Uvulo- palato- pharyngo- plasty (UPPP)

b) Contraindications

Active infection/Acute exacerbation, Aneurysm of internal carotid artery, age below 3 years, Active menstruation

Bleeding/Clotting disorders
Cervical spine pathology
Diphtheritic tonsillitis,
Drugs-aspirin, oral contraceptives etc
Endemic of polio

Failure to control systemic diseases like hypertension, diabetes, bronchial asthma, LRTI etc.

V. Material & Methods

After approval of the study protocol by the local Ethical Committee and obtaining fully informed written consents, 60 patients assigned for tonsillectomy enrolled in the study of age group 5 to 35 yr. The study conducted at Department of Otorhinolaryngology, MBS Hospital Kota Rajasthan from Dec. 2010 to Oct. 2012. Patients with history of bleeding diathesis allergy to study drugs, or tonsillar abscesses excluded from the study.

Patients randomly divided into 6 equal study groups (n=10); Group I (Negative control group) included patients assigned to receive PT saline infiltration as placebo, Group II (Positive control group) included patients assigned to receive xylocaine (1 %) PT infiltration. Group III included patients assigned to receive tramadol (2mg/kg) PT infiltration, Group IV included patients assigned to receive ketamine (0.5mg/Kg) PT infiltration, Group V received combination of Bupivacaine (5mg/ml) with Tramadol (2mg/kg), Group VI received Bupivacaine (5mg/ml) with Ketamine (0.5mg/Kg). All medications prepared as 2ml in volume and injected as 1ml per tonsil 3 min. prior to incision (pre-incisional).

All study patients premedicated with midazolan intravenously before the procedure and received nalbufine i.v. immediately after induction of general anesthesia.

VI. Operative Techniques

Tonsillectomy operation performed by dissection method. Before making incision, infiltration of tonsillar bed through ant. Pillar with various analgesic agents likes xylocaine, Ketamine. Tramadol & Placebo (Normal Saline), bupivacaine with tramadol/ketamine as their combination (regimen).

VII. Review of Literature

Tonsillectomies are done since 3000 years ago in india & also done now a days, now a days surgons are concentrated on the postoprative analgesia after tonsillectomy because after tonsillectomy patients suffer from pain, decrease in oral feeding also in psychological & financial burdon

Alhamarneh (2008) et al(2) reported that a significantly greater than normal secondary haemorrhage rate was noted in patients who had undergone tonsillectomy & experienced postoperative pain & concluded that adequate analgesics, for first week posttonsillectomy, is essential in order to keep the secondary haemorrhage rate within an acceptable range

Smith et al(2009) (3) reported that after tonsillectomy in children, postoperative pain management is essential yet often challenging task, In addition to discomfort, lack of pain management can leads to delays in oral intake of patients, resulting in external stays & increased costs.

Costas-gastiaburo (1998) et al (4) found peritonsillar infiltration decrease intraoprative bleeding & pain independent of the type of solution infiltrated

Dr. Akbar Pizadeh, Mo-Ali. Mohammadi, Sooreh Allaf-Akbari, Masood Entezarias (10)-The Effect Of Ketamine On Post-tonsillectomy Pain in Children: A Clinical Trial; Iranian Journal of Otolaryngology No.1, Vol. 24, Serial No.66, winter 2012.

Moller (2010) et al(11) showed that postoperative pain in the preoperative peritonsillar injection with bupivacaine was less compared with the control (placebo) group injected with no .In a large scale study on 1026 patients, pain levels in the ketamine group were shown to be lower than in the control group and patient satisfaction to be more.

VIII. Drugs

a) Lignocaine (Lidocaine)

This is a intermediate potency & duration agent of local anaesthetics (LAs), it is a amide linked LAs. introduced in 1948, currently most widly used ,injected around a nerve it blocks conduction within 3 min. it is used for surface application, infitration, nerveblock, epidural, spinal, i.v. (intravenous) and regional block anaesthesia. Cross sensitivity with ester LAs is not seen. early central effect of lignocaine are drowsiness,

mental clouding, altered taste & tinnitus. overdoses causes muscle twitching, convulsion, cardiac arrythmias, fall in BP, coma, respiratory arrest. lignocaine is popular antiarrythmic.

i. *Features of amide Las (compared to ester LAs)*

– produce more intense & longer lasting anaesthesia
– bind to α1 acid glycoprotein in plasma
– not hydrolysed by plasma esterase
– Rarely cause hypersensitivity reaction; no cross sensitivity with ester LAs

ii. *Mechanism of action*

– The LAs block nerve condution by decreasing the entry of Na+ ions during upstroke of action potential (AP) as the concentration of LAs is increased, the rate of rise of AP & maximum depolarization decreases causing slowing of conduction. Finally local depolarization fails to reach the threshold potential & conduction block ensues.

iii. *Local action*

The clinically used LAs have no/minimal local irritant action & block sensory nerve endings, nerve trunks, neuromuscular junction, ganglionic synapse & non selective receptors, i.e. structures which function through increased Na+ permeability. They also reduce release of acetylcholine from motor nerve endings. Injected around a mixed nerve they cause anaesthesia of skin & paralysis of voluntary muscle supplied by that nerve.

iv. *Addition of a vasoconstrictor, eg adrenaline (1:50000 to 1:200000)*

1. Prolongs duration of action of LAs
2. Reduce systemic toxicity of LAs
3. Provides a more bloodless field for surgery
4. May raise BP
5. Makes the injection more painful

v. *Systemic action*

Any LAs injected or applied locally is ultimately absorbed & can produce systemic effects depending on concentration attained in the plasma & tissuses.

C.N.S. - all LAs are capable of producing a sequence of stimulation followed by depression. Lignocaine on the contrary usually causes drowsiness & lethargy, but higher doses produce excitation followed by depression.

C.V.S.-little effect on contractility & conductivity, it abbreviates effective refractive period (ERP) &is used as an antiarrhythmic.

vi. *Pharmacokinetics*

Surface soluble anesthetics' are rapidly absorbed from mucous membrane & abraded areas but absorption from intact skin is poor lignocaine is degraded only in liver microsomes by dealkylation & hydrolysis.

vii. *Adverse effects*

Systemic toxicity on rapid i.v. injection is related to the intrinsic anesthetic potency of the LA. Toxicity after topical application or regional injection is influenced by relative rates of absorption & metabolism.

1. -CNS effects are light headedness, dizziness, auditory & visual disturbance, mental confusion, disorientation, shivering, twitching, tremors, finally convulsion & respiratory arrest.
2. -CVS toxicity of LAs is manifested as bradycardia, hypotension, cardiac arrhythmias & vascular collapse.
3. - injection of LAs may be painful, but local tissue toxicity of LAs is low
4. Hypersensitivity reactions like rashes, angioedma, dermatitis, asthma, & rarely anaphylaxis occurs. Common with ester group rare with lignocaine.

b) Bupivacaine

Bupivacaine Hydrochloride is a white odorless crystalline powder or colourless. Crystals. It is freely soluble in water; freely soluble in alcohol; slightly soluble in acetone and in chloroform. A 1% solution in water has a PH of 4.5 to 6.0 and should be protected from light. A potent & long acting amide LA: used for infiltration, nerve block, epidural & spinal anaesthesia of long duration. It has high lipid solubility; distribute more in tissue than in blood after spinal/epidural injection. Bupivacaine appears to be more cardiotoxic than other local anesthetics. Cardiac arrest due to bupivacaine can be resistant to electrical defibrillation and a successful outcome may require prolonged resuscitative efforts. it is more prone to prolong QTc interval & induce ventricular tachycardia or depression –should not be used for intravenous regional analgesia.

Local nerve blockade by bupivacaine Wong AK (1995) reduces short & long term pain in children undergoing tonsillectomy & adenoidectomy in the presence of general anesthesia.

c) Ketamine

It is pharmacologically related to hallucinogen phencyclidine; induces-profound analgesia, immobility, amnesia with light sleep & feeling of dissociation from one's own body & surroundings so called "DISSOCIATIVE ANAESTHESIA" the primary action is cortex & sub cortical areas; heart rate , cardiac output & BP are elevated due to sympathetic stimulation. A dose of 1-3(average 1.5) mg/kg i.v. or 6.5-13(average 10) mg/kg i.m. produces the above effect within a min, recovery starts after 10-15 min, and patient remains amnesic for 1-2 hrs. , emergence delirium, hallucination, & involuntary movements occur in up to 50%pts., but inj. Is not painful, children tolerate drug better. Its elimination t1/2 is 3-4 hrs. Ketamine also recommended for operation on the head & neck, in those who do not want to lose consciousness & for short operation. It may

be dangerous for hypertensive & ischemic heart disease but good for hypovolemic pts.

Ketamine al Yu M (2007) et al suppressed injury induced tumor necrosis factor (TNF)-α and IL-6prodution & nuclear factor –kappa-B activator.

d) Tramadol

It is centrally acting analgesic relieves pain by opioids as well as additional mechanism .its affinity for *μ* opioids receptor is modest while that for kappa & delta is weak, it inhibit reuptake of NA & 5-HT,& thus activates monoaminergic spinal inhibition of pain. Its analgesic action is only partially reversed by opioids antagonist naloxone. Injected i.v.100 mg tramadol is equanalgesic to 10 mg morphine; oral bioavailability is good (oral: parenteral dose ratio1.2) the t1/2 is 3-5 hrs & effect last 4-6 hrs. Tramadol causes less respiratory depression, sedation, constipation, urinary retention, & rise in inhibitory pressure than morphine it is well tolerated, side effect are dizziness, nausea, sleepiness, dry mouth, & sweating. Safer in compromised cardiovascular function, it is indicated for medium intensity short lasting pain due to diagnostic procedure, injury, surgery as well as chronic pain in cancer, but not effective in severe pain.

Tramadol (Ugur MB(2008) to prevent pain in children undergoing tonsillectomy & found peritonsillar infiltration with tramadol provided good intra-operative analgesic, less post operative pain on awaking &lower analgesics requirements after surgery with no significant difference between both routes of administration for any of these parameters

e) Bupivacaine And Ketamine

Bupivacaine (5 mg/kg) & ketamine (0.5 mg/kg), both combination decrease pain & prolong the duration of analgesia without increasing side effects

f) Bupivacaine and Tramadol

Bupivacaine (5 mg/ml) & tramadol (2 mg/kg),

*bupivacaine plus ketamine, bupivacaine plus tramadol Choudhuri AH (2008) for post operative pain management in children having surgery for inguinal hernia & reported that caudally administered 0.5ml\kg bupivacaine 0.25% plus tramadol 1 mg\kg provided significantly longer duration of analgesia without an increase in the adverse effects when compared to bupivacaine alone

All medication prepared as 2 ml in volume & was injected as 1 ml per tonsil 3 min. prior incision.

IX. Observation and Results

Patients randomly divided into 6 equal study groups (n=10); Group 1 (Negative control group) included patients assigned to receive PT saline infiltration as placebo; Group 2 (Positive control group) included patients assigned to receive xylocaine (1%) PT infiltration. Group 3 included patients assigned to receive tramadol (2mg/kg) PT infiltration, Group 4 included patients assigned to receive ketamine (0.5mg/Kg) PT infiltration, Group 5 received combination of Bupivacaine (5mg/ml) with Tramadol (2mg/kg), Group 6 received Bupivacaine (5mg/ml) with Ketamine (0.5mg/Kg)

Gp1-normal saline

Gp2-xylocaine (1%)

Gp3-tramadol (2mg/kg)

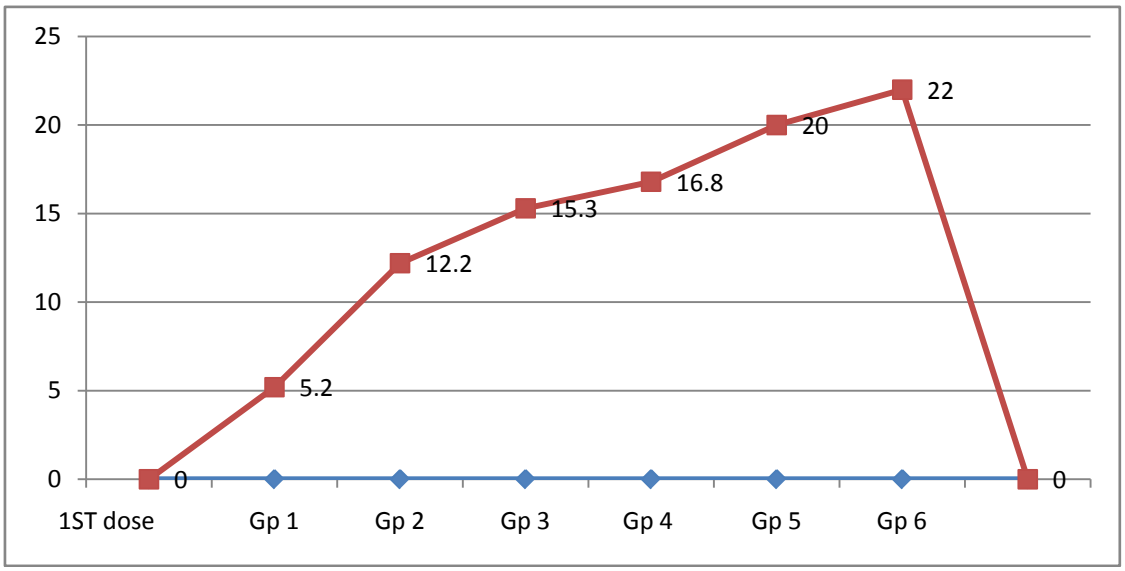
Gp4-ketamine (0.5mg/kg)

Gp5-bupivacaine (5mg/ml) with tramadol

Gp6-bupivacaine with ketamine

Requirement of 1st oral analgesic dose post-operatively(hrs.)

1ST dose	Hrs.	Mean
Gp 1	6,5,7,4,5,4,6,5,6,4	5.2
Gp 2	11,13,12,11,12,13,13,12,11,14	12.2
Gp 3	15,16,15,16,15,16,16,15,13,16	15.3
Gp 4	17,16,15,17,16,18,17,18,17,17	16.8
Gp 5	22,19,22,18,20,21,18,22,19,19	20
Gp 6	24,23,23,24,21,21,21,22,21,20	22



X. Disscussion

We have divided patients in six groups according to drugs which were injected to patients preoperatively in tonsillar fossa.

According to Table shows distribution of patients according to requirement of 1st analgesic dose after tonsillectomy. This depends on efficacy of analgesic dose. Patients asked 1st analgesic dose after surgery in gp1 (normal saline) 5.2 hours, in gp2 (xylocaine) is 12.2 hours, in gp3 (tramadol) 15.3 hours, in gp4 (ketamine) 16.8 hours, in gp5 (bupivacaine and tramadol) 20 hours and in gp6 (bupivacaine and ketamine) 22 hours. The analgesic efficacy of combination of drugs in gp5 gp6 is very good. Therefore requirement of 1st analgesic dose was very late, in control group the analgesic dose require very early.

The difference between all groups was statistically significant ($P<0.05$).

Our study references are similar to the study of Ehab Saaid MD in Ain shams Journal of Anesthesiology in vol.2.2 July 2009 and from the Journal of International medical research 2005; 33:188-195.

According to Ehab Saaid 2009 all patients enrolled in the control groups (gp1) requested for rescue analgesia and 14 patients (46.7%) requested it twice. However, 9 patients (30%) in positive control group (gp2) did not request for rescue analgesia till discharge.18 patients (60%) requested it once and 3(10%) requested it once. No patient in study drugs groups (gp3-6) requested rescue analgesia twice and 68(56.7%) patients; 16, 13, 21 and 18 respectively, did not requested it till discharge and 52 patients (43.3%) requested it once .In total, 77 patients received PT infiltration did not asked for rescue analgesia till discharge and 86 patients received it once with significant difference compared to patients who have received placebo.

Patients receiving PT drug infiltration had significantly longer duration of PO analgesia compared to those who received placebo infiltration. However, patients enrolled in group2 (xylocaine) had significantly shorter duration of PO analgesia compared to gp3 (tramadol), 4 (ketamine) and 6 (bupivacaine and ketamine), but non- significantly shorter compared to gp5 (bupivacaine and tramadol).There was a no-significant difference between duration of PO analgesia reported in gp3 compared to gps4-6; however infiltration of tramadol/bupivacaine produced significantly longer duration compared to ketamine groups, either alone or in combination.

XI. Conclussion and Summary

Preincisional infiltrations of various agents are effective method to reduce post-tonsillectomy pain. This method also effective for earlier start of oral feeding and discharge from the hospital

We recommend the routine use of pre incisional peritonsillar infiltration of various agents in all tonsillectomy cases, irrespective of the age of the patient to reduce the post-tonsillectomy pain and other morbidities

a) Summary

This is prospective, randomized, single blind controlled clinical trial to assess the effect of preincisional peritonsillar infiltration of various agents on pain after tonsillectomy, which was performed on Dec.2010 till Oct.2012 in the department of ENT, Govt. Medical College, Kota.

A volunteer sample of 60 patients, aged 5 to 35 yrs with history of recurrent or chronic tonsillitis were included in this study and planned for tonsillectomy with or without adenoidectomy

Patients were divided into 6 equal study groups (n=10); Group I (Negative control group) included patients assigned to receive PT saline

infiltration as placebo; Group II (Positive control group) included patients assigned to receive xylocaine PT infiltration. Group III include patients assigned to receive tramadol (2mg/kg) PT infiltration, Group IV included patients assigned to receive ketamine (0.5mg/Kg) PT infiltration, Group V received combination of Bupivacaine (5mg/ml) with Tramadol (2mg/kg), and Group VI received Bupivacaine (5mg/ml) with Ketamine (0.5mg/Kg).

All medications prepared as 2ml in volume and injected as 1ml per tonsil 3 min prior to incision (pre-incisional).

Postoperative pain was assessed using OPS and ALDRETE score for severity of pain at different time after the surgery. The time of oral intake start and total admission days after the surgery also were noted.

Comparision of various agents for pain, oral intake and postoperative admission days were noted.

No complication of preincisional peritonsillar infiltration of various agents was seen in this study.

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Surgical Treatment of Fractures of the Zygomatic Complex with Different Retainers: Osteosynthesis Features in the Zygomatic-Alveolar Crest Area

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Abstract- The article reflects the results of clinical and radiological examination to solve the matter of lock choice for osteosynthesis (resorptive titanium or polymer) in the zygomatic-alveolar crest area) in case of fracture. As a result of the research the author concluded different approaches to the use of various types of clamps. Thus, in cases of small debris fractures in the zygomatic-alveolar crest area and the presence of bone defect, a biodegradable polymer plate, as the only way to fix bone fragments, is impractical because in this area it is necessary to renew the buttresses. Polimerosteosynthetic rezorptive retainers author recommends in cases of restoration of the integrity measures.

Keywords: polimerosteosynthesis, resorptive bone plate, osteosynthesis for fracture of the zygomatic complex fracture, zygomatic-alveolar crest.

GJMR-J Classification: NLMC Code: WE 250

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Surgical Treatment of Fractures of the Zygomatic Complex with Different Retainers: Osteosynthesis Features in the Zygomatic-Alveolar Crest Area

E. Astapenko [α], V. Malanchuk [σ] & N. Timoshchenko [ρ]

Abstract- The article reflects the results of clinical and radiological examination to solve the matter of lock choice for osteosynthesis (resorptive titanium or polymer) in the zygomatic-alveolar crest area) in case of fracture. As a result of the research the author concluded different approaches to the use of various types of clamps. Thus, in cases of small debris fractures in the zygomatic-alveolar crest area and the presence of bone defect, a biodegradable polymer plate, as the only way to fix bone fragments, is impractical because in this area it is necessary to renew the buttresses. Polimerosteosynthetic rezorptive retainers author recommends in cases of restoration of the integrity measures.

Keywords: polimerosteosynthesis, resorptive bone plate, osteosynthesis for fracture of the zygomatic complex fracture, zygomatic-alveolar crest.

I. Introduction

Fractures of the zygomatic complex (ZCF) is the second in frequency among all fractures of the maxillofacial area [8]. Unfortunately, the frequency of criminal injury has increased, except fractures, moreover a zygomatic bone has become more complex in nature of damage [3, 8]. Nowadays some algorithms that provide surgical care for victims of zygomatic complex (ZC) fractures are defined [1,7,9]. To fix the bone fragments different types of the bone plates and screws are used, such as titanium and resorptive. Last, performing its function, without giving harmful effects to the body. The titanium ones remain in the tissues after consolidation of the bone fragments. Recently, many researchers emphasize the need to remove the metal braces after consolidation of fractures due to the inflammatory processes in the surrounding tissues, cold response, the patient's desire to remove the metal retaining structure after the fusion of the bone fragments, etc. [2]. However, there is a number of clinical situations where the removal of the metal retaining structure is undesirable because it performs a supporting and reconstructive function.

In our previous studies, we demonstrated the feasibility of bioactive plates' resorptive action EPU-GAP-LEV for fixing bone fragments of the middle zone face (MZF) [4,5,6]. Therefore, in this and subsequent studies we concentrate attention on the particular choice of clamps for osteosynthesis depending on the location of the fracture and the clinical situation. Thus, in the area of the zygomatic-alveolar crest (ZAC) which is MZF buttresses, the choice of lock depends on the nature and type of fracture.

The aim of our work is to decide how to choose the lock for osteosynthesis (titanium or resorptive) in the area of ZAC at various ZCF.

II. Materials and Methods

Observation group were 120 patients with fractures of the ZC, after which clinical and radiographic examination surgical treatment of fractures was performed using various types of clamps. The surgery included reposition and fixation of ZC fragments revision of maxillary sinus using intraoral and one of the extraoral accesses. Osteosynthesis of ZC was carried by titanium and polymer plates based on poliuretan (EPU-GAP-LEV). Planning surgery and braces selection was based on the data of computer tomography (CT) and the intraoperative picture of the fractures. Analysis of the treatment was carried out on the basis of the CT study, 6 months after surgery with the definition of bone density in the area of the fragments ZC fusion.

III. Research Results

The main role for the stable ZC fixation in the right position was given to the area of osteosynthesis of zygomatic-frontal suture. However, it is undeniable thesis on the necessity to fix 2-3 zones. This important support for stabilization ZC space is given in the ZAC areaosteosynthesis'.

Polymerosteosynthesis with the bone plates and screws in the survey was conducted to 79 patients. It was possible in case of absence of bone defects. In the vast majority of observations the fracture gap was accurately located, while the diagrams of X-ray density remained uniform due to a significant decrease in mineral saturation of the surrounding bone. In general

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radiographic bone density in the area offusion detected 20-30% less than the intact side.

Resorptive retainers for osteosynthesis EPU-GAP-LEV, that we proposed [3], have certain advantages. Due to the hydroxyapatite and levamisole they have a good biocompatibility and positive influence on the course of reparative regeneration of bone tissue in the area of the fracture. According to its physical and mechanical indicators they are close to the bone [6]. Therefore, during the fusion of bone fragments after osteosynthesis of their application, the load on the bone is shared equally, there is no effect of "mechanical shunt" and consolidation of fragments is on time. But this is possible only in the integrity recovery.

Based on the analysis of the results, it should be noted that if there are comminuted fractures in the area of ZAC and bone defects, biodegradable polymer platesis impractical as the only way to fix bone fragments because in this area it is necessary to renew buttresses. This is possible only if the application of more stringent not resorptive bone plates for osteosynthesis. Polymer fixation plates and screws EPU-GAP-LEV should be used as an extra, they simultaneously function as "depot" to improve conditions for wound healing and prevent inflammatory complications in the postoperative period.

Thus, for 41 patients titanium plates and screws were used in the areas of fracture and polymer retainers EPU-GAP-LEV were used as additional latches. In these cases, the observed bone defects of different sizes were detected because of the removal of free fragments, which lost contact with the periosteum, and till the time of the survey (6 months after the surgery) were not filled with bone tissue. Radial density in these areas averaged 138 + 59 HU, and was 5-16 times lower than the healthy unaffected side.

In the postoperative period, all patients administered the standard course of anti-inflammatory therapy.

Clinical Example № 1.

Patient S., 30, arrived for treatment in the emergency procedure. He had a right traumatic fracture with displacement (Fig. 1).

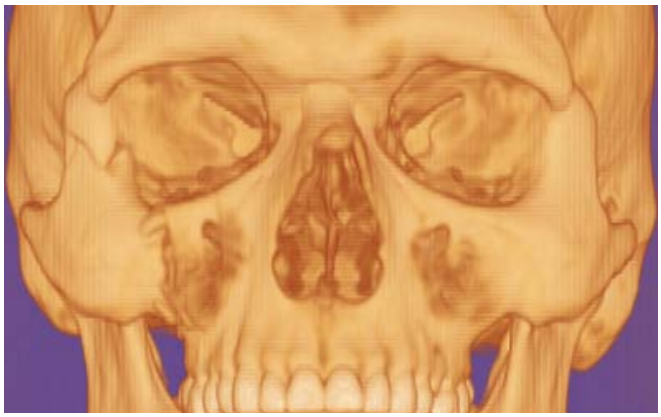
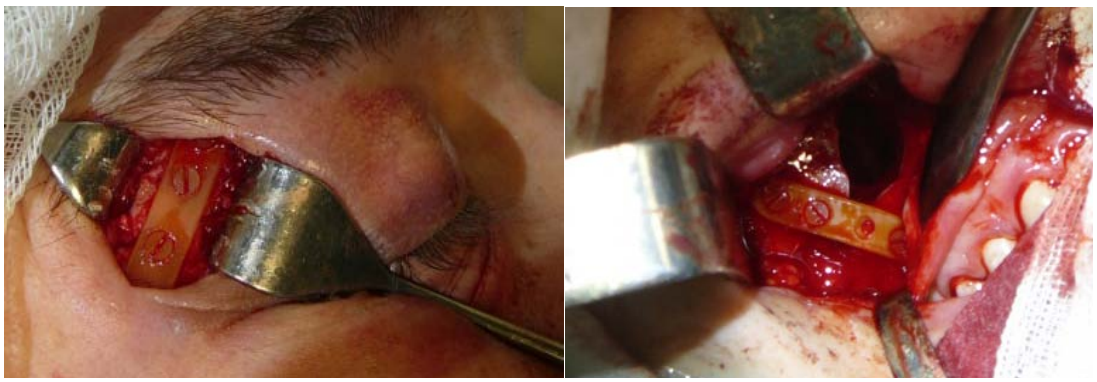


Figure 1: 3D CT facial reconstruction of the skull in the patient C. (condition after injury).

After clinical and radiographic examination operation was conducted- reposition, polimerosteosynthesis EPU-GAP-LEV of the right zygomatic complex. With an intraoral access and direct access to the right zygomatic-frontal suture ZC reposition was made, its fixation with plates EPU-GAP-LEV in the area of right zygomatic-frontal suture and ZAC. The operation was completed with revision and catheterization of the right maxillary sinus (Fig. 2).



A B

Figure 2 : Step operative care:

A - polimerosteosynthesis in the area of zygomatic-frontal suture with the plate and screws EPU-GAP-LEV.
B - polimerosteosynthesis in the ZAC area with the plate and screws EPU-GAP-LEV.

The postoperative period was uneventful. The X-Ray of the position of bone fragments of the zygomatic complex testified the correct position of the plates and screws. The stitches were removed. The patient was discharged from the office in satisfactory condition.

A survey in 3 months after the operation testified to the full rehabilitation of the patient. The polymer plate in the osteosynthesis areas was not palpated.

After 6 months CT 3D control of the facial skull showed a complete anatomic restoration of the affected area (Fig. 3). Indicators of mineral density bone

regenerated in the area of polimerosteosyntesis EPU-GAP-LEV approached to the mineral density of unaffected bones on the symmetrical side 879 + 124 HU versus 951 + 132 HU, indicating the timeliness of all phases of the regeneration of bone tissue, including the mineralization and restructuring (Fig. 4).

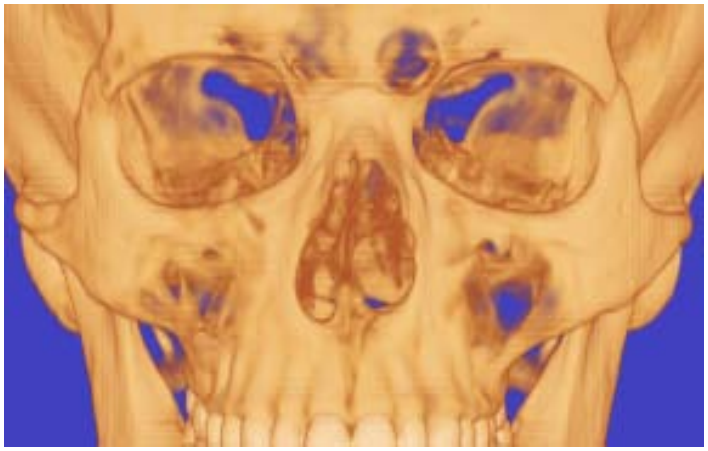


Figure 3 : 3D CT patient's status, 6 months after surgery.

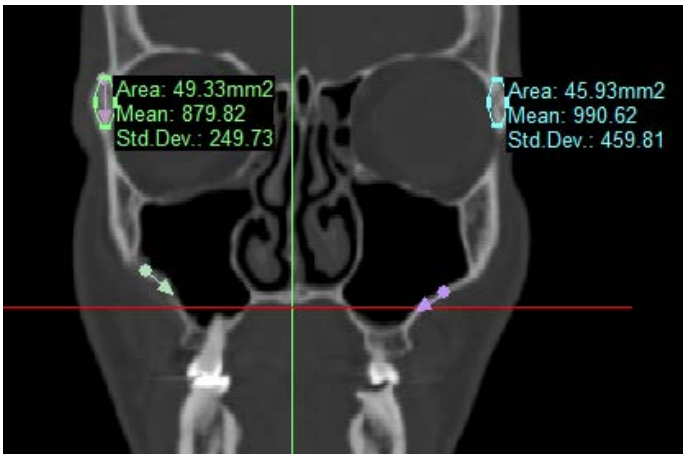
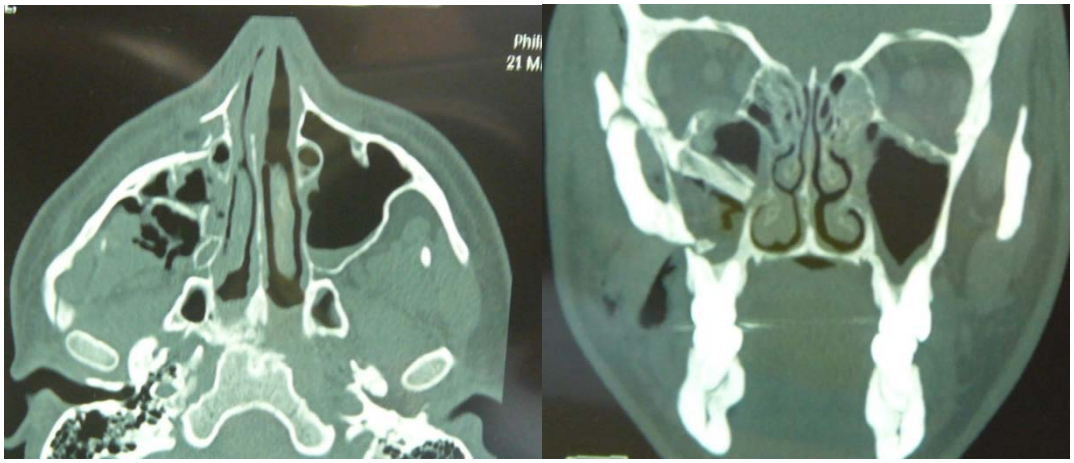


Figure 4 : The research density of bone fusion fragments, 6 months after surgery.

Comparison of the bone mineral density in polimerosteosyntheis and the symmetrical unaffected areas (in this slice MSCT indicators of the mineral bone density in the area with polimerosteosynthesis was 879,82 HU against 990,62 HU on the unaffected side).

Clinical example № 2. Patient S., 28, arrived for treatment in emergency procedure. He had a traumatic fracture of the right zygomatic complex with displacement. He addressed doctors 5 days after the injury.

At CT 3D determined violations of integrity skull bone clastic complex of the right zygomatic complex near the body of the ZC, the lower edge of the orbit and ZAC with the offset (Fig. 5).



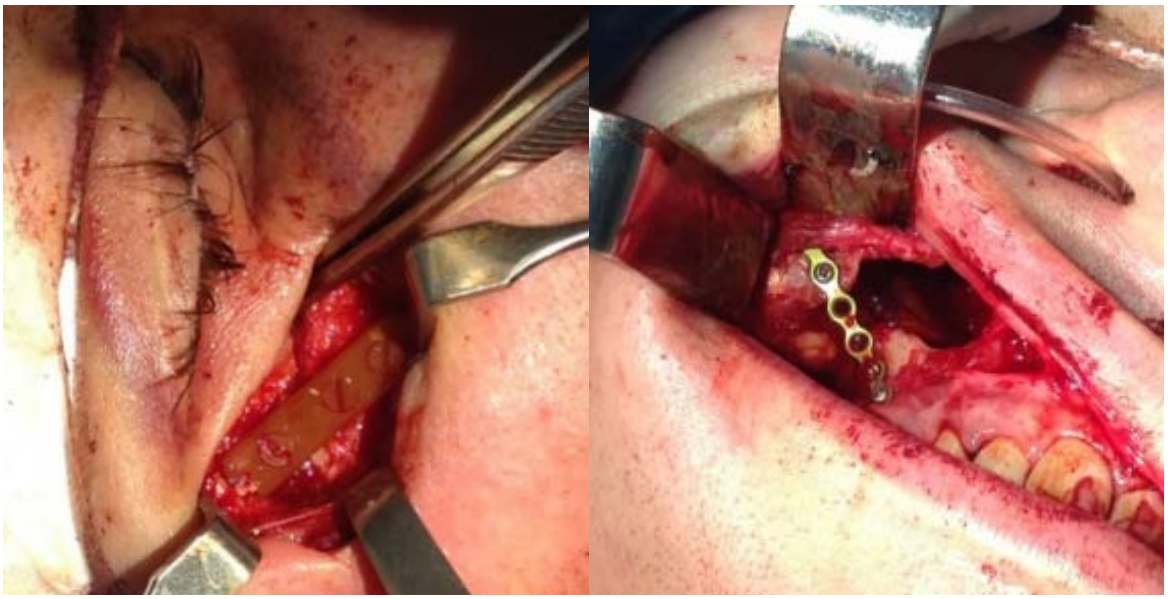
A B

Figure 5 : Patient S., Diagnosis: right traumatic ZC fracture with the offset:
A. Photo slice CT in axial projection.
B. Photo slice CT in frontal projection.

After clinical and radiographic examination an operation was conducted - reposition, osteosynthesis of the right ZC. With intraoral access and direct access reposition of ZC was made, it was fixed with the plate EPU-GAP-LEV near the body of ZC.

Taking into account that the fracture was debris and after the removal of free pieces a small bone defect was created the length of which was 1.4 mm, there was a need not only to fix this locus bone fragments, but also to play buttresses.

Therefore, a fixation on the ZC body was carried with a plate EPU-GAP-LEV, and in the area of scales with a bone titanium plate and screws (Fig. 6). The operation was completed with revision and catheterization of the right maxillary sinus.



A B

Figure 6 : Stage of the surgery of patient S.: A – polimerosteosynthesis (EPU-GAP-LEV) in ZC on the body; B – metaloosteosynthesis in the ZAC area.

The postoperative period was complicated.The X-ray testified the correct position of the fragments (Fig. 7). Within a year after the surgery there were no complications.

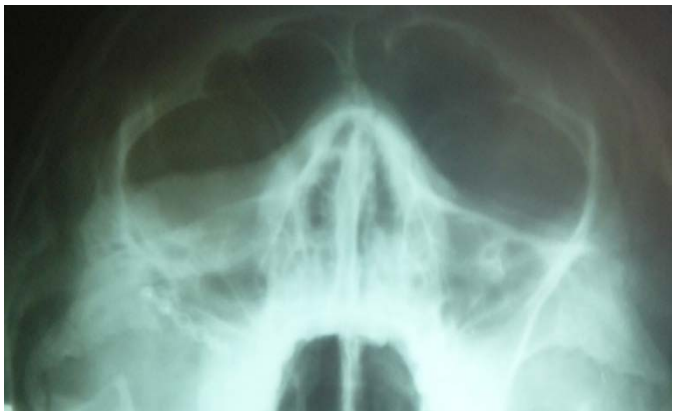


Figure 7: Axial projection X-ray of the patient 7 days after the surgery.

After 6 months of the operation as a result of the MSCT control consolidation of the fracture was detected in all the loci where the bone fragments were in contact during osteosynthesis. In the ZAC area a bone defect remained that was restored with a bone titanium plate (Fig. 8).

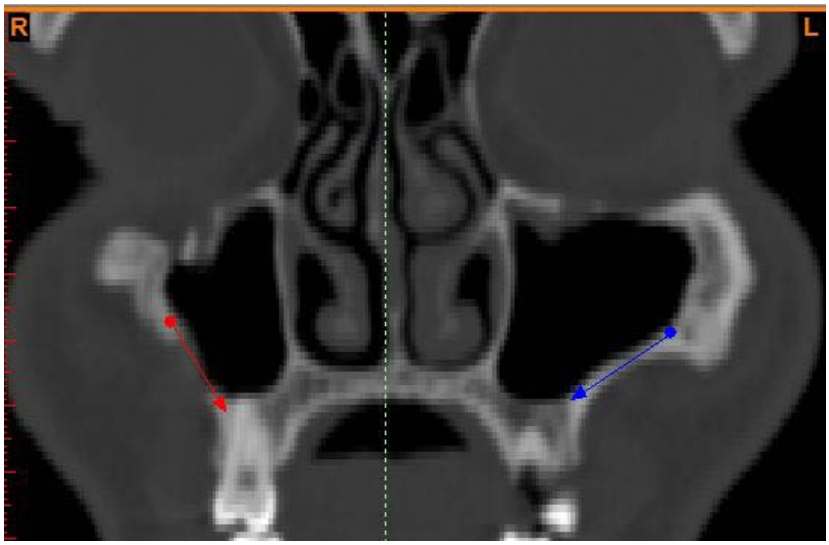


Figure 8 : MSCT facial bones of the skull of the patient S., 28 years, 6 months after osteosynthesis in the defected ZAC area.

IV. Conclusions

Analysis of clinical cases showed that the choice of retainers for osteosynthesis in the ZAC area should be treated differently. If the surgery in the area formed a bone defect and buttress should be restored,use hard not resorptive catches, including titanium. In cases of the ZAC integrity restoring resorptive bone plates and screws EPU-GAP-LEV should be used.

Prospects for further research: To evaluate the efficiency of osteosynthesis of resorptive accessory EPU-GAP-LEV in other areas of maxillo-facial area.

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Congenital Lobular Capillary Hemangioma of Nasalseptum in a 4 Year Old Child – A Case Report

By Jyoti Ranjan Das, Jayanta Saha, Debabrata Biswas, Ajay Manickam, Rajarshi Sannigrahi, Shaswati Sengupta & SK Basu

RG Kar Medical College, INDIA

Abstract- Lobular capillary haemangioma is a benign, rapidly growing lesion of skin and mucus membrane. It usually involves gingiva, lips, tongue, and buccal mucosa. Nasal cavity is a rare location. Generally cases of haemangioma have been reported in children with epistaxis and nasal obstruction. We report a case of a 4yr old boy with congenital lobular capillary haemangioma of nose without epistaxis.

Keywords: *LCH, nasal cavity, congenital, endoscopic approach.*

GJMR-J Classification: *NLMC Code: WV 320*

Strictly as per the compliance and regulations of:

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Jyoti Ranjan Das [α], Jayanta Saha [σ], Debabrata Biswas [ρ], Ajay Manickam [ω], Rajarshi Sannigrahi [¥], Shaswati Sengupta [§] & SK Basu [χ]

Abstract- **Lobular capillary haemangioma is a benign, rapidly growing lesion of skin and mucus membrane. It usually involves gingiva, lips, tongue, and buccal mucosa. Nasal cavity is a rare location. Generally cases of haemangioma have been reported in children with epistaxis and nasal obstruction. We report a case of a 4yr old boy with congenital lobular capillary haemangioma of nose without epistaxis.**

Keywords: LCH, nasal cavity, congenital, endoscopic approach.

I. Introduction

Capillary haemangioma are hamartomas and most commonly arise in head and neck, affects 2.6% of all live births.[1]They are noted soon after birth as pink to red macular lesion that rapidly increase in size[1]. The lesion becomes raised, popular or polypoidal[1].Then they enter a quiescent phase and subsequently regress with 70% disappearing by the age of seven.[1]

Lobular capillary haemangioma is a benign, rapidly growing lesion with microscopically distinctive lobular structre that affects the skin and mucus membrane of oral cavity.[2]Gingiva, lips, tongue, buccal mucosa have been reported to be common sites of involvement. It was first described as `botryomycosis` by Poncet and Dort in 1897.[3]It is rarely located in the nasal cavity. The most common site in the nose is nasal septum [4, 5.] it affectsmales more than females.[6]Micro trauma and hormonal factors are the most common etiological factors. In a typical presentation, lobular capillary haemangiomaappears at endoscopy as a red to purple mass not larger than 1cm associated with epistaxis. However, in more rare instances the lesion reaches a considerable size filling the nasal cavity and leading to a complain of nasal obstruction.The treatment is nasal endoscopic surgery[7].

We present a case of a 4yr old boy with intranasal lobular capillary haemangioma since birth, with nasal obstruction but without any complaint of nasal bleeding. It is considered in differential diagnosis of childhood endonasal mass without bleeding like dermoid cyst, nasoalveolar cyst, nasolacrimal cyst, meningocele, encephalocele, glioma, chordoma etc.[1]

II. Case Report

A 4yr old boy came to the outpatient department of a tertiary care hospital with a swelling in left side nasal cavity. According to his mother it was there since birth and progressively increasing in size with age. Patient had only complaint of nasal obstruction. There was no history of epistaxis, nasal discharge, and disturbance of smell, headache, facial pain or change of voice. Local examination of Ear, Throat, Head & neck was within normal limits. There were no enlarged neck glands or palpable neck nodes.

On anterior rhinoscopy, a non-tendergreyish-white mass with smooth surface and soft consistency was seen in left side of nasal cavity. There was no nasal discharge or sinus tenderness.Diagnostic nasal endoscopy showed its attachment to the anteroinferior portion of septum partially obstructing the left nasal passage. Also there was mild DNS to right. (Figure 1)

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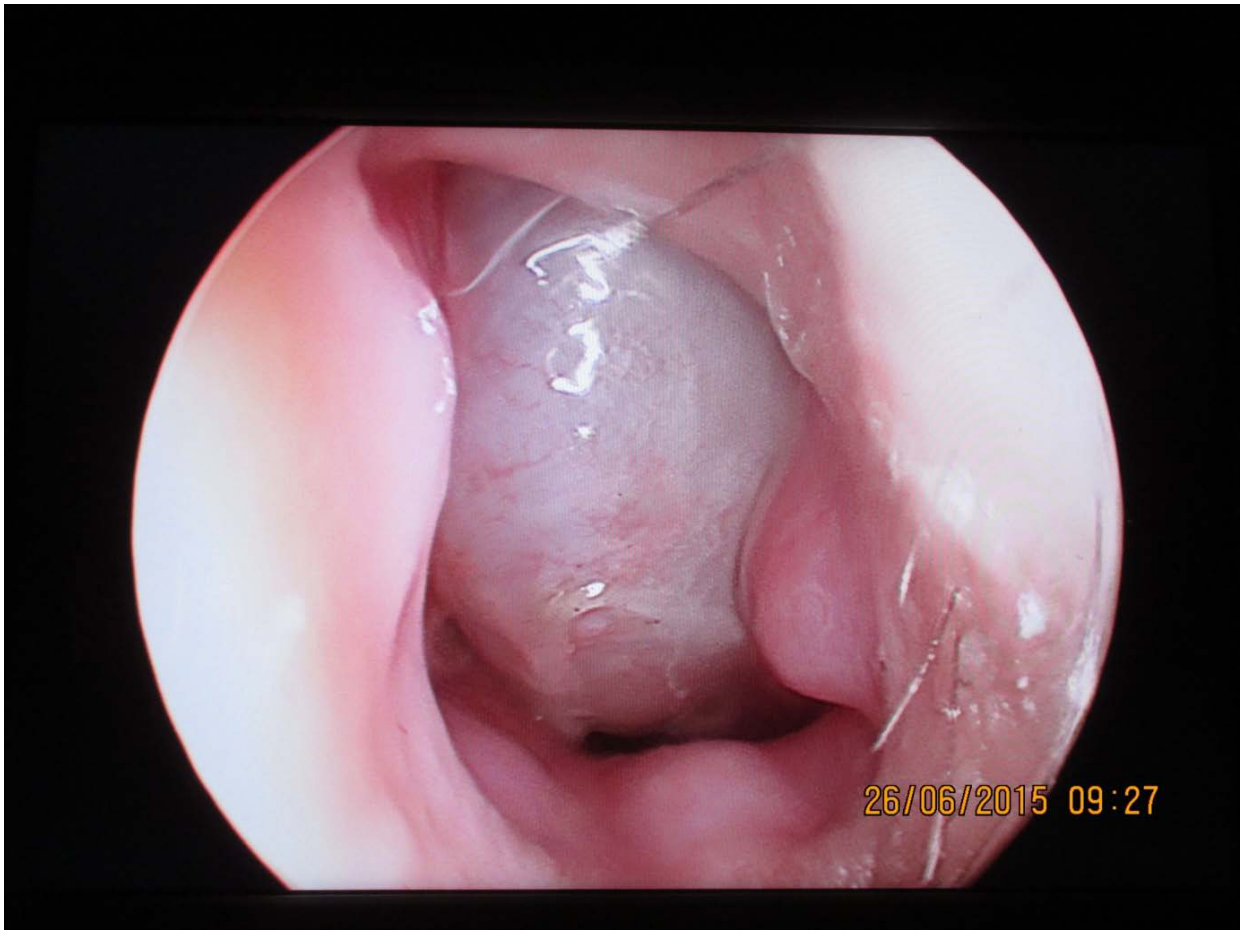

Figure 1: Endoscopic picture of Lobular capillary Haemangioma

Computed tomography scan of nose and paranasal sinuses revealed a wide-based soft tissue mass arising from anteroinferior portion of septum in left side of nasal cavity without any intracranial connection. There was no extension of the massinto paranasal sinuses. Septum was deviated to right. (Figure 2)

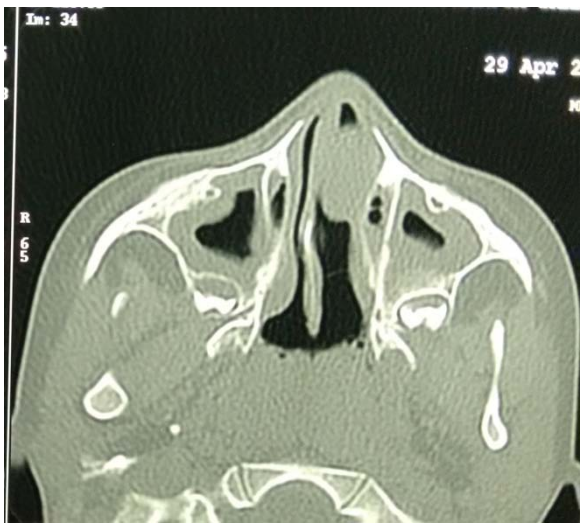

Figure 2 : CT scan showing the mass attached to the septum

Magnetic resonance imaging showed an elliptical non enhancing cystic lesion being hyper in T2 and STIR,hypo intense in T1 seen in anterior aspect of left side of nasal cavity, abutting adjacent parts of nasal septum and middle turbinate.The lesion measures about 22mmx9mmx13mm.

Endonasal endoscopic excision of the lesion was planned under general anaesthesia. The nasal mass was completely resected with a rim ofnormal septal mucoperiosteum and perichondrium under GA.There was no needfor any perioperative blood transfusion.The surgical specimen was sent for histopathological examination. (Figure 3)

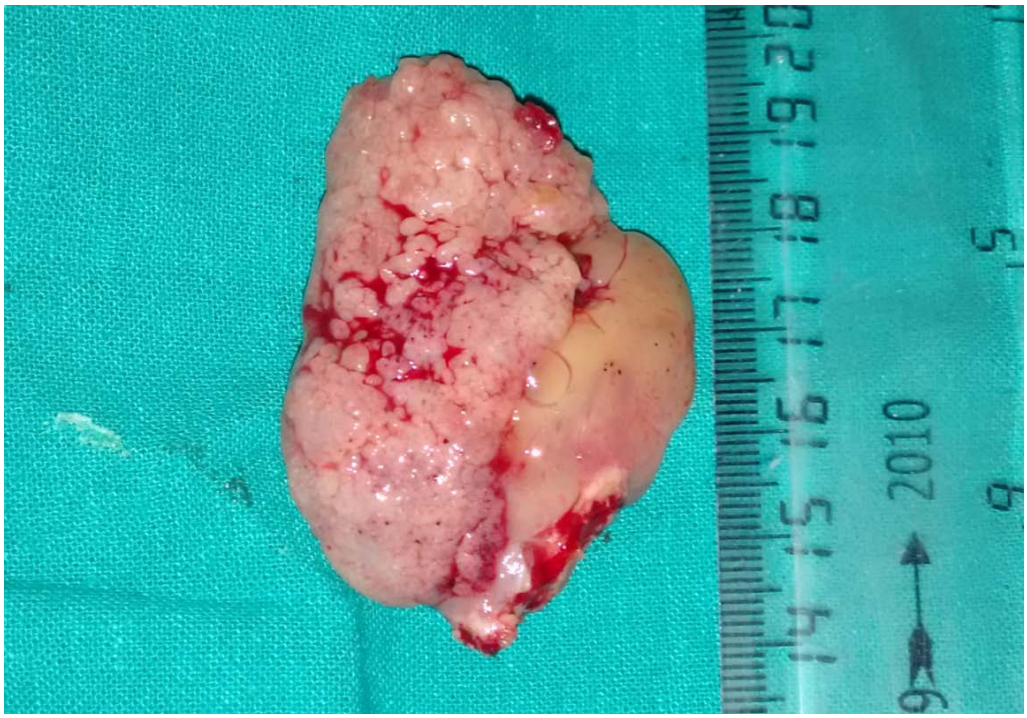

Figure 3 : specimen of Lobular capillary Haemangioma after excision

On gross examination, mass was whitish with smooth surface measuring 2x1.2 cm in size. On histopathological examination, section shows a lesion composed proliferating capillaries of various size lined by flattened endothelium lying in a fibrous stroma suggestive of lobular capillary haemangioma. There was no evidence of malignancy. (Figure 4)

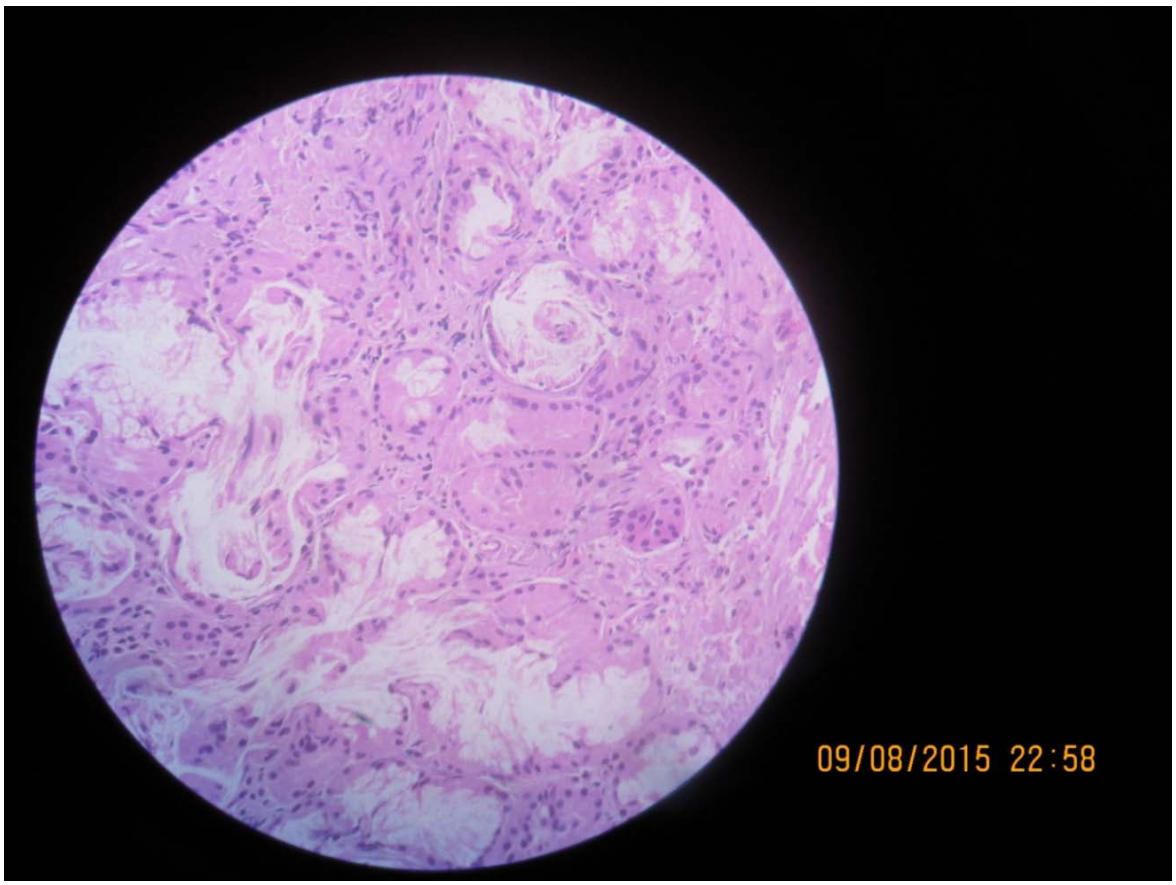

Figure 4 : Histopathology showing features of haemangioma

The patient has been followed up for a period of one year, and there is no recurrence of growth.

III. Discussion

Capillary haemangioma are hamartoma, most commonly arise on head and neck affecting 2.6% of all live births[1]. They are noted soon after birth as pink to red macular lesion that rapidly increase in size.[1]the lesions becomeraised, popular or polypoidal, then enter a quiescent stage and subsequently regress with 70% disappearing by the age of seven.[1]

LCH was first described by Poncet and Dor in the year of 1897where they referred these tumours as small vascular tumours in finger of four patients.[3]the authors referred to this condition as human botryomycosis thinking that the lesions were secondary to fungal infection.

In 1904, Hanziell coined the term pyogenic granuloma to describe these lesions which he suggested to be granulation tissue arising in response to bacterial infection.[8] In 1980 Mills et al propose the term lobular capillary haemangioma derived from its characteristic microscopic features.[9]

Aetiology of LCH remains unclear but trauma and hormonal influencesare considered to be the main factors. A retrospective study of 112 patients by Pagliai and Cohen shows a history of trauma in 5% with clinically diagnosed asLCH.[10] other possible aetiologiesare viral oncogenes, microscopic AV malformations and over production of angiogenic growth factors.[11]

There is a well-established relationship between LCH and pregnancy.LCH commonly occurs in women who are pregnant and those who use oral contraceptives. These signs regress after delivery indicating a role of hormone in the growth of LCH.[12]

Patients with LCH commonly present with nasal obstruction and epistaxis. In our case, patient only presented nasal obstruction. The differential diagnosis for nasal mass without any epistaxis will be meningocele, dermoid cyst, glioma, and polyp. These can be differentiated by CT scan and MRI.

Recommended treatment of LCH in nasal cavity is endoscopic guided local excision with cautery at the base of tumour for hemostasis.[10] this technique is associated with lower rate of recurrence.[9, 10]

IV. Conclusion

LCH is a rare lesion when it occurs in a nasal cavity. The exact is unknown. It may not be always presented with epistaxis or red colour polypoidal mass. It can be considered as a differential diagnosis of intranasal mass causing obstruction but no bleeding.

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Comparison of Epidermal Growth Factor Levels in the Gingival Crevicular Fluid of Patients with Gingivitis and Advanced Periodontitis

By Amir Alireza. Rasouli Ghahroudi, Afshin Khorsand, Mojtaba Bayani, Afsaneh Rezaee & Sepehr Torabi
Tehran University of Medical Sciences, Iran

Abstract- *Aims:* The aim of this study was to evaluate and compare epidermal growth factor (EGF) levels in gingival crevicular fluid (GCF) in patients with gingivitis and advanced periodontitis.

Study design: Department of Periodontics, Tehran University of Medical Sciences, between March 2012 and August 2013.

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GJMR-J Classification: *NLMC Code: WU 240*

Comparison of Epidermal Growth Factor Levels in the Gingival Crevicular Fluid of Patients with Gingivitis and Advanced Periodontitis

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Results: Mean EGF levels in the GCF samples of patients with gingivitis and advanced periodontitis were 68.07 ng/mL (SD=6.45) and 43.61 ng/mL (SD=6.18), respectively. Independent t-test showed significant differences between the two patient groups in EGF levels of GCF, with significantly higher levels in patients with gingivitis than those with advanced periodontitis ($P<.001$).There was significant correlation between EGF level and probing pocket depth ($P<.001$), and also between EGF level and clinical attachment level ($P<.001$).

Conclusion: The results showed significantly lower levels of EGF in the GCF of patients with periodontitis compared to those with gingivitis. It could be postulated that changes in EGF levels may be considered among important factors for predicting pathogenesis of periodontal diseases.

Keywords: epidermal growth factor, gingivitis, periodontitis, gingival crevicular fluid.

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I. Introduction

Periodontal diseases constitute one of the major health-related problems of teeth and their supporting structures, with a high prevalence rate in the general population all over the world [1,2]. Evidence indicates that major risk factors in periodontal diseases include poor oral hygiene, tobacco use, severe alcoholism, stress and diabetes.

Advanced chronic periodontitis results from the interaction between gram-negative bacteria and the host's inflammatory response, finally resulting in tissue destruction and loss of teeth [3-5]. Presence of various bacterial products in the cellular components of gingival tissues has been reported to be a factor involved in the activation of cellular processes, leading to the destruction of connective tissue and bone [3,6]. Pathogenic bacteria can evade recognition and elimination by the host defense system and can inactivate the cells and humoral factors of the host, directly and indirectly affecting tissues [6]. The immune cells of the periodontium secrete proinflammatory mediators in response to periodontal pathogens and their endotoxins [7], one of which is cytokines in the gingival crevicular fluid (GCF).

In the same context, active cytokines which destroy tissues have been introduced as the main factors involved in the destruction of connective tissue adhesion and bone loss. Different kinds of cytokines are released by lymphocytes, monocytes and non-immune cells, such as fibroblasts and epithelial and endothelial cells in the inflamed periodontal tissues [8]. Cytokines are soluble glycoproteins, which function as signaling molecules for the control, behavior harmony and cell function.

On the other hand, growth factors are generally considered subsets of cytokines. These factors are biologic mediators which regulate cellular migration in the connective tissue and proliferation and synthesis of proteins and other extracellular matrix cells. Reaction of target cells to growth factors depends on the expression of their specific receptors. These receptors are membrane antigens which produce intercellular signals when they bind to growth factors and induce

chemotaxis, cellular growth, and synthesis and differentiation of extracellular matrix [9]. It has been shown that receptors of growth factors are very important in inducing periodontal disease and regeneration in a rat model. [10].

Periodontal diseases comprise a number of chronic and acute inflammatory processes in response to bacterial products or components, which are diagnosed through resorption of some extracellular matrix components, including bone resorption. Severe destruction of periodontal tissues is probably related to an increased activity of proteinases derived from the host, including collagenase and gelatinase [11]. Since epidermal growth factor (EGF) is an important activator of collagenase and gelatinase, its presence in the gingival tissues of the rats has been evaluated and confirmed [12]. In addition, expression of gingival EGF has been reported during inflammatory processes in rat. So, it appears EGF is an important mediator in the pathogenesis of periodontal diseases [13].

Successful and effective treatment of chronic periodontitis depends on early diagnosis of the disease. As a result, even in the case of aggressive periodontitis, too, early diagnosis might to a great extent prevent subsequent problems and disturbances resulting from the condition. It can be concluded that recognition of risk factors involved in the pathogenesis of the condition is one of the most important factors contributing to the diagnosis and effective treatment of any disease condition [7].

Saliva, serum, urine and GCF samples have been used for evaluation of periodontal diseases. Some evaluations have shown that serum and urine can only be used for differential diagnostic tests because they pass through different body parts and a large number of constituents are incorporated into or deleted from serum and urine during these passes. Saliva, too, has some problems in the firm diagnosis because it contains many constituents derived from various sources, including salivary glands, serum, GCF, bacteria and foreign bodies [14]. However GCF is superior to other sources because it is easy to collect using a non-invasive procedure and it contains some products derived from the host, dental plaque and the products resulting from their interaction.

This study was carried out to evaluate and compare EGF levels in the GCF samples of patients with gingivitis and advanced periodontitis.

II. Materials and Methods

a) Population Samples

The present cross-sectional/analytical study was conducted according to the guidelines of the Helsinki Declaration of 1975, revised in 2000. The research protocol was approved by the Ethics Committee of the Dental Research Center of Tehran University of Medical Sciences. The study population consisted of patients referred to the Department of Periodontics, Tehran University of Medical Sciences, between March 2012 and August 2013 intended for periodontal treatment teeth that met the inclusion and exclusion criteria of the study.

11 patients with advanced periodontitis (5 females and 6 males with an age range of 30 to 65 years) and 13 patients with gingivitis (7 females and 6 males with an age range of 20 to 47 years) were included in the study. None-random sampling technique was applied based on the subjects available.

b) Inclusion Criteria

The inclusion criteria for patients with advanced periodontitis were as follows: attachment loss of ≥ 5mm, periodontal pocket depth > 3 mm, radiographic signs of bone loss and thorough systemic health.

The inclusion criteria for patients with gingivitis were as follows: presence of gingival inflammation with bleeding on probing, no attachment loss, any characteristics of periodontitis, any history of previous scaling or root planing, absence of bone loss on panoramic radiographs, periodontal pockets depth of ≤ 3 mm and thorough systemic health.

Based on our previous study, the amount of GCF is absolutely low and in many cases we were not able to calculate it [18]. Therefore, healthy controls were not included in this study and the control was considered as zero.

c) Exclusion Criteria

The exclusion criteria consisted of a history of systemic diseases with an effect on periodontal tissues, use of antibiotics six month before the study, periodontal treatment during the previous year, pregnancy and lactation, history of any prophylactic procedures, smoking, and lack of patient compliance.

d) Registration of Data

The patients received explanations about the study design and consent forms were obtained. The demographic data of the subjects were recorded, which consisted of name, age, sex, occupation, educational status, presence of systemic conditions, use of antibiotics and frequency of use, pregnancy and lactation as well as a history of any periodontal treatment.

e) Ethical considerations

In the present study, samples were collected using sample non-invasive techniques after the subjects signed informed written consent forms. In addition, all the laboratory steps of the study on patient samples, except for sampling procedures, were carried out in the absence of the patients.

f) Registery of clinical examination

The clinical indices of plaque Index (PI), bleeding on probing Muhlemann and Son 1971 (BOP), periodontal pocket depth (PPD) and clinical attachment level (CAL) were measured using a Williams' probe (Hu-Friedy, Chicago, IL, USA).

Subsequently, the patients' panoramic radiographs were used to evaluate and record bone loss (vertical and/or horizontal) generally in each patient (Figure 1). If patients were suffering from BOP without any bone loss, then they were assigned to the gingivititis group and if in addition to BOP, advanced bone loss (Advanced periodontitis) were observed these subjects were assigned to the periodontitis group.

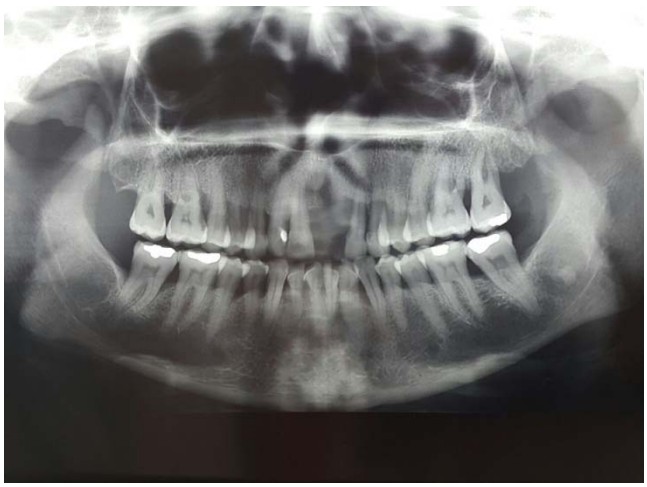

Figure 1 : Panoramic radiograph of a patient with advanced periodontitis.

Then, the number of teeth in each patient's mouth was recorded. Locations selected for sampling in the gingivititis and advanced periodontitis groups patients were 4 per-determined sites. (mesial, mid, distal aspect in buccal and mid lingual) , which included the deepest pocket in each quadrant and the following procedure was used to extract [15,16] GCF:

– Isolation of tooth/teeth with cotton rolls and placement of a strong saliva ejector
– Drying the teeth under question with an air syringe
– Removal of supragingival plaque, if any, with a curette
– Placement of absorbent paper pieces in the pre-determined locations

To this end, Whatman absorbent papers (P&R Labpak, united kingdom, catalog number #1001 110), which had previously been cut to 2×8 mm dimensions and sterilized in a dry oven, were used (Figure 2). Each paper strip was placed in a depth of 1 mm in the pocket for 1 minute (Figure 3).

Figure 2 : Whatmann absorbent papers.

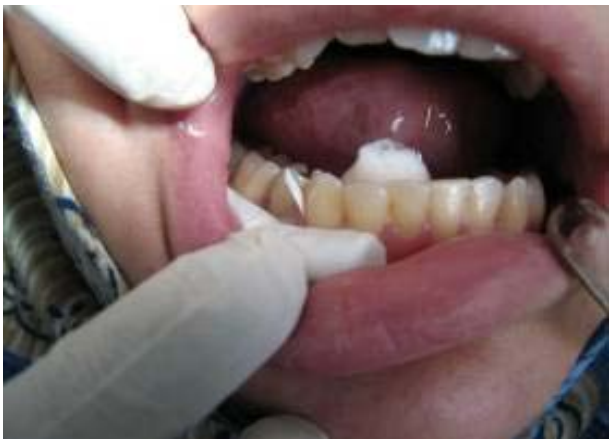

Figure 3 : Placement of absorbent papers in the pockets.

4 samples were collected and finally a sufficient amount of GCF was provided for measurements.

During the next stage, the absorbent papers were placed in Eppendorf tubes (manufactured by Eppendorf Company, UK catalog number #2015) containing Tris-HCL buffer solution (Rockland Inc., Limerick, Pennsylvania, USA.), immediately after the sampling procedure.

g) Laboratory procedure of samples and buffer preparation for ELISA test

The solution pH value was adjusted at 7.8 by stepwise adding of hydrochloric acid (0.5 mmol/L). Finally, the volume was adjusted at 100 mL by incorporating distilled water. Solutions produced this way are stable, capable of being preserved for a period of 6 months at -4°C. To achieve an identical test condition for all the samples, 300 μL of the solution was placed in each Eppendorf tube. The samples were preserved at -20°C in the laboratory until sufficient number of samples was collected for the use of an ELISA kit. Finally, the samples were simultaneously evaluated.

Before evaluation of the samples with ELISA, all the samples were placed in a mixer and homogeneously dissolved in the buffer solution. . In this way, each patient had only one sample for evaluation by ELISA.

h) ELISA Test

A standardized curve was used to determine the concentration of the samples in ng/mL.The labolatory steps of ELISA test procedurewas carried out carefully according to company instruction (R&D Systems, Minneapolis, MN, USA Catalog number # DEG00*).

i) Statistical analysis

SPSS 22 .0 was used for statistical analysis. To this end, central dispersion parameters of age and EGF levels of GCF were determined and reported. Independent t-test was used to compare EGF levels in the GCF samples of patients with gingivitis and advanced periodontitis at a significant level of $P<.05$. To determine the correlation of clinical parameters and EGF levels of GCF, Spearman's rho (2-tailed) test was used. Level of statistical significance for this test was set to $<.01$.

III. Results

Based on the results, evaluation of EGF levels in the GCF samples of the subjects showed that the mean levels in patients with gingivitis and advanced periodontitis were 68.07 ng/mL (SD=6.45) and 43.61 ng/mL (SD=.18), respectively (Table1). Independent t-test showed significant differences between the two groups of patients in EGF levels of GCF, with significantly higher levels in patients with gingivitis compared to those with advanced periodontitis ($P<.001$).

Table 1 : Central dispersion parameters of EGF in the GCF samples of patients with gingivitis and advanced periodontitis (ng/mL).

Group	No	Mean	SD	Std error	95% confidence interval	
					Upper bound	Lower bound
Gingivitis	13	68.07	6.45	1.79	71.97	64.17
Periodontitis	11	43.61	6.18	1.86	47.77	39.46

Clinical parameters of patients including PI, BOP, PPD, and CL for each study group are presented as mean ± SD in Table 2. Spearman rho (2-tailed) test showed significant correlation between PPD and EGF levels of GCF ($p<.001$) and also, between CAL and EGF levels of GCF ($P<.001$).(Table 3) Scatter plot of different levels of EGF in relation to PI, BOP, PPD, and CAL are shown in figures 4, 5, 6, and 7, respectively.

Table 2 : Mean ± SD of clinical parameters of patients for each study group.

	PI	BOP	PPD	CAL
Gingivitis	1.92 ± 0.76	28.46 ± 12.97	2.69 ± 0.48	0
Periodontitis	2.18 ± 0.87	35.45 ± 16.80	5.18 ± 1.16	5.45 ± 0.68

Table 3 : Correlation between EGF concentrations and clinical parameters.

		PI	BOP	PPD	CAL	Age
EGF	Correlation Coefficient	.063	.003	-.777**	-.866**	-.068
	Sig. (2-tailed)	.769	.990	.000	.000	.754
	N	24	24	24	24	24
PI	Correlation Coefficient		.147	.060	.209	-.113
	Sig. (2-tailed)		.493	.781	.328	.598
	N		24	24	24	24
BOP	Correlation Coefficient			.195	.129	-.156
	Sig. (2-tailed)			.361	.548	.467
	N			24	24	24
PPD	Correlation Coefficient				.831**	.009
	Sig. (2-tailed)				.000	.968
	N				24	24
CAL	Correlation Coefficient					-.063
	Sig. (2-tailed)					.769
	N					24

***Significant correlation*

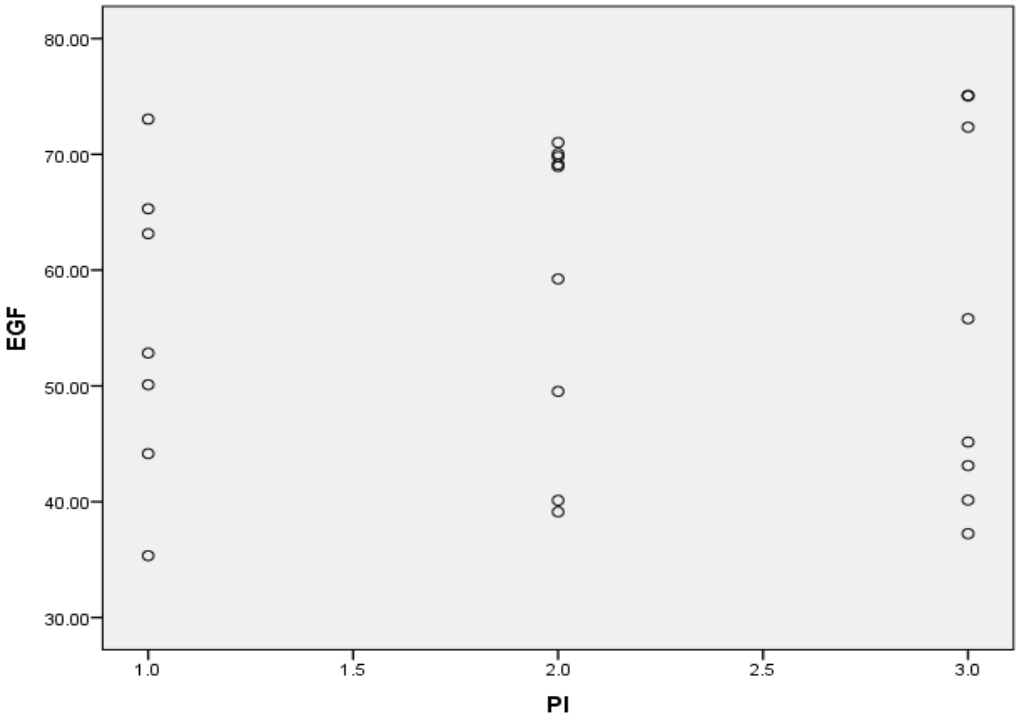

Figure 4 : EGF concentrations in individual plaque index values.

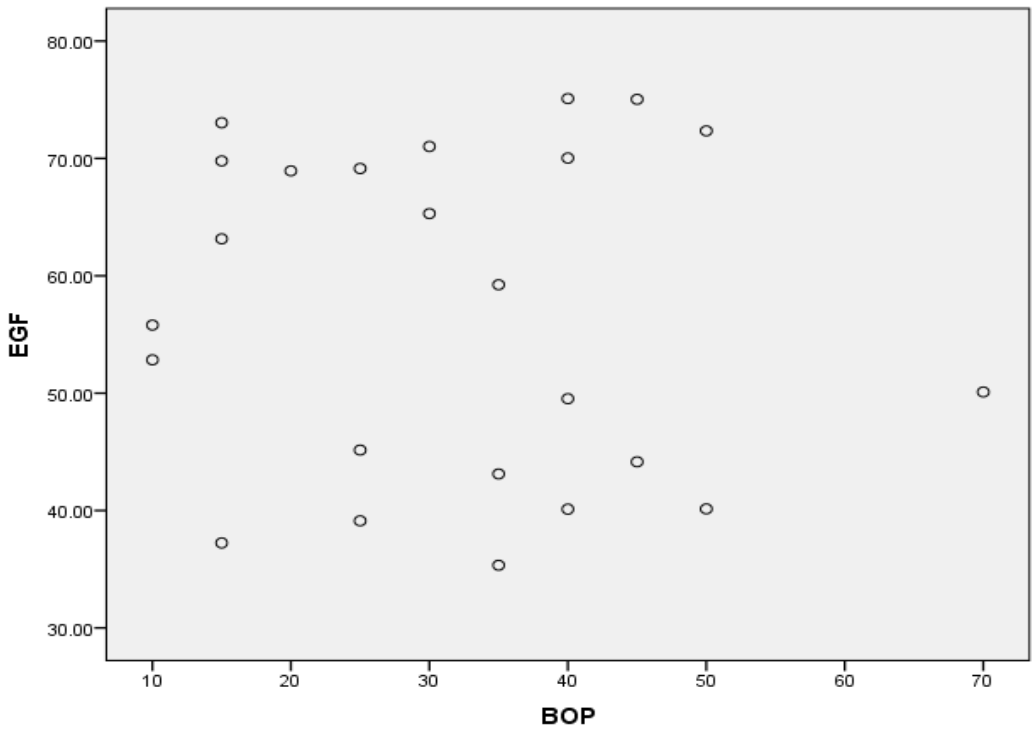

Figure 5 : EGF concentrations in individual bleeding for probing values.

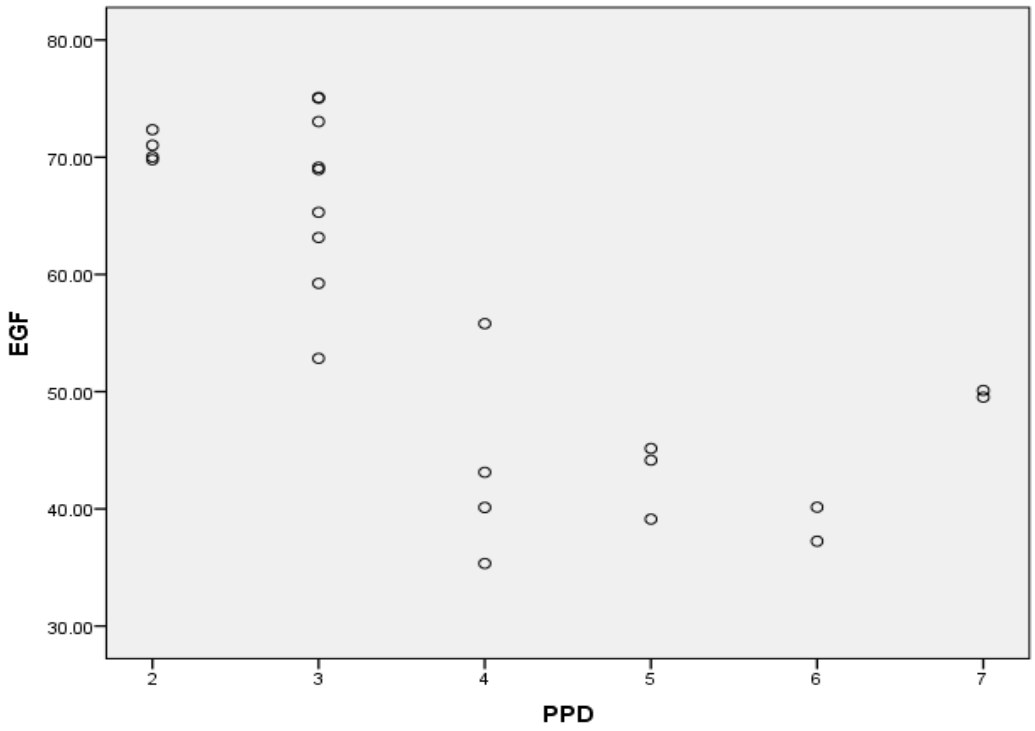

Figure 6 : EGF concentrations in individual probing pocket depth values.

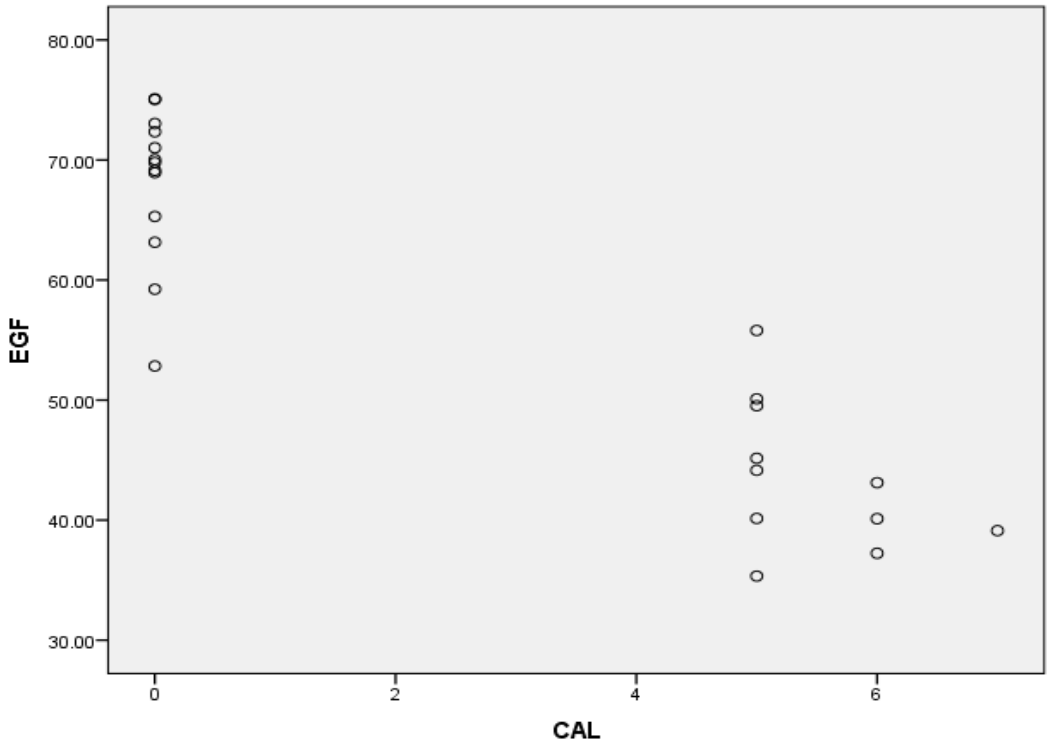

Figure 7 : EGF concentrations in individual clinical attachment loss values.

IV. Discussion

Evaluation of EGF in the GCF of patients revealed mean concentrations of 68.07 ng/mL and 43.61 ng/mL in patients with gingivitis and advanced periodontitis, respectively, demonstrating a significantly lower level of the factor in the GCF of patients with advanced periodontitis compared to those with gingivitis. Moreover, EGF concentrations in GCF have shown to be in significant negative correlation with PPD and CAL ($P<.001$). In other words, the concentration of EGF had significantly decreased with the progression of periodontal disease.

According to Oxford et al (2000) cells in the injured area or with periodontal disease are able to synthesize growth factors and can have an effective role in wound healing processes, evaluation of the mechanisms associated with the course of periodontal diseases or other oral manifestations is of great significance [17], although some studies [17, 18] demonstrated that the role of EGF in saliva may be similar to its role in GCF as a prognostic factor for periodontal disease, authors belive evaluating the EGF levels in GCF that carefully was isolated from the saliva contamination, can show more solidarity with progression of periodontal disease.

Moosavijazi et al (2014) reported that significant differences between the three understudy groups (patient with periodontitis and patient with gingivititis and healthy controls) in the salivary level of EGF, with a significant decrease in EGF levels with the progression of periodontal disease. Given a significant decrease in the salivary level of EGF in patients with periodontal disease, it appears that change in EGF level is an important mechanism associated with the pathogenesis of periodontal disease [18]. This conclusion is in agreement with our findings in the GCF. It is suggested to design studies in the future that can evaluate and compare EGF concentrations in saliva and GCF in different periodontal health conditions. By the suggested study design, we can find which one of saliva or GCF can be more helping in the determination of periodontal deterioration.

It must be stated that although commonly in studies where more than one cytokine evaluated, the concentration is adjusted for the whole mg of proteins, however, in the present study, only EGF was evaluated, Therefore, there was no need to adjust the concentration for the whole mg of proteins.In a study by Chang et al (1996), concentration of EGF in the GCF samples collected from deep pockets (≥5 mm) was reported to be approximately one-third of that in samples collected from shallow pockets (<5 mm) [19]. Since deep pockets have gingival indexes and GCF flow rates higher than those of shallow pockets, it appears this decrease in the concentration of EGF is associated with an increase in the severity of inflammation. The results of the present study confirmed the results of the mentioned study because there was a decrease in the EGF levels of GCF with an increase in PPD and CAL, which were higher in patients with periodontitis compared to patients with gingivitis. An increase in the GCF flow,

which is one of the complications of inflammation, might exert a dilutive effect on the concentration of EGF. This dilutive effect might also be attributed to an increase in its stasis in the area after an increase in its volume in the more superficial areas of the pockets or an increase in the permeability of vessels, leading to more leakage.

On the other hand, not all studies reported the same findings. Mogi et al (1999) evaluated and compared the concentrations of a number of cytokines including EGF in the GCF in different conditions of periodontal tissues. They found no statistically significant difference between EGF concentrations in comparison of healthy controls and periodontitis patients [20]. Laurina et al (2009) reported that the highest expression of growth factors and their receptors are found in the gingival epithelium in patients with periodontitis and at the same time, normal gingival tissues exhibit low levels of growth receptors compared to inflamed tissue [21].

Generally, growth factors are considered a kind of cytokines and it appears EGF has an important role in the pathogenesis of periodontal disease because it induces the production of plasminogen, collagenase and gelatinase activators [12,22]. Plasminogen activator can convert plasminogen into plasmin, which consists of a broad range of proteins and has the potential to decrease extracellular matrix components, such as laminin and fibronectin [12]. In addition, it can degrade collagen by activating latent collagenase [12]. Furthermore, EGF can increase endothelial cell migration and production of plasminogen activators, which are inhibited by TNF [23]. On the other hand, it has been shown that EGF can induce proliferation of epithelial cells in inflammatory periapical lesions [24]. This inductive activity might be effective in the proliferation of junctional epithelium during formation of periodontal pockets.

Since activators of collagenase, gelatinase and plasminogen and TNF, IL-1 and prostaglandin E2 all have a role in tissue destruction in periodontal diseases, including bone loss, the results of the present study, in relation to decreases in growth factor levels concomitant with the progression of periodontal disease, showed that EGF might be an important regulator of the pathogenesis of periodontal disease due to its complex reactions with the factors mentioned above.

The low molecular weight polypeptide, EGF, plays important roles in epithelial growth and differentiation and in wound healing by binding to a cell surface receptor. In 1991, the gingival specimens of periodontally healthy subjects and patients with adult (AP) and juvenile periodontitis (JP) were examined by immunohistochemistry and a monoclonal antibody (mAb) directed against the EGF receptor [25]. They reported that EGF receptors were highly expressed on the surface of basal cell layers of gingival epithelium. However, in normal junctional epithelium, specific labeling was faint or negative. These findings showed that receptors are poorly expressed or absent in these cells. Therefore, EGF is involved in control of epithelial growth and differentiation in periodontal tissues. Considering that EGF receptors have been studied [25], we suggest that future studies should be designed, so that the expression of gingival receptors of EGF together with other cytokines in different types of periodontal diseases to be evaluated. This will help in obtaining more accurate results.

The action of some polypeptide growth factors in patients with rapidly progressive periodontitis (RPP) during periodontal therapy was studied in 1995 using alloplastic grafts [26]. They measured the levels of epidermal growth factor (EGF), fibroblastic growth factor (FGF), platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF beta) in both blood serum and saliva. The results showed significant differences in the behaviour of growth factors in blood referred to EGF and PDGF. It was found that serum concentration of RPP patients were higher at the beginning of the study and after three months as compared to control group. On the other hand, the concentrations of EGF, PDGF and FGF were not significantly different in salivary samples as compared with control group.

Cytokines derived from resident and inflammatory cells during inflammation have important roles for diagnostic purposes. In 2003, the evidences of a study was released in which the area fraction (AA%) occupied by collagen fibers and the amount of cytokines including interleukin (IL)-1beta, IL-4, IL-6, tumor necrosis factor (TNF)-alpha, transforming growth factor (TGF)-beta, and epidermal growth factor (EGF) had been investigated [27]. They aimed to show correlation between such cytokines, collagen degradation, and the gingival index. The study was designed on culturing gingival tissue specimens of patients with mild, moderate and severe gingival inflammation to be compared to the samples obtained from healthy. The cytokines present in the culture media were then quantified by enzyme-linked immunosorbent assay (ELISA). They calculated then the area fraction (AA%) occupied by the gingival fibers through automated image analysis. Based on their results, significant differences were observed between means of AA% in examined groups for collagen fibers as compared to controls. They reported significant increases of IL-1beta (groups 3 and 4), IL-6, and TNF-alpha (group 3); a significant decrease of IL-4 (groups 2, 3, and 4) and TGF-beta (groups-2 and, 3); and no change of EGF. It was also reported that collagen AA% was significantly correlated with the amounts of IL-4 and TGF-beta, and significantly inversely correlated with the amounts of IL-1beta for all 3 inflamed groups and IL-6 and TNF-alpha for groups 2 and 3. It was concluded that EGF was not changed in inflamed gingival tissue

and that IL-1beta and IL-4 were particularly and intensively correlated with collagen loss. These results expressed that cytokines could be markers of clinical severity during active periodontitis.

It is suggested that detecting alternations in different compounds present in gingival crevicular fluid (GCF) could be considered as potent indicators of periodontal disease activity. In a 2006 study, human cytokine array V, was used in order to determine the profile of cytokines in GCF from chronic periodontitis patients and to be compared with healthy subjects [28]. Their statistically analyzed results showed the presence of only 10 cytokines in periodontally healthy sites, while this number raised to about 4 times (36 cytokines) in the cases with periodontal disorder. Among the evaluated cytokines, EGF and some others were reported to be significantly higher in diseased sites than healthy sites. In contrast to the present study in which a quantitative method was utilized, in the above-mentioned research a semi-quantitative one was used. So, it is not possible to compare the EGF concentrations between the two studies. Moreover, in the current study, EGF was found to be at lower amounts in periodontits in comparison to gingivitis. Overally, from the results of the above-mentioned and the present studies, it can be hypothesized that EGF expression in GCF will increase eventually as gingivitis emerges and then will decrease as periodontitis develops, but to a level still significantly higher than health condition. But this hypothesis has to be confirmed by further studies.

The effect of epidermal growth factor (EGF) on the expression of MMPs and TIMPs in cultured human gingival fibroblasts has also been reported [29]. It was found that MMP-1, 3, 7 and 11 expressions were increased at all EGF concentrations. However, at the lowest EGF concentration, MMP-1, 3 and 7 showed only small expression while MMP-11 presented the greatest expression. On the other hand, at higher EGF concentrations, MMP-1, 3 and 7 presented greater up-regulation, and MMP-11 lower up-regulation. The study suggested that EGF may play a role in periodontal destruction and wound repair.

Porphyromonas gingivalis is one of the most important periodontal pathogens. It has been shown that this bacteria have the ability to inactivate EGF by its peptidylarginine deiminase enzyme [30]. This finding may suggest a potential mechanism for the progression of periodontal disease. Because, based on the discussed articles, EGF has a protective role in the periodontium. Based on results of our present study, there is a significant decrease in EGF levels in the GCF with progression of periodontal disease from gingivititis to periodontitis. So, it may propose another potential mechanism for periodontal destruction; reduction in the quantity of EGF in the GCF. But this suggestion has to be confirmed by performing studies regarding the possible reasons for this reduction.

V. Conclusions

There is a significant decrease in EGF levels with exacerbation of periodontal disease. On the whole, given the significant decrease in EGF levels in the GCF samples of patients with periodontal disease, it is suggested that alterations in the concentrations of EGF in the GCF may predict the pathogenesis of periodontal diseases. Future studies regarding the effect of periodontal treatment on EGF concentrations in GCF samples of patients with periodontal disease is suggested.

VI. Acknowledgement

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Consent

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this study and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

Ethical Approval

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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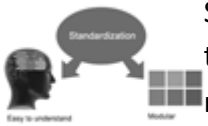

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21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

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.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

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33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

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.

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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.

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To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- 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
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

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· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

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

· Shun use of extra pictures - include only those figures essential to presenting results

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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.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
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- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

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The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- 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.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

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- 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.

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- Shape the theory/purpose specifically - do not take a broad view.
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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:

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- 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.

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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.

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- 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.
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- 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

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- 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

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- 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
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- Submit to generally acknowledged facts and main beliefs in present tense.

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Topics	Grades		
	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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