THE EFFICACY OF SYSTEMIC ENZYME THERAPY FOR EDEMA CONTROL IN MANDIBULAR THIRD MOLAR IMPACTION SURGERY

Dissertation Submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment for the Degree of

MASTER OF DENTAL SURGERY

BRANCH III

ORAL AND MAXILLOFACIAL SURGERY

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THE TAMIL NADU Dr. MGR MEDICAL UNIVERSITY CHENNAI

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled **"THE EFFICACY OF SYSTEMIC ENZYME THERAPY FOR EDEMA CONTROL IN MANDIBULAR THIRD MOLAR IMPACTION SURGERY"** is a bonafide and genuine research work carried out by me under the guidance of **Prof.Dr. B.VIKRAMAN, M.D.S.,** Professor and Unit Head, Department of Oral & Maxillofacial Surgery, Ragas Dental College and Hospital, Chennai.

Date:

Place: Chennai

Dr. N. Sriram Choudary
Post Graduate Student
Department of Oral & Maxillofacial Surgery
Ragas Dental College and Hospital
Chennai

CERTIFICATE

This is to certify that this dissertation titled **"THE EFFICACY OF SYSTEMIC ENZYME THERAPY FOR EDEMA CONTROL IN MANDIBULAR THIRD MOLAR IMPACTION SURGERY"** is a bonafide record of work done by **Dr. N. Sriram Choudary** under our guidance and to our satisfaction during his postgraduate study period **2013-2016.**

This Dissertation is submitted to **THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY,** in partial fulfillment for the award of the Degree of **MASTER OF DENTAL SURGERY– ORAL AND MAXILLOFACIAL SURGERY, BRANCH III.** It has not been submitted (partial or full) for the award of any other degree or diploma.

Guided by:

Dr. B. Vikraman, M.D.S.,
Professor & Unit Head
Dept of Oral & Maxillofacial Surgery
Ragas Dental College & Hospital,
Uthandi, Chennai.

Dr. M. Veerabahu, M.D.S., IBOMS.,
Professor and Head
Dept of Oral & Maxillofacial Surgery,
Ragas Dental College & Hospital,
Uthandi, Chennai

Dr. S. Ramachandran, M.D.S.,
Principal
Ragas Dental College & Hospital
Uthandi, Chenna

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ABSTRACT

PURPOSE:

The purpose of this prospective study was to determine the efficacy of systemic enzyme therapy for edema, mouth opening, and pain control in impacted mandibular third molar surgery.

MATERIALS AND METHODs: -

42 mandibular 3rd molar impactions assigned to the study (14 for each group – A, B, C). Systemic enzyme therapy administered postoperatively and compared between study groups A (Disperzyme) & B (phlogam) and control group C on 1st, 3rd, 5th postoperative days for changes in facial swelling, mouth opening and visual analog scale as parameters and analysed statistically.

RESULTS:

FACIAL SWELLING ASSESSMENT:-

The Disperzyme group exhibited an increase in facial swelling by 11% on day 1, gradually the swelling reduced to 7% on day3 , on day 5 still a 3% increase in facial swelling from actual measurements were noted, there by the study group reduced 8% of total increase in swelling from post-operative day1.

The Phlogam group exhibited an increase in facial swelling by 11% on day 1, gradually the swelling reduced to 7% on day3 , on day 5 still a 3%

increase in facial swelling from actual measurements were noted, there by the study group reduced 8% of total increase in swelling from post-operative day1.

The control group exhibited an increase in facial swelling by 15% on day 1, gradually the swelling reduced to 9% on day3 , on day 5 still a 7% increase in facial swelling from actual measurements were noted, there by the Control group reduced 8% of total increase in swelling from post-operative day1.

MAXIMUM MOUTH OPENING ASSESSMENT:-

The disperzyme group exhibited a mean mouth opening of 57% (31.43mm) on day1, increasing to 69% (37.93mm) on day3, reaching a maximum mouth opening of 78% (42.43mm) on day5.

The Phlogam group exhibited a mean mouth opening of 58% (29.29mm) on day1, increasing to 68% (34.36mm) on day3, reaching a maximum mouth opening of 79% (39.86mm) on day5.

The Control group exhibited a mean mouth opening of 40% (20.86mm) on day1, increasing to 49% (25.14mm) on day3, reaching a maximum mouth opening of 55% (28.21mm) on day5.

VISUAL ANALOG SCALE (PAIN ASSESSMENT):-

In Disperzyme group, patients reported with moderate pain in post-operative day 1 with mean value of 4 on VAS, which gradually reduced to

mean value VAS score of 1 on day 3 which remained to be at VAS score of 1 till day5.

In Phlogam group, patients reported with moderate pain in post-operative day 1 with mean value of 5 on VAS, which gradually reduced to mean value VAS score of 3 on day 3 & remained to be at VAS score of 1 till day 5.

In Control group, patients reported only mild pain in post-operative day 1 with mean value of 3 on VAS, which gradually reduced to mean value VAS score of 1 on day 3 which remained to be at VAS score of 1 till day 5.

CONCLUSION:

The control group had statistically significant residual edema of 4% when compared with study groups, concluding that **SYSTEMIC ENZYME THERAPY (SET)** is comparatively efficient in reducing edema than NSAID's.

The study groups have shown significant statistical difference with improved mouth opening by 23.5% (12.93mm) when compared with control group, concluding that systemic enzyme therapy (SET) is comparatively efficient for mouth opening than NSAID's.

Subjective assessment of pain using visual analog scale revealed mean score of 4.5 (moderate pain) for both study groups , while control group mean score of VAS was 1 (mild pain) on follow-ups, Concluding that control group - NSAID'S was better in reducing pain than the study groups

KEY WORDS:

mandibular third molar surgery, complications of mandibular third molar surgery, methods for edema control, routes of drug administration, role of NSAID'S, steroids, and systemic enzyme therapy.

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Introduction

INTRODUCTION

Removal of mandibular third molar teeth is the most commonly and frequently performed dentoalveolar surgery in Oral & Maxillofacial Surgery.

It requires sound understanding of surgical principles and patient management skills. The surgical procedure is considerably traumatic to the

1) Alveolar bone
2) The surrounding musculature attached to the bone encircling third molar

Various surgical tools are employed to remove third molars like Bi-beveled chisel, Burs, Peizo & Laser. But though the procedure of surgery – Flap incision, Flap elevation, Flap Retraction, Bone removal, Tooth sectioning remains the same.

Leading to considerable post-operative pain, swelling, edema, trismus, resulting in bed rest, absence to work, & reduced food intake - which therefore becomes essential in management thereby improving quality of life & enhancing speedy recovery from extra oral swelling, pain & to deliver improved mouth opening at the earliest.

Existing protocols described & followed widely to decrease postoperative swelling are – application of pressure dressings & ice packs,

modification by surgical method, modified placement of suture & drain tubes, post-operative medications.

Current medical management that is widely followed, with certain limitations or contraindication to control edema in oral surgery are

1) NSAIDS
2) Steroid therapy
3) Systemic Enzyme Theraphy

The proteolytic properties exhibited by enzyme tablet DISPERZYME to control edema, are

1) Trypsin (96mg)
2) Bromelian (180mg)
3) Rutoside Trihydrate (200mg)

Trypsin:- acts as a thrombolytic and fibrinolytic agent, thus cleaving the fibrin mantle and ensuring proper blood flow during wound healing.

Bromelian:- converts plasminogen into plasmin, exerting mild anti-inflammatory and antiedematous effects.

Rutoside trihydrate:- increases the strength of the walls of the blood capillaries and regulates their permeability to normalize pathologically increased vessel

permeability. It also has antioxidant activity and anti-inflammatory, antihistaminic, and antiviral properties.

"The present study is designed to assess the efficacy of Systemic Enzyme Therapy for edema control in mandibular third molar impaction surgery between DISPERZYME & PHLOGAM as post-operative medications"

Aims and Objectives

AIMS AND OBJECTIVES

AIMS:

The aim of this study is to determine the efficacy of systemic enzyme therapy for the control of edema following removal of impacted mandibular third molars.

OBJECTIVES:

Pre & Post-operative measurements at fixed anthropometric points in face among the study groups & control group will be recorded

Clinical assessment of extension of swelling

Clinical assessment of range of mouth opening

Clinical assessment of pain felt

Review of Literature

REVIEW OF LITERATURE

Couch JF et al (1952): Rutin content of Sophora japonica L explains that Rutoside trihydrate increases the strength of the walls of the blood capillaries and regulates their permeability to normalize pathologically increased vessel permeability. It also has antioxidant activity and anti-inflammatory, antihistaminic, and antiviral properties.

Vangool and Tenbosch (1977) state that the relation between Sectioning, Position and Width was emphasized by the finding that surgical removal of third molar was followed by more edema when the greatest width of the tooth was surrounded by bone.

According to David et al (1982) the swelling & pain was significantly greater in primary closure for 5 days following surgery than in secondary closure. Following the fifth postoperative day, no difference was observed in patient discomfort between the two groups.

Dubois et al (1982) concluded that primary closure technique gave rise to more postoperative problems than secondary closure technique. Secondary closure was found to minimize swelling and pain, helping to reduce discomfort.

Mohamed A et al (1983) says tight suturing and primary closure in third molar surgery will give rise to more postoperative discomfort to the patient

Miles M, et al (1985) The results suggest that the method was accurate to within 5% in measuring swellings of known volume. The reproducibility of replicate measures also showed a low level of error (3.3%)

Roynesdal et al (1993) talks about the effect of soft laser application on postoperative morbidity after 3rd molar surgery, it was concluded that soft-laser treatment has no beneficial effect on swelling, trismus, and pain after third molar surgery.

S. Schultze-Mosgan et al (1995) state that ultrasound was directly assessing the Facial swelling by increased the distance between the mucosa and the skin surface produced by edema as the ultrasound was quick, noninvasive and time saving method also where as other method such as visual analog scale, photograph, stero - photograph and face- bows are indirect assessment of Facial swelling of skin.

Rakprasitkul et al (1997) discusses the postoperative problems, in general, were less in the small surgical drain group as compared to the no drain group.

Esen, FerdaTasar (1999) sate that Ultrasound and CT were among the most accurate diagnostic techniques. These techniques made it possible to performed precise measurements of the facial soft tissues. However, during examination of the soft tissue with ultrasound, some alterations occurred in the measurement because the transducer was applied with a slight pressure. CT

examination ensured the visualization of the soft tissue in a passive state, and it was more reliable for measurement of edema. Also because of the diffused characteristic of edema, it was best detected on 2 dimensional CT scans.

Emin E et al (1999) clarifies one of the factors most closely linked to the intensity of postoperative pain & swelling is the type of healing of the surgical wound

Suarez-Cunqueiro et al (2003) compares the paramarginal and marginal flaps in surgical extraction of lower impacted 3rd molars and found no statistically significant difference in using the two.

Bui C et al (2003) states overall complication rate was 4.6%. The operative and inflammatory complication rates were 2.2 and 7.5% respectively. Complications were generally minor (91.9%) and were managed non-operatively on an outpatient basis. Major complications (8.1%) were mostly inferior alveolar nerve injuries. All nerve injuries except 1, resolved within 1 year.

According to Sugiura et al (2004) third molars are the most commonly impacted teeth and their removal is one of the most commonly performed procedures by an Oral and maxillofacial surgeon, even today.

Arteagoitia et al (2005) compare the use of Amoxicillin/Clavulanic acid versus placebo, after 3rd molar surgery and concluded by reporting an increased chance of being affected with Infective endocarditis in the placebo group, than the antibiotic group.

D. Pasqualine et al (2005) has conducted a comparative study and concluded that Pain and swelling were less severe with secondary healing than with that of primary healing.

According to Grossi et al (2007) Serious infections and permanent nerve damage occurred at a very low rate, but they were considered as the most severe complications after third molar surgery.

Al-Khateeb TH et al (2007) significant reduction in the extent of cheek swelling and pain intensity in the seratiopeptase group at the 2nd, 3rd and 7th postoperative days, but no significant difference in mean maximal interincisal distance was found between the 2 groups.

Baqain et al (2008) concluded that the postoperative morbidity increases with increasing age, deeper level of impaction, longer procedures and the impaction side differing from the handedness of the operator.

Forouzanfar et al (2008) in a single blinded randomized controlled trial, talk about ice compression being a valuable tool in reducing postoperative pain after 3rd molar surgery.

Sortino et al (2008) reported a statistically significant decrease in postoperative swelling and trismus, but an increase in time by 25.83% in the piezosurgery group compared to the rotary osteotomy group, in surgical removal of impacted mandibular third molars.

Chang A, (2009) describes trypsin acts as a thrombolytic and fibrinolytic agent, thus cleaving the fibrin mantle and ensuring proper blood flow during wound healing.

Chang A, et al (2009) states bromelian:- converts plasminogen into plasmin, exerting mild anti-inflammatory and antiedematous effects.

Danda et al (2010) have said that the patients in the secondary closure group had a significantly lesser amount of pain and swelling postoperatively than the primary closure group.

Dolanmaz D, Esen A, Isik K, Candirli C (2012) evaluate 2 flap designs (envelope and modified triangular flap) for postoperative pain and swelling after mandibular impacted third molar surgery and showed that there were no significant differences between the 2 incision techniques regarding post operative pain and swelling ($P > .05$).

Vikram Shetty, MBBS, DNB, MDS,* and Amit Mohan, (2013) MDS conclude that systemic enzyme therapy significantly decreases postoperative edema in orthognathic surgery, precluding long-term corticosteroid use.

Materials and Methods

MATERIALS AND METHODS

The present study was conducted at the Department of Oral and Maxillofacial Surgery, Ragas Dental College and Hospitals, Chennai.

Forty two patients who had given their consent were randomly assigned to 3 groups (A,B & C), requiring surgical removal of impacted mandibular third molars under Local anaesthesia. The study is a prospective study & approved by IRB committee.

The primary outcome variables were swelling, Mouth opening, pain. These were recorded on the first, third and fifth postoperative days respectively.

INCLUSION CRITERIA:-

- Group A, B, C - All impacted, partially impacted mandibular third molars indicated for trans-alveolar extraction.
- Age group – individuals from 18 years to 35 years with no medical history.
- Patients who are willing to participate in study and report for follow up visits.
- Procedure completed within 45 mins.

EXCLUSION CRITERIA:-

- Pregnant or lactating mothers.
- History of smoking,
- alcohol consumption habits.
- Systemic conditions – un-controlled Diabetes, Renal, Hepatic, Cardiac, Bleeding disorders.
- Acute infection in the area of surgery.
- Males with beard due to differences that might lead to error in linear measurements.
- Patients unwilling to commit post-operative follow up visits
- Procedure that lasted more than 45 mins.

CASE SHEET IMPACTION

OP NO: ***DATE:***

NAME: ***AGE/SEX:***

OCCUPATION: ***RELIGION:***

ADDRESS:

CHIEF COMPLAINTS AND DURATION:

HISTORY OF PRESENT ILLNESS:

PAST MEDICAL HISTORY:

PAST DENTAL HISTORY:

PERSONAL HISTORY:

GENERAL EXAMINATION

CLINICAL EVALUATION:

ERUPTED / PARTIALLY ERUPTED / NON ERUPTED

INTERPRETATION OF RADIOGRAPH:

PELL AND GREGORY'S CLASSIFICATION

CLASS II ***CLASS III***

POSITION B ***POSITION C***

INVESTIGATIONS:

DIAGNOSIS:

TREATMENT PLAN:

CONSENT FORM

Date:-

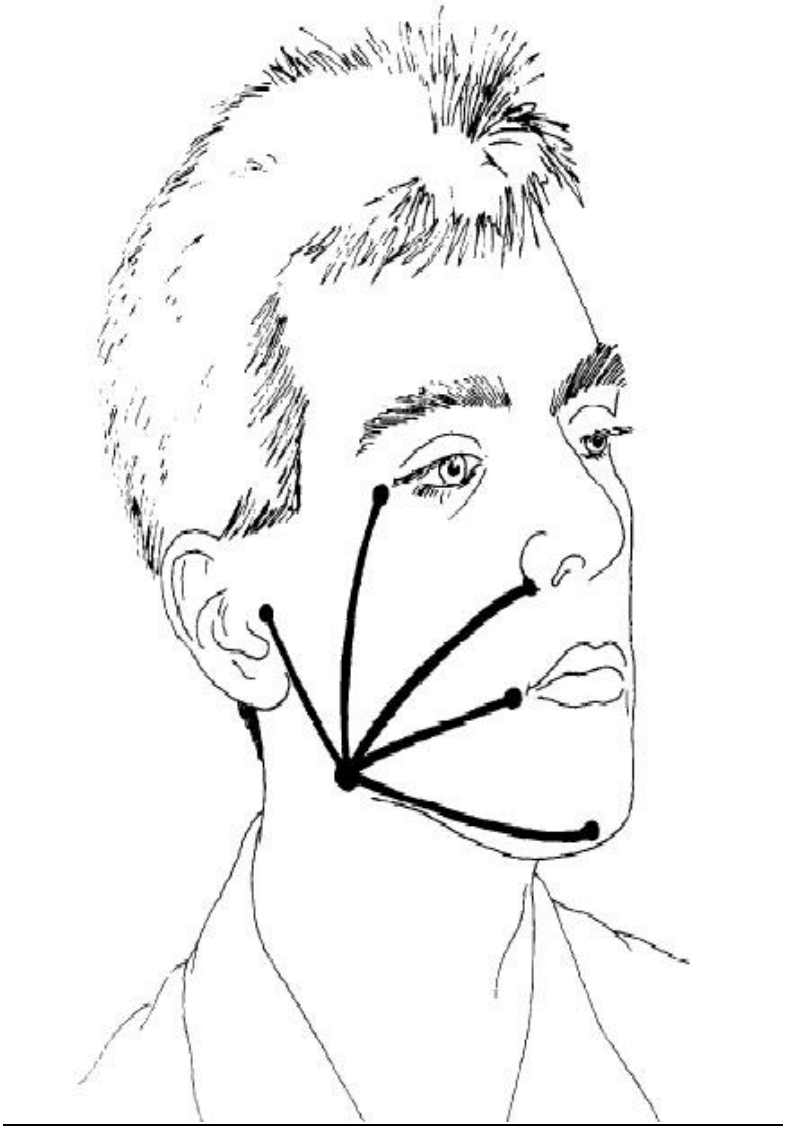
Name :- Age/Sex:-

Address :- Mob:-

1. I have been explained in detail regarding the surgical complications of removing impacted teeth in detail, including post-operative swelling.
2. I understand that post-operative medications are compulsory for management of post-operative swelling.
3. The choice using of "Systemic Enzyme Therapy" in managing post-operative swelling was explained to me.
4. I know that drug may cause adverse reactions like vomiting, gastritis, diahorrhea, allergy just as any other regular drugs.
5. I understand that radiographs (OPG, IOPA) are necessary & would be taken to study third molar eruption, angulation against the adjacent second molar.
6. I am aware that the surgical procedures would be performed by postgraduate residents of oral and maxillofacial surgical unit.
7. I therefore state to clearly understand the intended purpose and consent to be on "Systemic Enzyme Therapy" as prescribed by the surgeon in managing post-operative swelling.

Signature of the Guardian Signature of the Patient

FACIAL SWELLING ASSESSMENT



Linear measurements were made using inch tape at fixed anthropometric points in face pre-op and post-op for assessing the facial swelling following surgical procedure.

Tick the prescribing post-operative medication

• Disperzyme	• Phlogam	• Control

EDWARD, A. NEUPERT et al assessment chart

Pre-operative:- (in mm)	Post-operative:- 1st, 3rd, 5th days		
Gonion – Tragus –			
Gonion – L.Canthus –			
Gonion – Alar base –			
Gonion – Commisure –			
Gonion – Pogonion -			

MAXIMUM MOUTH OPENING ASSESSMENT

(Inter-incisal distance between 11–41)

Pre- op	Post-op Day - 1	Post – op Day - 2	Post – op Day - 3

(Measurements in mm)

Visual Analog Scale (VAS)

1st post-op day	2nd post-op day	3rd post-op day

QUALITY OF LIFE QUESTIONNAIRE

1. Morning stiffness:-

(i) Significant (ii) Moderate (iii) Insignificant

2. Disturbed sleep: - (i) Yes (ii) No

3. Pain on palpation extra orally: –

Musculotendinous pain, (i) Yes (ii) No

4. Pain on physiological movements

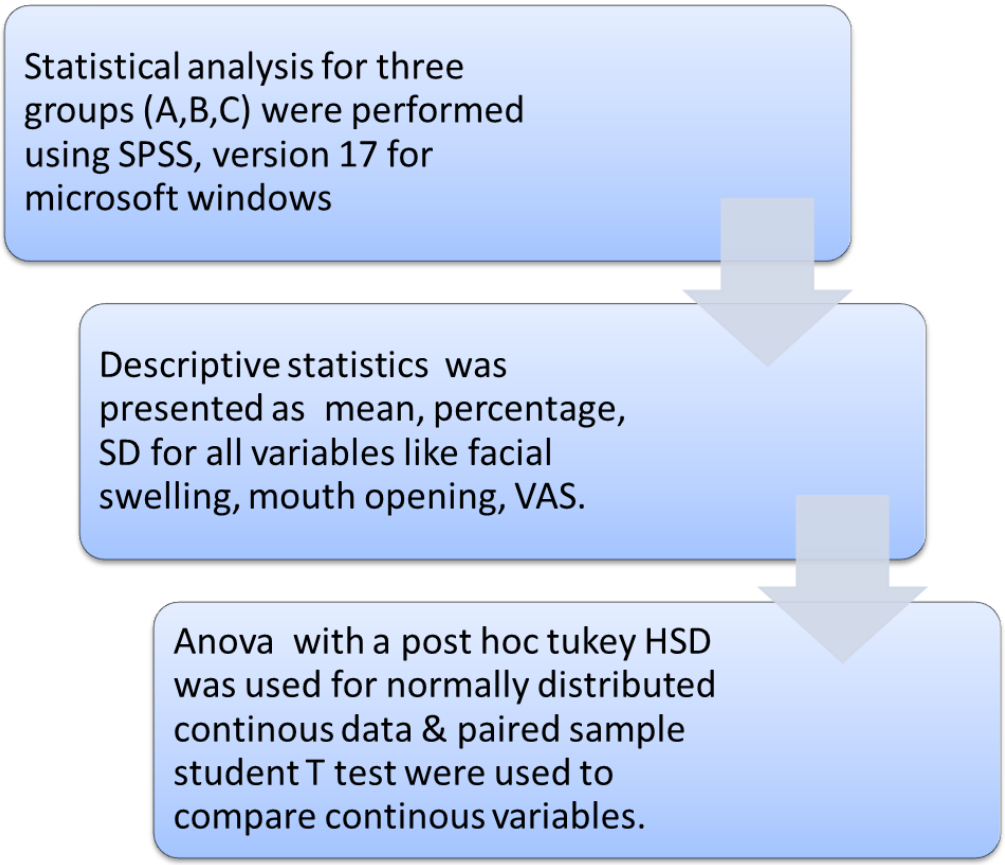
(i) Speech (i) Eating

5. Has your appearance changed since the surgical procedure?

(i) Yes (ii) No

Patient's signature

All statistical analysis was performed using Statistical Package for Social Science (SPSS, version 17) for Microsoft windows. The data were normally distributed. And therefore parametric tests were performed. Descriptive statistics were presented as numbers and percentages. The data were expressed as Mean and SD.A one way analysis of variance with a post hoc Tukey HSD was used for normally distributed continuous data. Paired sample student t test were used to compare continuous variables within groups. A two sided p value < 0.05 was considered statistically significant.



Surgical Protocol

ARMAMENTARIUM:-

- 2% Lignocaine with 1:80,000 Adrenaline
- 3ml Unolock syringe (Luer lock safety system)
- No #15 Bard Parker scalpel with no #3 handle
- No #9 Molts periosteal elevator
- Howarths periosteal elevator
- Rubber mouth prop
- Austins cheek retractor
- Tongue depressor
- Marathon Ki-20 surgical motor & straight handpiece (Korea)
- No #702 & #703 SS white burs (USA)
- Couplands elevator
- Tooth delivery forceps – molars
- Bone file
- Toothed forceps
- Fergusson's suction tip
- Curved needle holder
- 3-0 silk suture material as it encourages patient to report for suture removal on 7th post op day.

MEDICATIONS:-

- Tab. Disperzyme (Trypsin-96mg, Bromelion-200mg, Rutoside Trihydrate-100mg)
- Tab. Phlogam (Trypsin-48mg, Bromelion-100mg, Rutoside Trihydrate-50mg)

Surgical Procedure:

All the patients underwent surgical removal of impacted mandibular third molars under local anesthesia performed by final year post graduates with same level of experience and surgical handling skills.

Inferior alveolar nerve, lingual nerve and the long buccal nerve block was administered on the indicated side.

Using Bard parker scalpel no #15 & handle no #3, a standard Ward's incision was made. A Molts periosteal elevator was used to reflect muco-periosteal flap from distal aspect of second molar extending mesially over the releasing incision & distally along the external oblique ridge.

Using Howarth's, the flap was adequately raised on all planes to access adequate surgical field & placed sub-periosteally on lingual aspect of mandibular ramus, thereby protecting the lingual nerve from any possible inadvertent iatrogenic injury caused by high speed surgical burs.

A Rubber mouth prop of proper size was placed between the teeth on the contralateral side and patient asked to bite on, to maintain adequate mouth opening during surgery. This step relieves constant muscle strain, thereby increasing cooperation in terms of decreased muscle fatigue. The other end of the chain is rolled over the lingually placed howarth elevator, thus stabilizing the howarth in place & securing the mouth opening for surgery.

Marathon Ki-20 surgical motor & straight handpiece (Korea) was used in 1:1 gear ratio @ 40,000rpm to remove overlying bone if present followed by minimal buccal guttering with SS White #702 bur (USA) from mesial aspect of third molar till the entire distal bone is relieved maintaining close proximity to the crown structure under constant irrigation of sterile isotonic Saline solution. In certain cases, the distal cusp of crown was sectioned tangentially to facilitate easy removal of distal bone close to crown structure.

At this juncture, a buccal groove in between second and third molar is deepened if necessary. Tooth is luxated with a Couplands elevator by using the groove and/or the buccal bone as fulcrum before sectioning. The tooth was extracted in full or after sectioning, bony margins were checked for sharp edges using index finger palpation & smoothened with bone file. The wound was irrigated with Betadine mixed sterile isotonic solution as an antisepsis measure & also to flush out if any possible bone or tooth chips displaced into socket inadvertently during bone trephining or tooth sectioning.

The gingival margins were approximated & trimmed and secured using non-absorbable black 3-0 silk suture at mesial, distal, relieving incision to attain closure, subsequently removed after a week.

Postoperatively, Group A patients received Cap. Amoxycillin 500 mg thrice daily, Tab. Metronidazole 400 mg thrice daily and Tab. Dolo 500 mg twice daily. Tab. Disperzyme twice daily 30 mins before food & Tab. Rantac 150mg twice daily 30 mins before Food - (Course of 5 days)

Group B patients received Cap. Amoxycillin 500 mg thrice daily, Tab. Metronidazole 400 mg thrice daily and Tab. Dolo 500 mg twice daily. Tab. Phlogam twice daily 30 mins before food & Tab. Rantac 150mg twice daily 30 mins before Food - (Course of 5 days)

Group C patients received Cap. Amoxycillin 500 mg thrice daily, Tab. Metronidazole 400 mg thrice daily and Tab. Dolo 500 mg twice daily. Tab. Rantac 150mg twice daily 30 mins before Food - (Course of 5 days)

All patients were recalled for linear measurements between anthropometric points in face & VAS forms were recorded on 1^{st}, 3^{rd} and 5^{th} day after the surgery. Quality of life questionnaire was also filled by the patient.

Figures

Fig.1: LANDMARKS OF FACIAL ANTHROPOMETRIC POINTS

- **1.Gonion (Go)**
  2.Tragus (Tr)
  3.Lateral canthus (Lc)
  4.Ala of Nose (Al)
  5.Commisure (Co)
  6.Pogonion (Po)

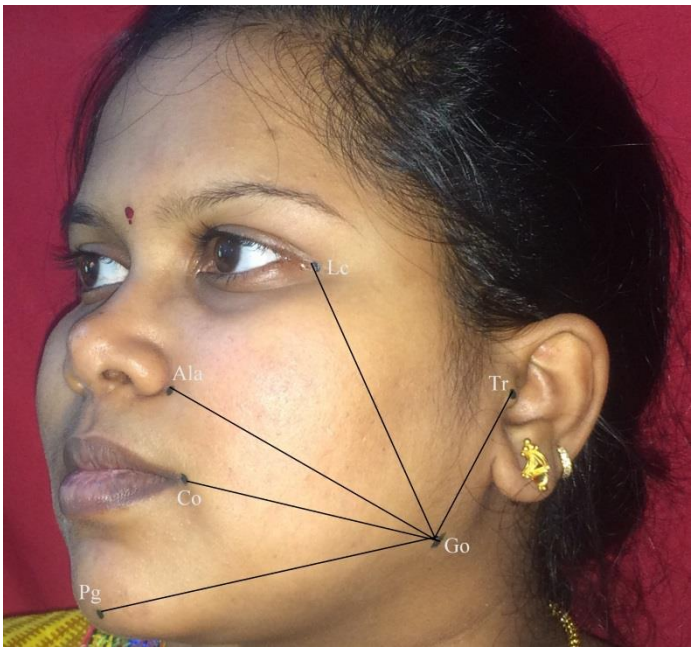


Fig.2: GONION – POGONION LINEAR MEASUREMENT

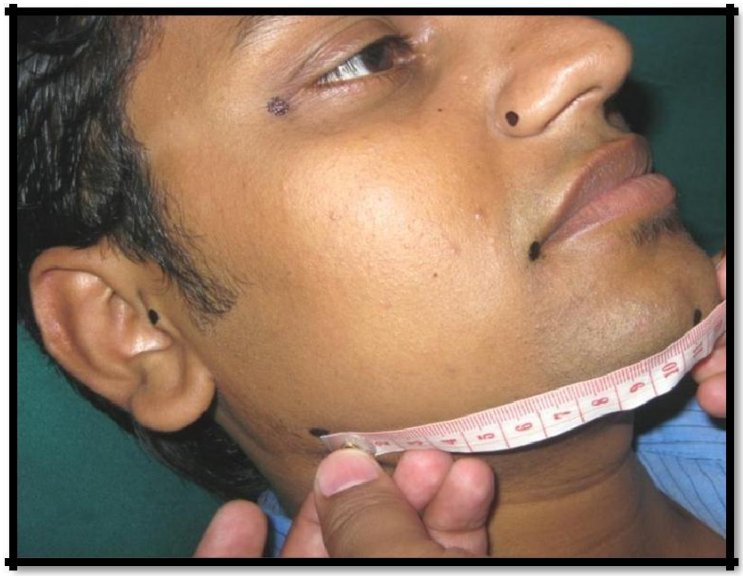


Fig.3: GONION – COMMISURE LINEAR MEASUREMENT

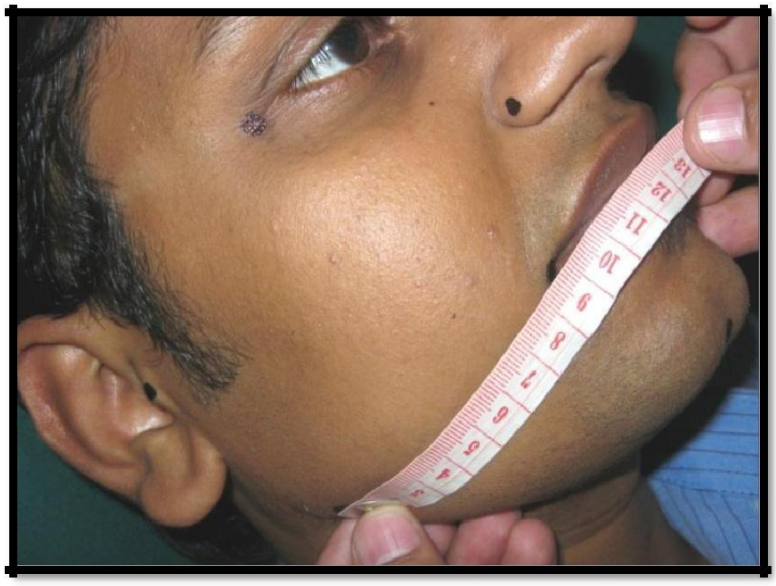


Fig.4: GONION – ALA LINEAR MEASUREMENT

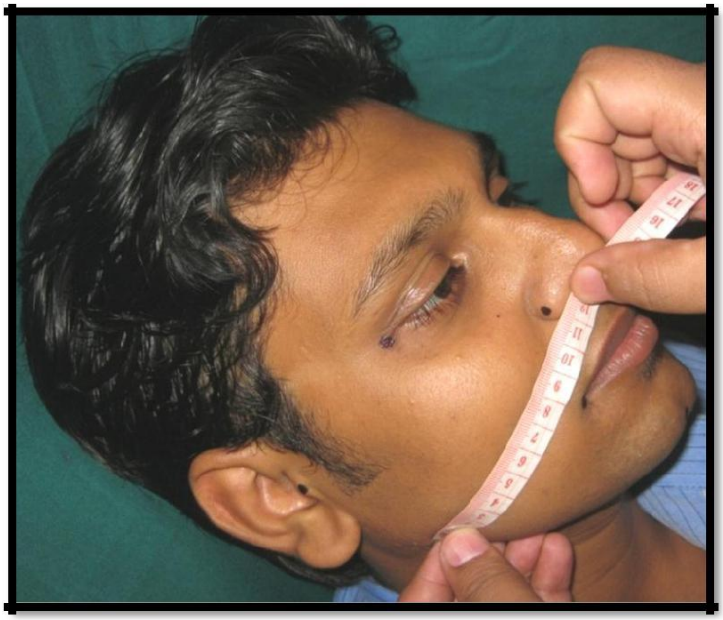


Fig.5: GONION – L.CANTHUS LINEAR MEASUREMENT

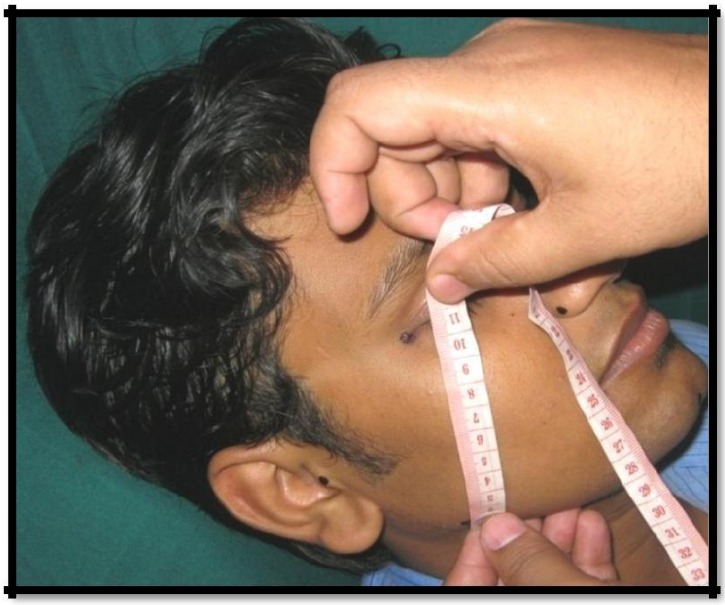


Fig.6: GONION – TRAGUS LINEAR MEASUREMENT

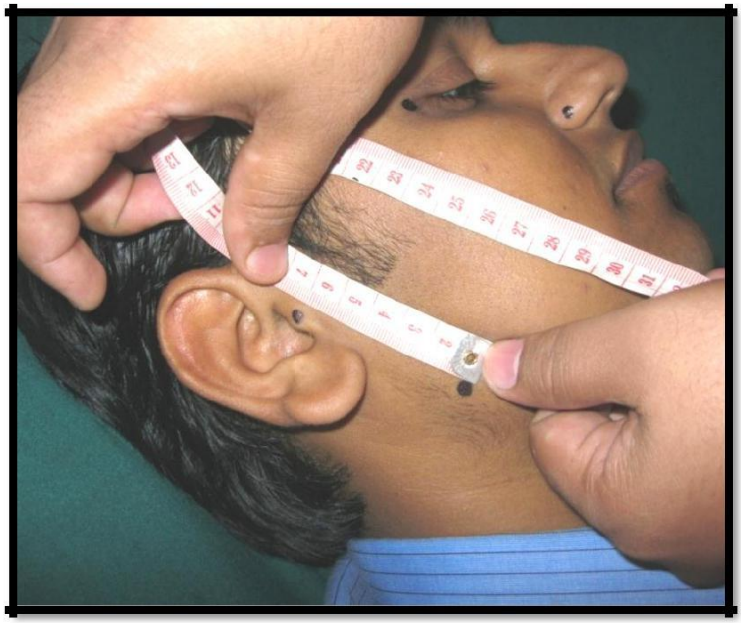


Fig.7: MEASUREMENT OF MAXIMUM MOUTH OPENING WITH VERNIER CALIPER

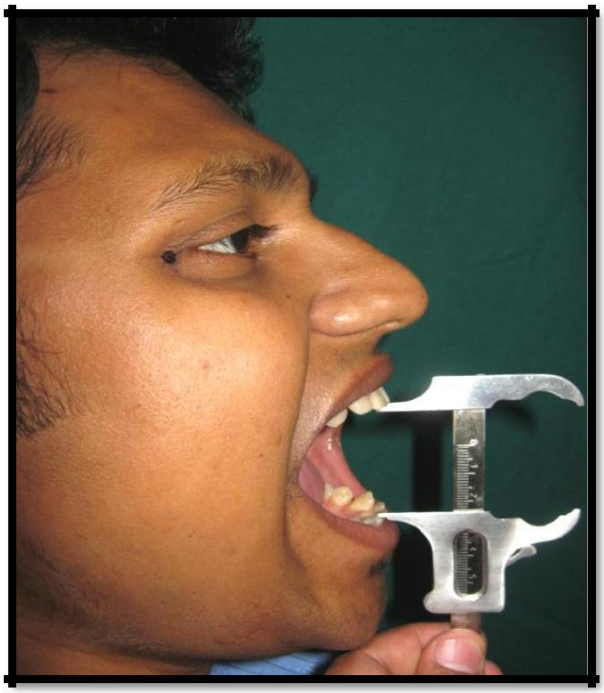


Fig.8 A: OPG (48 indicated for impaction)

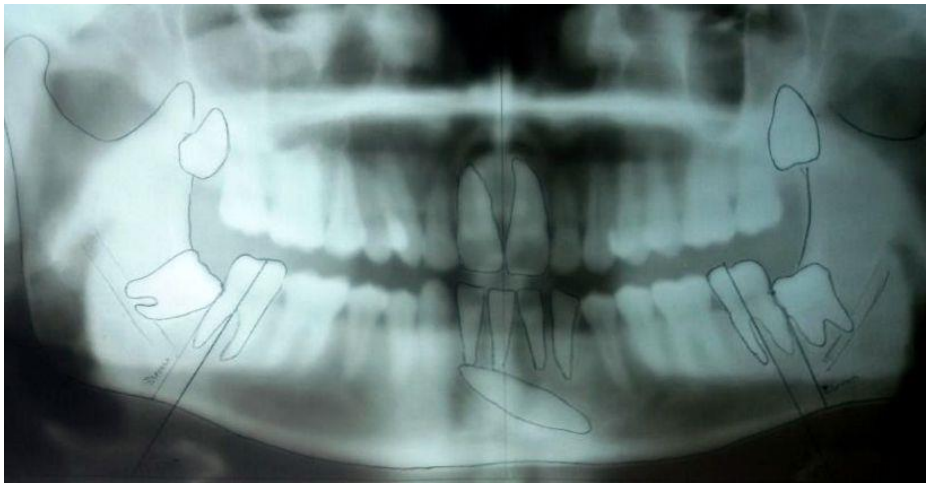


Fig.8 B: OPG (38 indicated for impaction)

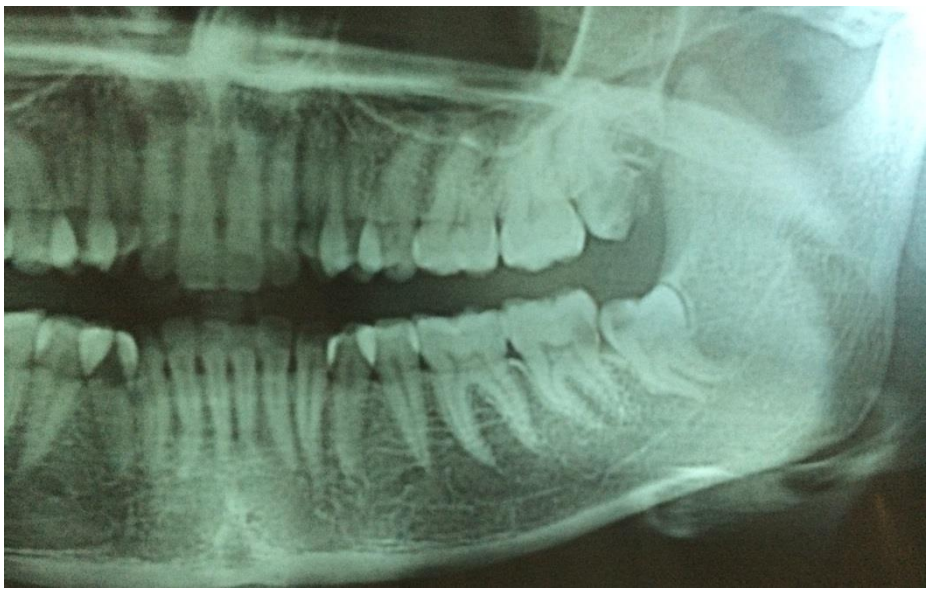


Fig.9 A: SURGICAL INSTRUMENTS

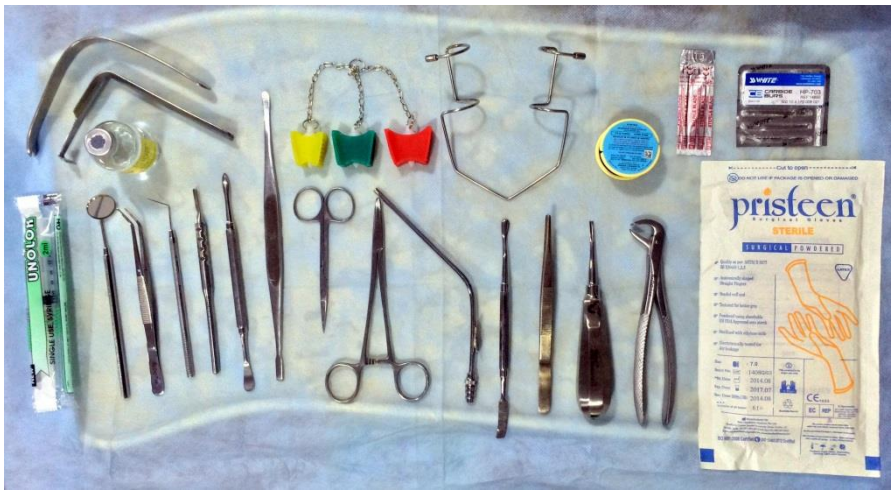


Fig.9 B: MARATHON KI-20 SURGICAL MOTOR & STRAIGHT HANDPIECE (Korea)

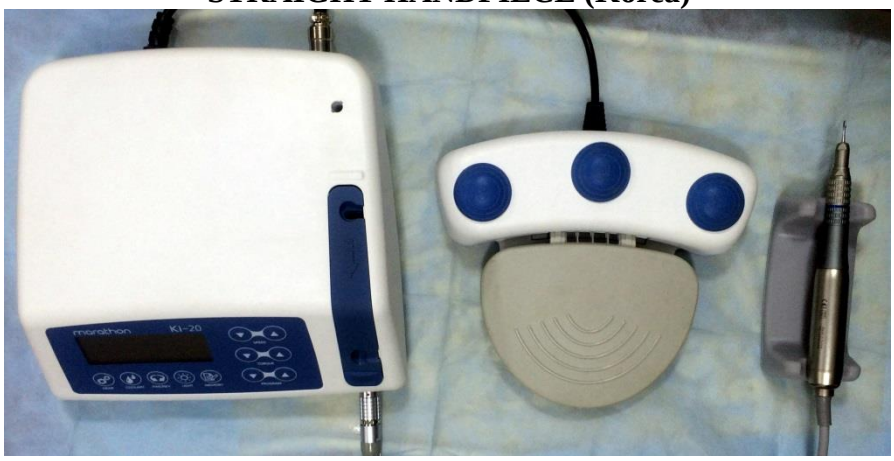
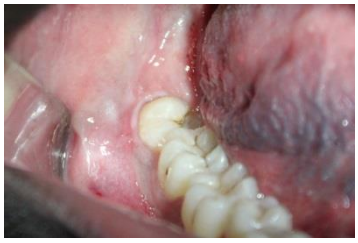


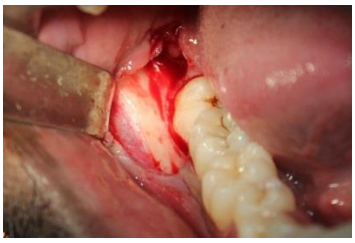
Fig.9 C: SURGICAL PROGRAM

Fig.10 A-E: Surgical procedure

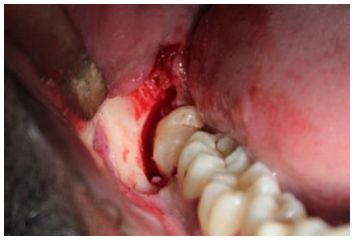
A) Pre operative



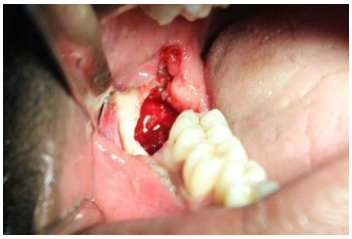
B) Mucoperiosteum raised



C) Bone guttering



D) Tooth elevated



E) Placement of 3-0 silk suture

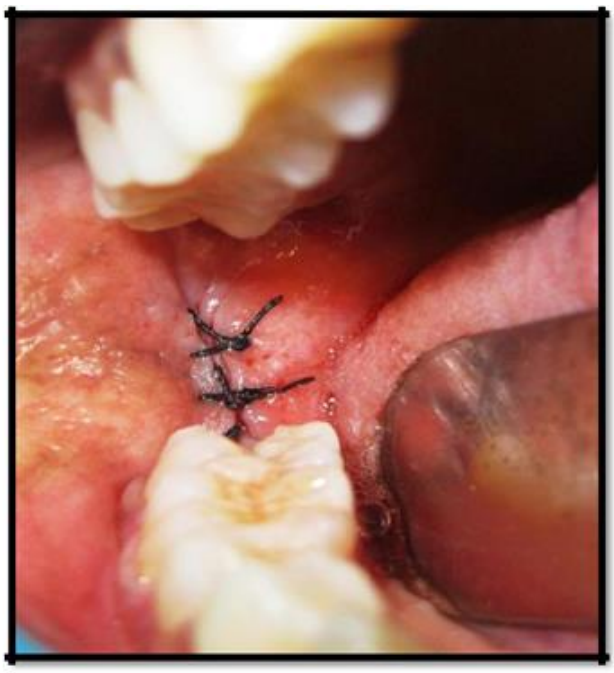


Fig.11 A: IOPA of mesioangular 48 & split specimen

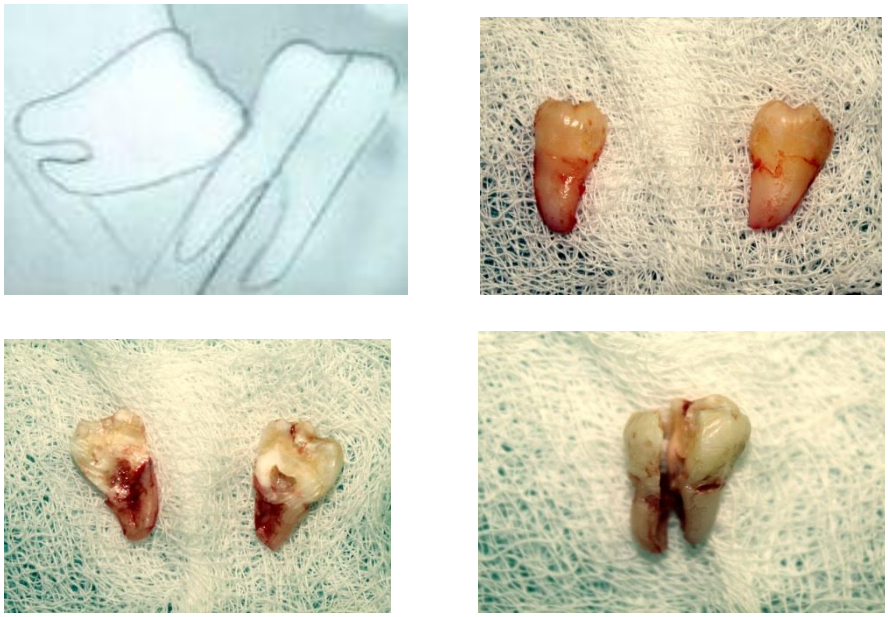


Fig.11 B: RVG of 38 & specimen of whole tooth in toto with dilacerated distal root

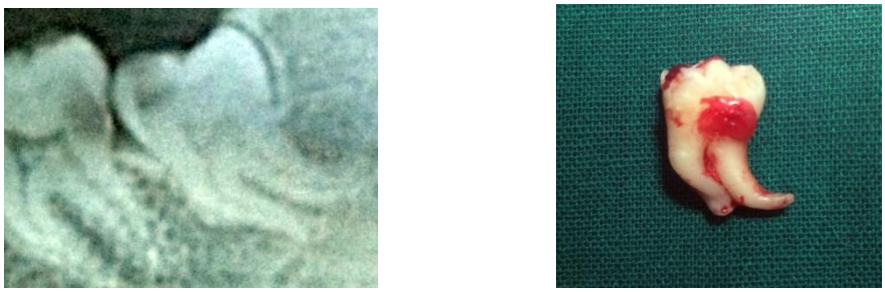
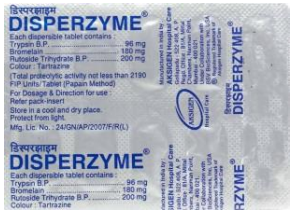


Fig.12: DISPERZYME PATIENT – GROUP A

A) PRE OPERATIVE

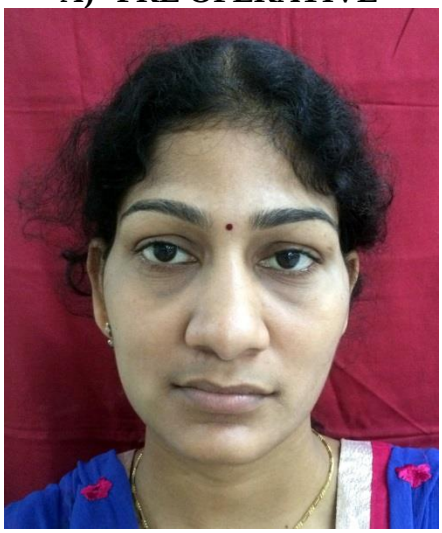
TAB.DIPERZYME SAMPLE



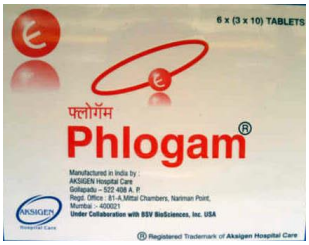
B) POST OPERATIVE 5TH DAY

Fig.16: PHLOGAM PATIENT – GROUP B

A) PRE OPERATIVE



T.PHLOGAM SAMPLE



B) POST OPERATIVE 5TH DAY

Fig.17: CONTROL PATIENT – GROUP C

A) PRE OPERATIVE

B) POST-OPERATIVE 5TH DAY

Results

RESULTS

A total of 42 patients requiring surgical removal of a single impacted mandibular third molar under local anesthesia, on fulfilling the inclusion & exclusion criteria were evaluated in the study. The mean patient age was 24.69 + 8.92 years. No statistically significant differences were found in the demographic and clinical characteristics among the study groups.

A pilot study of 5 cases each in group A,B,C was done and power of sample size was calculated using statistical method as follows:-

Two means – Hypothesis testing for two means (equal variances)

Standard deviation in the 1st group S1 = 9.61

Standard deviation in the 2nd group S2 = 12.87

Mean difference between 1st & 2nd sample = 12.2

Effect size = 1.08540925266904

Alpha error (%) = 5

Power (%) = 80

Sided = 2

Number needed (n) = 14

I. SWELLING (Graph 1)

When compared with preoperative & postoperative cumulative linear measurements of facial landmarks between anthropometric points

The Disperzyme group exhibited an increase in facial swelling by 11% on day 1, gradually the swelling reduced to 7% on day3 , on day 5 still a 3% increase in facial swelling from actual measurements were noted, there by the study group reduced 8% of total increase in swelling from post-operative day1.

The Phlogam group exhibited an increase in facial swelling by 11% on day 1, gradually the swelling reduced to 7% on day3 , on day 5 still a 3% increase in facial swelling from actual measurements were noted, there by the study group reduced 8% of total increase in swelling from post-operative day1.

The control group exhibited an increase in facial swelling by 15% on day 1, gradually the swelling reduced to 9% on day3 , on day 5 still a 7% increase in facial swelling from actual measurements were noted, there by the Control group reduced 8% of total increase in swelling from post-operative day1, leaving behind statistically significant residual edema of 4% when compared with study groups, concluding that systemic enzyme therapy (SET) is efficient in reducing edema than NSAID's comparatively.

II. MOUTH OPENING (Graph 2)

The mouth opening was compared with their respective group, considering actual mouth opening at 100% (Disperzyme group had 54.43mm, Phlogam group had 50.36mm and Control group had 51.36 mm)

The disperzyme group exhibited a mean mouth opening of 57% (31.43mm) on day1, increasing to 69% (37.93mm) on day3, reaching a maximum mouth opening of 78% (42.43mm) on day5. (Graph 2)

The Phlogam group exhibited a mean mouth opening of 58% (29.29mm) on day1, increasing to 68% (34.36mm) on day3, reaching a maximum mouth opening of 79% (39.86mm) on day5. (Graph 2)

The Control group exhibited a mean mouth opening of 40% (20.86mm) on day1, increasing to 49% (25.14mm) on day3, reaching a maximum mouth opening of 55% (28.21mm) on day5. (Graph 2)

Concluding that neither of the groups (study or control) failed to achieve the actual preoperative mouth opening at postoperative day 5. Whereas, the study groups have shown significant statistical difference with improved mouth opening by 23.5% (12.93mm) when compared with control group.

III. PAIN (Graph 3)

In Disperzyme group, patients reported with moderate pain in post-operative day 1 with mean value of 4 on VAS, which gradually reduced to mean value VAS score of 1 on day 3 which remained to be at VAS score of 1 till day5.

In Phlogam group, patients reported with moderate pain in post-operative day 1 with mean value of 5 on VAS, which gradually reduced to mean value VAS score of 3 on day 3 & remained to be at VAS score of 1 till day 5.

In Control group, patients reported only mild pain in post-operative day 1 with mean value of 3 on VAS, which gradually reduced to mean value VAS score of 1 on day 3 which remained to be at VAS score of 1 till day 5.

Concluding that control (NSAID'S) group was better in reducing pain on subjective assessment on scale of Visual analog score.

Tables and Graphs

STATISTICAL ANALYSIS FOR FACIAL SWELLING

Descriptives

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
Facial Swelling - Preop	Disperzyme	14	508.93	23.193	6.199	495.54	522.32	471	550
	Phlogam	14	493.79	37.481	10.017	472.15	515.43	416	555
	Control	14	482.36	26.789	7.160	466.89	497.82	427	520
	Total	42	495.02	31.062	4.793	485.34	504.70	416	555
Facial Swelling - Day1	Disperzyme	14	565.29	25.772	6.888	550.41	580.17	510	600
	Phlogam	14	547.71	36.649	9.795	526.55	568.87	478	609
	Control	14	553.64	39.626	10.591	530.76	576.52	485	595
	Total	42	555.55	34.481	5.321	544.80	566.29	478	609
Facial Swelling - Day3	Disperzyme	14	546.29	21.218	5.671	534.03	558.54	500	584
	Phlogam	14	525.21	36.987	9.885	503.86	546.57	465	589
	Control	14	524.07	31.861	8.515	505.68	542.47	465	565
	Total	42	531.86	31.706	4.892	521.98	541.74	465	589
Facial Swelling - Day5	Disperzyme	14	524.36	18.703	4.998	513.56	535.16	492	561
	Phlogam	14	508.57	36.306	9.703	487.61	529.53	441	569
	Control	14	514.14	27.052	7.230	498.52	529.76	460	555
	Total	42	515.69	28.366	4.377	506.85	524.53	441	569

Table 1

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Facial Swelling - Preop	Between Groups	4974.476	2	2487.238	2.805	.073
	Within Groups	34584.500	39	886.782		
	Total	39558.976	41			
Facial Swelling - Day1	Between Groups	2237.476	2	1118.738	.938	.400
	Within Groups	46508.929	39	1192.537		
	Total	48746.405	41			
Facial Swelling - Day3	Between Groups	4381.000	2	2190.500	2.319	.112
	Within Groups	36834.143	39	944.465		
	Total	41215.143	41			
Facial Swelling - Day5	Between Groups	1794.619	2	897.310	1.122	.336
	Within Groups	31196.357	39	799.907		
	Total	32990.976	41			

Table 2

Multiple Comparisons

Tukey HSD

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Facial Swelling - Preop	Disperzyme	Phlogam	15.143	11.255	.379	-12.28	42.56
		Control	26.571	11.255	.059	-.85	53.99
	Phlogam	Disperzyme	-15.143	11.255	.379	-42.56	12.28
		Control	11.429	11.255	.572	-15.99	38.85
	Control	Disperzyme	-26.571	11.255	.059	-53.99	.85
		Phlogam	-11.429	11.255	.572	-38.85	15.99
Facial Swelling - Day1	Disperzyme	Phlogam	17.571	13.052	.379	-14.23	49.37
		Control	11.643	13.052	.649	-20.16	43.44
	Phlogam	Disperzyme	-17.571	13.052	.379	-49.37	14.23
		Control	-5.929	13.052	.893	-37.73	25.87
	Control	Disperzyme	-11.643	13.052	.649	-43.44	20.16
		Phlogam	5.929	13.052	.893	-25.87	37.73
Facial Swelling - Day3	Disperzyme	Phlogam	21.071	11.616	.178	-7.23	49.37
		Control	22.214	11.616	.149	-6.09	50.51
	Phlogam	Disperzyme	-21.071	11.616	.178	-49.37	7.23
		Control	1.143	11.616	.995	-27.16	29.44
	Control	Disperzyme	-22.214	11.616	.149	-50.51	6.09
		Phlogam	-1.143	11.616	.995	-29.44	27.16
Facial Swelling - Day5	Disperzyme	Phlogam	15.786	10.690	.313	-10.26	41.83
		Control	10.214	10.690	.609	-15.83	36.26
	Phlogam	Disperzyme	-15.786	10.690	.313	-41.83	10.26
		Control	-5.571	10.690	.861	-31.62	20.47
	Control	Disperzyme	-10.214	10.690	.609	-36.26	15.83
		Phlogam	5.571	10.690	.861	-20.47	31.62

Table 3

PAIRED T-TEST FOR DISPERZYME GROUP ON FACIAL SWELLING:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Facial Swelling - Preop	508.93	14	23.193	6.199
	Facial Swelling - Day1	565.29	14	25.772	6.888
Pair 2	Facial Swelling - Day1	565.29	14	25.772	6.888
	Facial Swelling - Day5	524.36	14	18.703	4.998

Tables 4 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Facial Swelling - Preop - Facial Swelling - Day1	-56.357	19.178	5.125	-67.430	-45.284	-10.996	13	.000
Pair 2	Facial Swelling - Day1 - Facial Swelling - Day5	40.929	14.673	3.922	32.457	49.401	10.437	13	.000

PAIRED T-TEST FOR PHLOGAM GROUP ON FACIAL SWELLING:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Facial Swelling - Preop	493.79	14	37.481	10.017
	Facial Swelling - Day1	547.71	14	36.649	9.795
Pair 2	Facial Swelling - Day1	547.71	14	36.649	9.795
	Facial Swelling - Day5	508.57	14	36.306	9.703

Tables 5 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Facial Swelling - Preop - Facial Swelling - Day1	-53.929	21.713	5.803	-66.465	-41.392	-9.293	13	.000
Pair 2	Facial Swelling - Day1 - Facial Swelling - Day5	39.143	16.081	4.298	29.858	48.428	9.108	13	.000

PAIRED T-TEST FOR CONTROL GROUP ON FACIAL SWELLING:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Facial Swelling - Preop	482.36	14	26.789	7.160
	Facial Swelling - Day1	553.64	14	39.626	10.591
Pair 2	Facial Swelling - Day1	553.64	14	39.626	10.591
	Facial Swelling - Day5	514.14	14	27.052	7.230

Tables 6 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Facial Swelling - Preop - Facial Swelling - Day1	-71.286	45.862	12.257	-97.765	-44.806	-5.816	13	.000
Pair 2	Facial Swelling - Day1 - Facial Swelling - Day5	39.500	47.891	12.799	11.849	67.151	3.086	13	.009

STATISTICAL ANALYSIS FOR MOUTH OPENING

Descriptives

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
Mouth Opening - Preop	Disperzyme	14	54.43	4.569	1.221	51.79	57.07	45	63
	Phlogam	14	50.64	5.611	1.499	47.40	53.88	40	60
	Control	14	51.36	3.054	.816	49.59	53.12	48	58
	Total	42	52.14	4.724	.729	50.67	53.62	40	63
Mouth Opening -Day 1	Disperzyme	14	31.43	4.519	1.208	28.82	34.04	25	40
	Phlogam	14	29.29	6.696	1.790	25.42	33.15	20	42
	Control	14	20.86	8.132	2.173	16.16	25.55	12	37
	Total	42	27.19	7.936	1.225	24.72	29.66	12	42
Mouth Opening - Day 3	Disperzyme	14	37.93	4.411	1.179	35.38	40.48	32	46
	Phlogam	14	34.36	8.643	2.310	29.37	39.35	22	50
	Control	14	25.14	7.263	1.941	20.95	29.34	15	39
	Total	42	32.48	8.735	1.348	29.75	35.20	15	50
Mouth Opening - Day 5	Disperzyme	14	42.43	3.857	1.031	40.20	44.66	34	48
	Phlogam	14	39.86	8.018	2.143	35.23	44.49	32	55
	Control	14	28.21	7.876	2.105	23.67	32.76	20	42
	Total	42	36.83	9.162	1.414	33.98	39.69	20	55

Table 7

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Mouth Opening - Preop	Between Groups	113.286	2	56.643	2.755	.076
	Within Groups	801.857	39	20.560		
	Total	915.143	41			
Mouth Opening -Day 1	Between Groups	874.476	2	437.238	9.984	.000
	Within Groups	1708.000	39	43.795		
	Total	2582.476	41			
Mouth Opening - Day 3	Between Groups	1218.619	2	609.310	12.442	.000
	Within Groups	1909.857	39	48.971		
	Total	3128.476	41			
Mouth Opening - Day 5	Between Groups	1606.333	2	803.167	17.065	.000
	Within Groups	1835.500	39	47.064		
	Total	3441.833	41			

Table 8

Multiple Comparisons

Tukey HSD

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Mouth Opening - Preop	Disperzyme	Phlogam	3.786	1.714	.082	-.39	7.96
		Control	3.071	1.714	.185	-1.10	7.25
	Phlogam	Disperzyme	-3.786	1.714	.082	-7.96	.39
		Control	-.714	1.714	.909	-4.89	3.46
	Control	Disperzyme	-3.071	1.714	.185	-7.25	1.10
		Phlogam	.714	1.714	.909	-3.46	4.89
Mouth Opening -Day 1	Disperzyme	Phlogam	2.143	2.501	.670	-3.95	8.24
		Control	10.571*	2.501	.000	4.48	16.67
	Phlogam	Disperzyme	-2.143	2.501	.670	-8.24	3.95
		Control	8.429*	2.501	.005	2.33	14.52
	Control	Disperzyme	-10.571*	2.501	.000	-16.67	-4.48
		Phlogam	-8.429*	2.501	.005	-14.52	-2.33
Mouth Opening - Day 3	Disperzyme	Phlogam	3.571	2.645	.377	-2.87	10.02
		Control	12.786*	2.645	.000	6.34	19.23
	Phlogam	Disperzyme	-3.571	2.645	.377	-10.02	2.87
		Control	9.214*	2.645	.003	2.77	15.66
	Control	Disperzyme	-12.786*	2.645	.000	-19.23	-6.34
		Phlogam	-9.214*	2.645	.003	-15.66	-2.77
Mouth Opening - Day 5	Disperzyme	Phlogam	2.571	2.593	.586	-3.75	8.89
		Control	14.214*	2.593	.000	7.90	20.53
	Phlogam	Disperzyme	-2.571	2.593	.586	-8.89	3.75
		Control	11.643*	2.593	.000	5.33	17.96
	Control	Disperzyme	-14.214*	2.593	.000	-20.53	-7.90
		Phlogam	-11.643*	2.593	.000	-17.96	-5.33

*. The mean difference is significant at the .05 level.

Table 9

PAIRED T-TEST FOR DISPERZYME GROUP ON MOUTH OPENING:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Mouth Opening - Preop	54.43	14	4.569	1.221
	Mouth Opening -Day 1	31.43	14	4.519	1.208
Pair 2	Mouth Opening -Day 1	31.43	14	4.519	1.208
	Mouth Opening - Day 5	42.43	14	3.857	1.031

Tables 10 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Mouth Opening - Preop - Mouth Opening -Day 1	23.000	8.057	2.153	18.348	27.652	10.681	13	.000
Pair 2	Mouth Opening -Day 1 - Mouth Opening - Day 5	-11.000	4.804	1.284	-13.774	-8.226	-8.568	13	.000

PAIRED T-TEST FOR PHLOGAM GROUP ON MOUTH OPENING:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Mouth Opening - Preop	50.64	14	5.611	1.499
	Mouth Opening -Day 1	29.29	14	6.696	1.790
Pair 2	Mouth Opening -Day 1	29.29	14	6.696	1.790
	Mouth Opening - Day 5	39.86	14	8.018	2.143

Tables 11 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Mouth Opening - Preop - Mouth Opening -Day 1	21.357	5.904	1.578	17.948	24.766	13.534	13	.000
Pair 2	Mouth Opening -Day 1 - Mouth Opening - Day 5	-10.571	3.652	.976	-12.680	-8.463	-10.830	13	.000

PAIRED T-TEST FOR CONTROL GROUP ON MOUTH OPENING:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Mouth Opening - Preop	51.36	14	3.054	.816
	Mouth Opening -Day 1	20.86	14	8.132	2.173
Pair 2	Mouth Opening -Day 1	20.86	14	8.132	2.173
	Mouth Opening - Day 5	28.21	14	7.876	2.105

Tables 12 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Mouth Opening - Preop - Mouth Opening -Day 1	30.500	7.491	2.002	26.175	34.825	15.234	13	.000
Pair 2	Mouth Opening -Day 1 - Mouth Opening - Day 5	-7.357	7.571	2.024	-11.729	-2.986	-3.636	13	.003

STATISTICAL ANALYSIS FOR VISUAL ANALOG SCALE

Descriptives

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
VAS - Day 1	Disperzyme	14	3.43	.514	.137	3.13	3.73	3	4
	Phlogam	14	4.57	1.284	.343	3.83	5.31	2	6
	Control	14	3.21	.579	.155	2.88	3.55	3	5
	Total	42	3.74	1.037	.160	3.41	4.06	2	6
VAS - Day 3	Disperzyme	14	1.07	.917	.245	.54	1.60	0	3
	Phlogam	14	2.50	.855	.228	2.01	2.99	0	3
	Control	14	1.07	.267	.071	.92	1.23	1	2
	Total	42	1.55	.993	.153	1.24	1.86	0	3
VAS - Day 5	Disperzyme	14	.21	.426	.114	-.03	.46	0	1
	Phlogam	14	.86	.770	.206	.41	1.30	0	2
	Control	14	1.00	.392	.105	.77	1.23	0	2
	Total	42	.69	.643	.099	.49	.89	0	2

Table 13

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
VAS - Day 1	Between Groups	14.905	2	7.452	9.949	.000
	Within Groups	29.214	39	.749		
	Total	44.119	41			
VAS - Day 3	Between Groups	19.048	2	9.524	17.391	.000
	Within Groups	21.357	39	.548		
	Total	40.405	41			
VAS - Day 5	Between Groups	4.905	2	2.452	7.923	.001
	Within Groups	12.071	39	.310		
	Total	16.976	41			

Table 14

Multiple Comparisons

Tukey HSD

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
VAS - Day 1	Disperzyme	Phlogam	-1.143*	.327	.003	-1.94	-.35
		Control	.214	.327	.791	-.58	1.01
	Phlogam	Disperzyme	1.143*	.327	.003	.35	1.94
		Control	1.357*	.327	.001	.56	2.15
	Control	Disperzyme	-.214	.327	.791	-1.01	.58
		Phlogam	-1.357*	.327	.001	-2.15	-.56
VAS - Day 3	Disperzyme	Phlogam	-1.429*	.280	.000	-2.11	-.75
		Control	.000	.280	1.000	-.68	.68
	Phlogam	Disperzyme	1.429*	.280	.000	.75	2.11
		Control	1.429*	.280	.000	.75	2.11
	Control	Disperzyme	.000	.280	1.000	-.68	.68
		Phlogam	-1.429*	.280	.000	-2.11	-.75
VAS - Day 5	Disperzyme	Phlogam	-.643*	.210	.011	-1.16	-.13
		Control	-.786*	.210	.002	-1.30	-.27
	Phlogam	Disperzyme	.643*	.210	.011	.13	1.16
		Control	-.143	.210	.777	-.66	.37
	Control	Disperzyme	.786*	.210	.002	.27	1.30
		Phlogam	.143	.210	.777	-.37	.66

*. The mean difference is significant at the .05 level.

Table 15

PAIRED T-TEST FOR DISPERZYME GROUP ON VAS:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	VAS - Day 1	3.43	14	.514	.137
	VAS - Day 5	.21	14	.426	.114

Tables 16 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	VAS - Day 1 - VAS - Day	3.214	.426	.114	2.968	3.460	28.244	13	.000

PAIRED T-TEST FOR PHLOGAM GROUP ON VAS:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	VAS - Day 1	4.57	14	1.284	.343
	VAS - Day 5	.86	14	.770	.206

Tables 17 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	VAS - Day 1 - VAS - Day	3.714	.825	.221	3.238	4.191	16.837	13	.000

PAIRED T-TEST FOR CONTROL GROUP ON VAS:-

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	VAS - Day 1	3.21	14	.579	.155
	VAS - Day 5	1.00	14	.392	.105

Tables 18 A & B

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	VAS - Day 1 - VAS - Day	2.214	.579	.155	1.880	2.549	14.311	13	.000

Non Parametric Tests:-

KRUSKAL-WALLIS TEST FOR VISUAL ANALOG SCALE:-

Ranks

	Group	N	Mean Rank
VAS - Day 1	Disperzyme	14	19.36
	Phlogam	14	29.82
	Control	14	15.32
	Total	42	
VAS - Day 3	Disperzyme	14	16.07
	Phlogam	14	32.46
	Control	14	15.96
	Total	42	
VAS - Day 5	Disperzyme	14	13.07
	Phlogam	14	23.89
	Control	14	27.54
	Total	42	

Tables
19 A & B

Test Statistics[a,b]

	VAS - Day 1	VAS - Day 3	VAS - Day 5
Chi-Square	12.394	18.937	13.028
df	2	2	2
Asymp. Sig.	.002	.000	.001

a. Kruskal Wallis Test

b. Grouping Variable: Group

WILCOXON SIGNED RANKS TEST FOR DISPERZYME GROUP VAS:-

Ranks

		N	Mean Rank	Sum of Ranks
VAS - Day5 - VAS - Day1	Negative Ranks	14[a]	7.50	105.00
	Positive Ranks	0[b]	.00	.00
	Ties	0[c]		
	Total	14		

Tables
20 A & B

a. VAS - Day5 < VAS - Day1

b. VAS - Day5 > VAS - Day1

c. VAS - Day5 = VAS - Day1

Test Statistics[b]

	VAS - Day5 - VAS - Day1
Z	-3.494[a]
Asymp. Sig. (2-tailed)	.000

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

WILCOXON SIGNED RANKS TEST FOR PHLOGAM GROUP VAS:-

Ranks

		N	Mean Rank	Sum of Ranks
VAS - Day5 - VAS - Day1	Negative Ranks	14[a]	7.50	105.00
	Positive Ranks	0[b]	.00	.00
	Ties	0[c]		
	Total	14		

a. VAS - Day5 < VAS - Day1

b. VAS - Day5 > VAS - Day1

c. VAS - Day5 = VAS - Day1

Tables 21 A & B

Test Statistics[b]

	VAS - Day5 - VAS - Day1
Z	-3.352[a]
Asymp. Sig. (2-tailed)	.001

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

WILCOXON SIGNED RANKS TEST FOR CONTROL GROUP VAS:-

Ranks

		N	Mean Rank	Sum of Ranks
VAS - Day5 - VAS - Day1	Negative Ranks	14[a]	7.50	105.00
	Positive Ranks	0[b]	.00	.00
	Ties	0[c]		
	Total	14		

a. VAS - Day5 < VAS - Day1

b. VAS - Day5 > VAS - Day1

c. VAS - Day5 = VAS - Day1

Test Statistics[b]

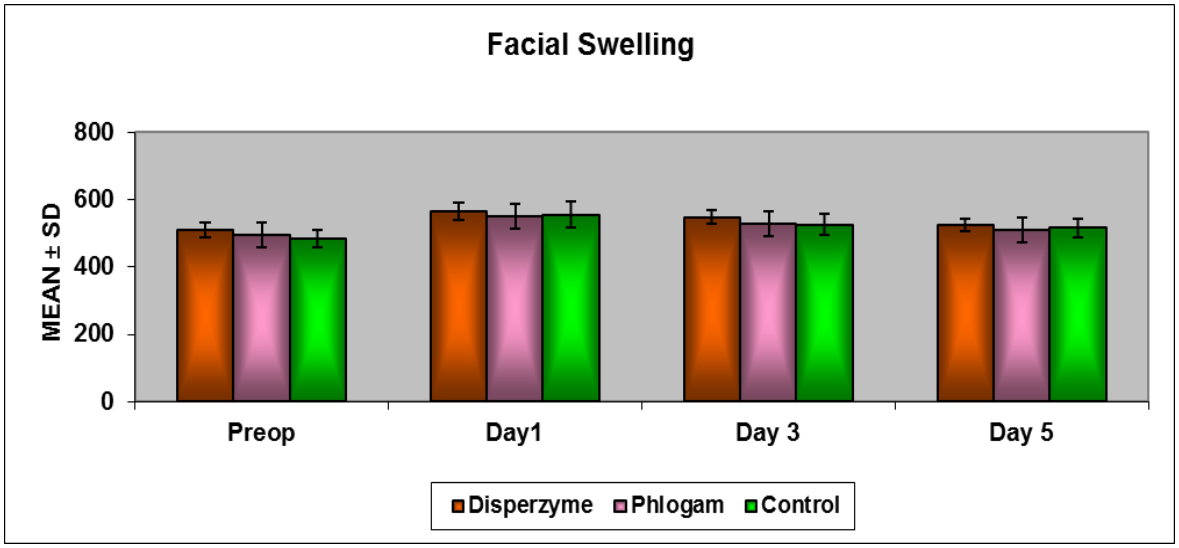
	VAS - Day5 - VAS - Day1
Z	-3.556[a]
Asymp. Sig. (2-tailed)	.000

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

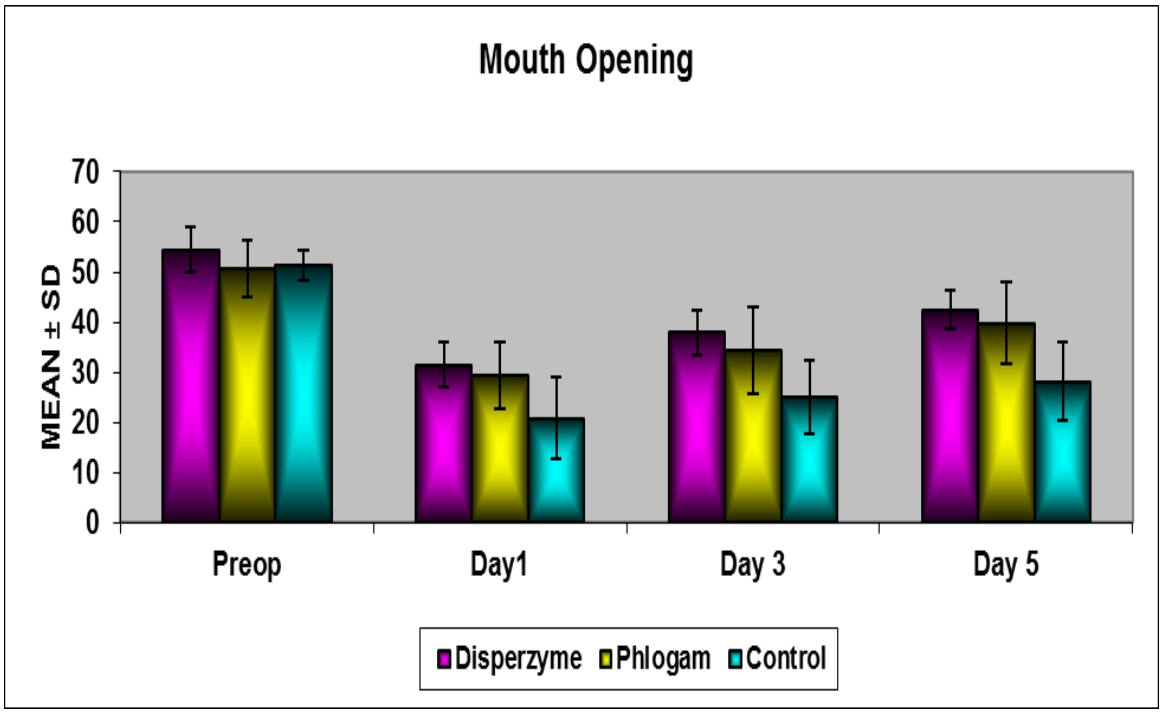
Tables 22 A & B

Graph 1



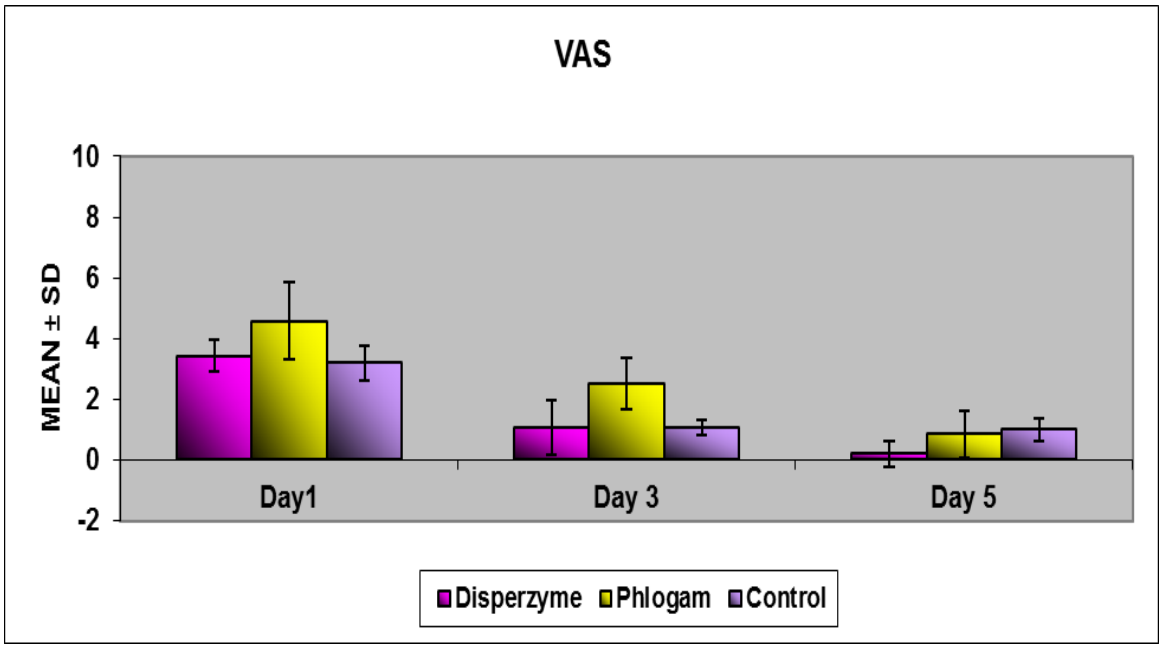
Mean value	Preop	Day1	Day 3	Day 5
Disperzyme	508.93	565.29	546.29	524.36
Phlogam	493.79	547.71	525.21	508.57
Control	482.36	553.64	524.07	514.14
SD				
	23.19	25.77	21.21	18.7
	37.48	36.64	36.98	36.3
	26.78	39.62	31.86	27.05

Graph 2



Mean value		Preop	Day1	Day 3	Day 5
Disperzyme		54.43	31.43	37.93	42.43
Phlogam		50.64	29.29	34.36	39.86
Control		51.36	20.86	25.14	28.21
	SD	4.56	4.51	4.41	3.85
		5.61	6.69	8.64	8.01
		3.05	8.13	7.26	7.87

Graph 3



Mean value	Day1	Day 3	Day 5
Disperzyme	3.43	1.07	0.21
Phlogam	4.57	2.5	0.86
Control	3.21	1.07	1
	0.51	0.91	0.42
	1.28	0.85	0.77
	0.57	0.26	0.39

Discussion

DISCUSSION

A mandibular third molar is considered to be impacted when its eruption into normal functional occlusion is interfered by the bone lying above, other teeth, or soft tissue and if it does not fully erupt by the expected chronological age. The most commonly impacted tooth is the 3rd molar, with an incidence of approximately 18-32%[1]

CLASSIFICATION PRINCIPLES:

Winter's gave a classification for impaction based on the angulation of the lower 3rd molar in relation to the lower 2nd molar - as mesioangular, distoangular, horizontal and vertical[55].

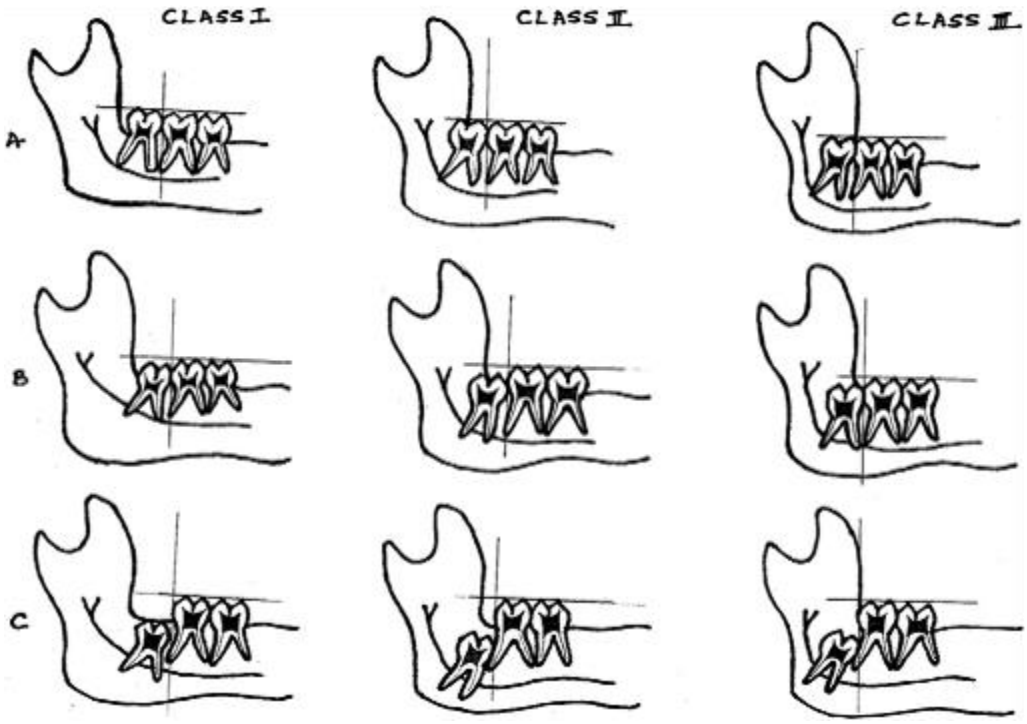
Pell & Gregory classified based on the distance between the anterior border of ascending ramus of the mandible and the 2nd molar[42.]

Class I: Sufficient space is present between the distal aspect of the 2nd molar and the anterior border of ascending ramus, for the third molar to erupt.

Class II: The space between the distal aspect of the 2nd molar and the anterior border of the ascending ramus is lesser than the mesiodistal width of the 3rd molar; hence the distal aspect of the 3rd molar crown is covered with bone from the ramus.

Class III: There is total lack of space; hence the 3rd molar is completely covered by bone from the ramus.

A diagrammatic representation by Padhye[36]



According to the level of eruption of the 3rd molar, it can be classified into levels A, B and C. (Diagrammatic representation by Padhye et al, 2013)

Level A: The highest portion of the 3rd molar is higher or at the same level of the 2nd molar occlusally

Level B: the highest portion of the 3rd molar is below the occlusal plane, but above the cervical line of the 2nd molar.

Level C: The highest portion of the 3rd molar is even below the cervical line of the 2nd molar.

THIRD MOLAR SURGERY

The indications for mandibular 3rd molar surgery usually are localized pain, pericoronitis, odontogenic abscess, trismus, distal caries and periodontal pocket in relation to the second molar, development of follicular cysts and crowding of lower incisors[23]; hence they need to be frequently extracted to prevent these signs. This involves the usual steps - mucoperiosteal flap elevation, ostectomy, tooth sectioning, root removal once luxated, removal of any sharp bony spicule or pathologic condition if present, debridement and wound closure[32]

This can lead to postoperative discomfort; Post-operative discomfort may due to the surgical technique, but also because of the physiological response of the system[**23**]

The extent of swelling and severity of pain are the chief indicators of patients comfort during the postoperative period after third molar surgery**.** Swelling evaluated with clinical measurement between anatomical points and pain evaluated with VAS scale, which is efficacious tool to evaluate clinical parameters that influence the subjective experience of an individual, as VAS scale is a reliable and repeatable method[28]

Studies conducted to compare primary and secondary closure techniques in terms of the same variables swelling and pain, conclude pain and swelling were less severe with secondary healing than sutured wound[**43**]

Drains were also used and compared with primarily closed wound & drain placed to facilitate drainage and was removed after 72 hours and found that swelling in the drain group was significantly less than in the no drain group, with no change in the pain severity in both groups[44]

The inflammatory process is an essential part of post-surgical healing after surgical procedures. Once initiated it may exceed the necessary physiological limits and result in excessive swelling, pain, and limited mouth opening. There has been a constant search for ways to control the inflammatory process, starting with the use of ice pack application, pressure dressings and thermal agents and extending to the use of various pharmacological agents.[10]

Medication administered to limit the physiological response of the system by NSAID's & Steroid's. Corticosteroids act by inhibiting, through a variety of proposed mechanisms, the body's inflammatory response to injury, with a reduction of fluid transudation and therefore reduction in edema[24]

Sub mucosal injection of dexamethasone 4 mg is an effective therapeutic strategy for improving the quality of life after surgical removal of impacted lower third molars with a comparable effect on postoperative sequelae to intramuscular injection. It offers a simple, safe, painless, non-invasive, and cost effective therapeutic option for moderate and severe cases[41].

Commonly used are NSAID's, they have effects of analgesia, anti-inflammatory, they act as non-selective inhibitors on the enzyme cycloxynase (COX), inhibiting both cox – 1, Cox -2. This is reversible, leads to inhibitions of PG, TXA[52]

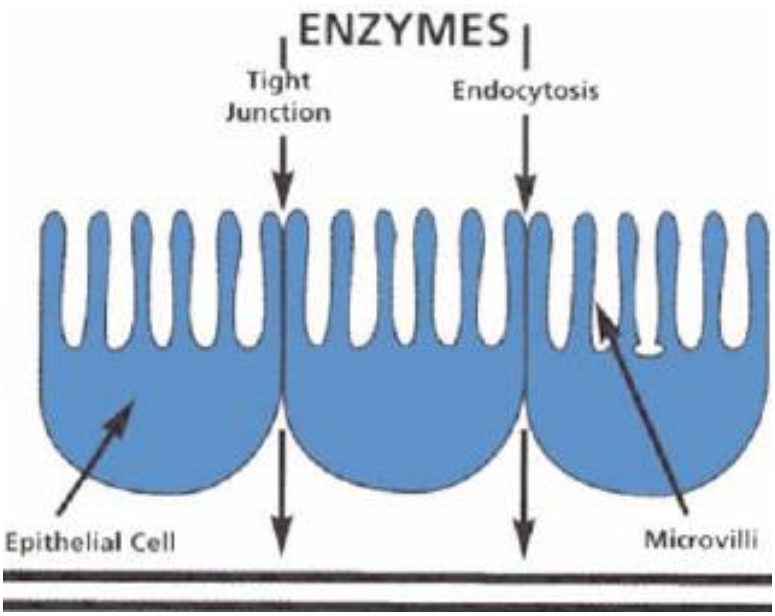
Contraindications of NSAID's – irritable bowel syndrome, gastrointestinal problems, peptic ulcers, uncontrolled hypertension, kidney disorders, cannot be in third trimester of pregnancy[52]

Adverse effects of NSAID's are gastrointestinal tract disturbances, dyspepsia, and drug interactions[52]

Enzymes such as hyaluronidase, streptokinase/streptodornase, trypsin, bromelion, rutoside trihydrate, papase and ananase were among the earliest agents used[3].

Oral proteolytic enzymes such as serratiopeptidase, chymotrypsins, etc., are aggressively prescribed for their anti-inflammatory action and are prescribed in a variety of conditions like facial edema, trauma, surgery, parotitis, and carpal tunnel syndrome[51], conclusively shown by various means histological, biochemical, immunological and biological, including marking them with radioactive dyes that enzymes do pass the intestinal barrier in an undamaged macromolecular form and realize their activities in the system[38]

There are three mechanisms of absorption: by pinocytosis (endocytosis), binding to specific receptors at the top of the intestinal villi; Via the so called 'M' cells which overlay the Peyer's patches; and through the opening of 'tight junctions' of the intestinal epithelium[30], Once absorbed they find their way to where they are needed to reduce inflammation, lessen pain, diminish edema, aid detoxification, maintain efficient blood circulation, speed up wound healing, fight infections, and lessen the side effects of some conventional procedures[39]



PATHOPHYSIOLOGY:-

The pathway of an injury starts from the initial tissue damage trauma through to the vascular reaction, vessel permeability disturbance, immune response, local vascular connective tissue proliferation and finally scar tissue. Enzymes are able to influence each stage of this pathway. They have the ability to break down fibrin, inhibit aggregation of platelets, break up fresh clots and accelerate blood flow. Local blood circulation is normalized, the chemicals that give rise to pain are eliminated more quickly, oxygenation is improved and edema is reduced[40]

SET uses specific enzyme compounds to increase enzyme levels throughout the body and improve the function of the various body systems primarily by modulating, controlling, and balancing the inflammatory and oxidative processes that occur throughout the various body systems[53]

These enzymes work on balancing the immune system. These enzymes bind with a2-macroglobulin and activate it. This activated a2-macroglobulin acts like a magnet to all unwanted and excessive mediators of inflammation and attracts them to form a complex. This complex is cleared by the abundance of macrophages in the liver[53]

The main reservations about the use of proteolytic enzymes are as follows according to various authors - Proteolytic enzymes are large protein molecules and there exist a doubt whether they will be absorbed in an active

form from the gastrointestinal tract. To overcome their destruction in stomach by hydrolysis, these tablets are given in enteric coated dosage form. There are very few reports of well controlled randomized clinical trials. Thus, anti-inflammatory activity after oral administration has not been convincingly demonstrated. Most of the clinical data are not adequately controlled, and is based on the subjective observations. Very little is known about their mechanism of action. No clinical data is available on the fate and excretion of proteolytic enzymes[51]

Apart from the above all discussion, literatures have described few mild complaints in SET like soft stools or meteorism, fullness of stomach, flatulence, which is not a serious complication[56]

It has been concluded that SET, when prescribed in heavier doses over prolonged period also, does not reveal any changes in hematological parameters on investigations[30]

Kleine M. Introduction to oral enzyme therapy. International Journal of Immunotherapy. XIII(3/4): 5965, 1997

hemoglobin	monocytes	sodium	ALT (GPT)
hematocrit	glucose	potassium	AST (GOT)
WBC	ESR	calcium	GLDH
RBC	MCV	chloride	γ-GT
platelets	MCH	urea	bilirubin (total)
lymphocytes	MCHC	uric acid	alk. phosphatase
polymorphs	Quick's time	creatinine	protein (total)
basocytes	PTT	hemoccult	α2-macroglobulin
eosinocytes	antithrombin III	urinalysis	blood pressure
		general side effects	

Fig. 5 No side effects on these parameters after a total of 84 enzyme tablets within 8 days

Summary and Conclusion

SUMMARY AND CONCLUSION

Oral enzymes are highly effective have nearly no side effects. They seem to reduce the body's physiologically overshooting reactions to injuries and allows the body to use its own repair mechanisms earlier and more effectively and regenerate the disturbed structures more quickly, reducing the convalescent time.

The only real contraindications are risk of allergic reactions to enzymes. Although many of the theoretical questions still have no answers, in many clinical trials the efficacy and tolerance of oral enzyme therapy have been proven in variety of injuries.

In our prospective study - though a small group of sample size, the efficacy of systemic enzyme Tab. Disperzyme & Tab. Phlogam has been proven to be statistically significant with regard to marked reduction of the post-operative edema, early & rapid mouth opening ability, but its efficiency is found limited pertaining to pain supressing property.

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Annexures

Complete Data Chart

s.no	age	sex	group	MM-P	MM-D1	MM-D3	MM-D5	GT-P	GT-D1	GT-D3	GT-D5	GL-P	GL-D1	GL-D3	GL-D5	GA-P	GA-D1	GA-D3	GA-D5	GC-P	GC-D1	GC-D3	GC-D5	GP-P	GP-D1	GP-D3	GP-D5	VAS-1	VAS-3	VAS-5
1	18	F	A	58	30	33	40	77	82	80	80	111	130	123	114	106	126	115	109	110	129	119	112	115	129	123	116	4	2	0
2	33	F	A	58	30	36	42	80	85	83	81	115	125	122	117	130	140	136	132	105	125	119	108	120	125	124	123	4	2	0
3	27	F	A	52	35	42	46	75	80	78	76	110	115	113	111	115	120	118	116	85	90	88	87	100	105	103	102	4	2	1
4	30	F	A	55	25	35	39	73	78	75	74	109	125	120	111	104	115	110	106	100	110	109	103	115	125	120	118	3	1	0
5	19	M	A	58	33	39	43	75	79	77	76	117	122	120	118	120	125	123	121	95	110	107	101	120	125	123	121	3	1	0
6	31	F	A	55	33	38	40	70	74	74	72	110	125	121	115	115	128	123	120	95	110	107	100	110	130	127	119	3	0	0
7	22	M	A	45	40	42	43	70	75	73	72	112	117	115	114	120	124	123	122	97	100	99	98	117	120	119	118	4	1	1
8	23	M	A	50	40	42	45	85	95	92	86	118	125	120	120	123	135	125	125	95	115	115	100	105	120	115	105	3	1	0
9	25	F	A	58	30	33	38	69	73	72	70	102	115	112	107	107	120	116	110	88	117	112	100	105	125	120	115	4	1	0
10	30	M	A	50	27	32	34	72	75	72	72	105	120	110	105	113	132	125	122	89	105	100	100	104	120	120	109	3	1	0
11	24	F	A	55	27	38	46	72	78	75	73	103	122	110	105	125	135	125	125	120	130	125	122	125	130	128	127	3	0	0
12	19	M	A	63	28	33	46	73	76	75	74	105	120	118	110	110	133	130	120	100	110	108	100	119	125	122	113	3	0	0
13	18	F	A	54	30	42	44	60	72	71	70	107	119	117	115	115	126	122	117	97	113	107	101	110	125	120	113	3	0	0
14	26	M	A	51	32	46	48	67	75	71	68	110	123	120	113	115	129	124	120	101	129	123	110	113	129	122	116	4	3	1
15	26	M	B	49	28	34	34	70	80	75	73	100	113	110	106	120	127	123	121	100	105	105	105	120	125	120	120	6	3	2
16	20	M	B	48	24	30	34	75	79	79	75	125	135	132	129	130	139	135	133	110	126	120	114	115	130	123	118	5	3	1
17	26	M	B	60	25	27	34	80	87	84	83	110	118	113	111	115	128	125	119	93	115	105	95	112	138	130	120	6	3	2
18	24	F	B	50	30	33	38	71	76	74	73	103	108	106	104	98	108	105	102	79	85	83	81	89	101	97	91	3	2	0
19	25	F	B	50	34	40	45	74	76	75	74	105	112	108	106	115	124	118	115	98	111	105	100	120	120	120	120	6	3	1
20	31	F	B	40	22	26	32	65	69	68	66	105	115	111	109	100	114	110	104	95	104	99	94	110	120	115	113	5	3	1
21	21	M	B	57	35	43	52	75	80	78	76	95	100	99	98	105	115	113	111	95	106	100	98	115	126	118	115	6	3	1
22	32	F	B	49	20	22	37	65	65	65	65	100	111	105	103	103	123	115	110	93	113	100	98	105	125	110	108	5	3	1
23	20	M	B	55	42	50	52	73	78	76	75	100	108	105	103	105	113	110	108	87	93	90	90	110	110	110	110	5	3	2
24	21	F	B	60	40	50	55	70	78	73	73	110	115	113	105	125	130	128	126	100	105	102	100	128	135	130	128	4	2	1
25	26	M	B	50	22	28	32	60	72	69	65	90	120	115	95	95	120	108	100	73	98	82	78	98	110	100	103	3	3	0
26	26	F	B	45	28	30	33	70	78	77	75	105	120	112	110	115	130	126	120	100	115	110	109	125	135	132	125	4	2	0
27	29	M	B	49	32	37	40	69	75	74	70	94	110	106	101	110	127	124	119	99	112	107	102	121	137	130	125	4	2	0
28	22	M	B	47	28	31	40	76	82	79	78	110	119	117	115	115	129	124	119	110	129	121	116	117	133	127	121	2	0	0

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Affiliated to The Tamilnadu Dr. M.G.R. Medical University, Chennai
2/102, East Coast Road, Uthandi, Chennai - 600 119. INDIA.
Tele : (044) 24530002, 24530003 - 06. Principal (Dir) 24530001 Fax : (044) 24530009

TO WHOM SO EVER IT MAY CONCERN

DATE: 28/12/2015
CHENNAI.

FROM:-
THE INSTITUTIONAL REVIEW BOARD,
RAGAS DENTAL COLLEGE AND HOSPITAL,
UTHANDI,
CHENNAI.

THE THESIS TOPIC **"THE EFFICACY OF SYSTEMIC ENZYME THERAPY FOR EDEMA CONTROL IN MANDIBULAR THIRD MOLAR IMPACTION SURGERY"**

SUBMITTED BY **Dr. N.SRIRAM CHOUDARY** HAS BEEN APPROVED BY THE INSTITTUTIONAL REVIEW BOARD OF RAGAS DENTAL COLLEGE AND HOSPITAL ON 5th May 2014.

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