

---

## Trypsin and Chymotrypsin Usage in Reduction of Pain Following the Surgical Extraction of Mandibular Third Molars

---

HARINI G<sup>1</sup>, DR. DINESH PRABU<sup>2\*</sup>, DR. BALAKRISHNAN R N<sup>3</sup>

<sup>1</sup>Saveetha dental college, Saveetha institute of technical and medical sciences, Saveetha University, Chennai - 600077

<sup>2</sup>Department of oral and maxillofacial surgery, Saveetha dental college, Saveetha institute of technical and medical sciences, Saveetha University, Chennai- 600077

<sup>3</sup>Department of oral and maxillofacial surgery, Saveetha dental college, Saveetha institute of technical and medical sciences, Chennai- 600077

\*Corresponding Author

Email ID: 151401014.sdc@saveetha.com<sup>1</sup>, dineshprabum.sdc@saveetha.com<sup>2</sup>, balakrishnarn.sdc@saveetha.com<sup>3</sup>

---

**Abstract:** The aim of the article is to evaluate the effect of trypsin and chymotrypsin (proteolytic enzyme ) on pain and swelling after the surgical removal of mandibular third molar. A prospective randomised clinical study was conducted among 30 patients requiring the surgical removal of impacted mandibular third molars. All the impacted molars were surgically removed and the patients were administered trypsin and chymotrypsin orally along with amoxicillin. The postoperative pain was assessed on 3rd and 7th consecutive days after extraction. 30 patients requiring the extraction of mandibular third molars were taken in this study.16 patients are male and 14 patients are females. There was the reduction in pain post operatively. The comparison was taken between 3rd and 7th postoperative days. Chymoral Forte can be used as a successful oral enzyme therapy for oral surgery patients, especially after the removal of impacted third molars.

**Keywords:** chymoral, impacted third molars, innovation, postoperative edema, third molars, trypsin

---

### INTRODUCTION

Impacted wisdom teeth is a disorder where the third molars (wisdom teeth) are prevented from erupting into the mouth. This can be caused by a physical barrier, such as other teeth, or when the tooth is angled away from a vertical position. Surgical removal of impacted third molars is one of the main procedures performed on young adults and adolescents, it is recommended when they present with certain symptoms, namely pain, food lodgement or with certain pathologic lesions. Sometimes prophylactic extraction of asymptomatic impacted third molars is also indicated by some professionals. Studies have shown that the most commonly impacted tooth are third molars(88%) and the canine was (12%). (Santosh, 2015). Removal of impacted teeth needs a surgical procedure,where the soft tissue flap is raised and the associated tooth or bone or both are cut and the tooth is removed from its socket, such surgical procedure results in injury of tissue involving inflammation repair process (Das et al., 2015). In order to avoid and minimize post surgical complications such as pain, swelling and trismus, surgeons have either modified surgical techniques such as using lasers and cryotherapy, patient are advised to use proteolytic enzymes such as trypsin, chymotrypsin, pappain, serratopeptidase and bromine along with the few routine antibiotics such as amoxicillin and metronidazole (Wala et al., 2020)(Islam et al., 2020). Thus the following study was undertaken to evaluate the analgesic and anti-inflammatory efficacy of Proteolytic enzymes: Trypsin and Chymotrypsin on Swelling, Pain and Trismus after extraction of impacted mandibular third molars. The benefits of administering proteolytic enzymes after the surgical procedure are demonstrated both in in-vitro and in-vivo studies are anti-inflammatory, anti-thrombotic and thereby minimizing the complications .The proteolytic enzymes such as trypsin and chymotrypsin when administered fasten the healing of damaged tissue and help in the fast complication free recovery. Various studies have been conducted by Al-sandook et al, showed the effective reduction of the complications ,reduction of inflammation after extraction and anti-edematous action .

Our department is passionate about research we have published numerous high quality articles in this domain over the past years ( Kavitha et al., 2014 ) , (Praveen et al., 2001),(Devi and Gnanavel, 2014), (Putchala et al., 2013), (Vijayakumar et al., 2010), (Lekha et al., 2014a, 2014b) (Danda, 2010) (Danda, 2010) (Parthasarathy et al., 2016)

(Gopalakannan, Senthilvelan and Ranganathan, 2012), (Rajendran et al., 2019), (Govindaraju, Neelakantan and Gutmann, 2017), (P. Neelakantan et al., 2015), (PradeepKumar et al., 2016), (Sajan et al., 2011), (Lekha et al., 2014a), (Neelakantan, Grotra and Sharma, 2013), (Patil et al., 2017), (Jeevanandan and Govindaraju, 2018), (Abdul Wahab et al., 2017), (Eapen, Baig and Avinash, 2017), (Menon et al., 2018), (Wahab et al., 2018), (Vishnu Prasad et al., 2018), (Uthrakumar et al., 2010), (Ashok, Ajith and Sivanesan, 2017), (Prasanna Neelakantan et al., 2015). Thus the following study was undertaken to evaluate the analgesic and anti-inflammatory efficacy of Proteolytic enzymes: Trypsin and Chymotrypsin on Pain and Trismus after extraction of impacted mandibular third molars.

## **MATERIALS AND METHODS**

A total of 30 subjects requiring extraction of impacted mandibular third molars who reported to the Department of oral and maxillofacial surgery in the age range of 18 to 50 years were selected randomly. Patients selected had no preexisting medical conditions or medications that would influence their ability to undergo surgery or alter their wound healing after surgery. Ethical Committee clearance was obtained for the study SDC/SIHEC/2020/DIASDATA/0619-0320. A detailed case record was taken and written consent was obtained from each subject before surgery.

### **Inclusion Criteria**

- ❖ Patient of age 18-50 years of age
- ❖ Patients with unilateral/ bilateral impacted mandibular third molars diagnosed for surgical extraction

### **Exclusion Criteria**

- ❖ Patient with known severe systemic disease contraindicating extraction
- ❖ Mentally challenged patients
- ❖ Pregnant and lactating women
- ❖ Immunocompromised patients

A complete history of all the patients was taken and examinations were ruled out by using OPG and IOPA for the impacted tooth. Difficulty index for removal of teeth was assessed by winter's war lines. Preoperative mouth opening was measured. The subject was injected for an inferior alveolar nerve block and a long buccal nerve block. Ward's incision was taken and a full thickness mucoperiosteal flap was erected using a periosteal elevator and osteotomy around the crown of the impacted mandibular third molar was carried out along with odontectomy. After all due procedures, the tooth was luxated using elevators and then extracted. Following removal of the impacted tooth, the surgical site was irrigated with sterile saline solution. Sharp bony edges were rounded off and the site was closed to achieve primary closure with 3-0 black-braided silk suture. All the subjects were given post-operative instructions .. Subjects were examined for pain, trismus (maximum mouth opening) on the third and seventh day post-operatively.

### **Statistic Analysis**

The data was analysed using SPSS software by means of the value to be recorded and the significance test was applied in the chi-square test.

## **RESULTS AND DISCUSSION**

A total of 30 patients ( 16 males and 14 females) were enrolled in the prospective study with mean age of 21-25 years. This study was conducted from 1st april 2019-1st april 2020. This was male predominance study with 16 males(54%) and 14 females(46%)(figure-1). Out of 30 patients, 11 patients had mesio angular impaction, 9 patients had horizontal impactions ,5 patients each with distoangular and vertical impactions(Figure-2). The mean time taken for the surgery was 30 +/- 5 mins. .. On the third day(Figure-3) of extraction patients experienced moderate-40% to severe pain-60%, On 7th day(figure-4) no pain was observed in 50% of the study population followed by mild pain-33%, few experienced severe pain-3%,and moderate pain- 13%. In comparison about 50% experienced the reduction of pain on 7th postoperative day based on VAS score(Table-1).

Association between the type of impaction and severity of pain on 7th postoperative day was seen. Majority of patients with mesio-angular impaction(20%) experienced no pain on the seventh day followed by no pain in horizontal(16.67%)impaction and vertical impaction-10%. . Chi-square test was done and Pearson chi-square value-8.949, P-value-0.44 which is found to be statistically insignificant.

Strategy for managing the clinical symptoms after third molar removal is aimed at interfering with the inflammatory process in order to limit the intensity and shorten the duration of the clinical signs of inflammation: pain, edema, local hyperthermia, erythema, and loss of function. In maxillofacial surgery, various methods are used to decrease

postoperative swelling, including pressure dressings, ice packs, and placement of drains. Various studies have been done in our institution on the study population (12-27). Excessive pressure in the lower third of the face and neck result in severe discomfort and can compress the airway in some patients. Moreover, intraoral drains are (Shetty and Mohan, 2013) usually not well tolerated by most patients. The use of ice bags to control edema after a maxillofacial procedure also has limited (Ambrus, Lassman and De Marchi, 1967) application. The use of enzymes like trypsin, chymotrypsin, bromelain as anti-inflammatory agents came into practice after it was observed during the 1950s in the USA. Enzymes are considered as extremely potent substances and the possibility of their therapeutic application is attractive. Trypsin and chymotrypsin is a proteolytic enzyme that provides better resolution of inflammatory symptoms and promotes the speedy recovery of other existing enzyme preparations.

Out of 30 patients, 16 were males and 14 were females. The mean age of the patients was 21-25 years. Overall this study is found to be effective in reducing the pain, swelling and healing time, however its action has been found to vary in different tissue in different patients

Abdul Wahab, P. U. et al. (2017) 'Risk Factors for Post-operative Infection Following Single Piece Osteotomy', *Journal of maxillofacial and oral surgery*, 16(3), pp. 328–332.

Ambrus, J. L., Lassman, H. B. and De Marchi, J. J. (1967) 'Absorption of exogenous and endogenous proteolytic enzymes', *Clinical Pharmacology & Therapeutics*, pp. 362–368. doi: 10.1002/cpt196783362.

Ashok, B. S., Ajith, T. A. and Sivanesan, S. (2017) 'Hypoxia-inducible factors as neuroprotective agent in Alzheimer's disease', *Clinical and experimental pharmacology & physiology*, 44(3), pp. 327–334.

Danda, A. K. (2010) 'Comparison of a single noncompression miniplate versus 2 noncompression miniplates in the treatment of mandibular angle fractures: a prospective, randomized clinical trial', *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*, 68(7), pp. 1565–1567.

Das, J. et al. (2015) 'Use of Corticosteroids in third molar surgery: Review of literature', *Universal Research Journal of Dentistry*, p. 171. doi: 10.4103/2249-9725.162800.

Devi, V. S. and Gnanavel, B. K. (2014) 'Properties of Concrete Manufactured Using Steel Slag', *Procedia Engineering*, 97, pp. 95–104.

Eapen, B. V., Baig, M. F. and Avinash, S. (2017) 'An Assessment of the Incidence of Prolonged Postoperative Bleeding After Dental Extraction Among Patients on Uninterrupted Low Dose Aspirin Therapy and to Evaluate the Need to Stop Such Medication Prior to Dental Extractions', *Journal of maxillofacial and oral surgery*, 16(1), pp. 48–52.

Gopalakannan, S., Senthilvelan, T. and Ranganathan, S. (2012) 'Modeling and Optimization of EDM Process Parameters on Machining of Al 7075-B4C MMC Using RSM', *Procedia Engineering*, 38, pp. 685–690.

Govindaraju, L., Neelakantan, P. and Gutmann, J. L. (2017) 'Effect of root canal irrigating solutions on the compressive strength of tricalcium silicate cements', *Clinical oral investigations*, 21(2), pp. 567–571.

Islam, A. A. et al. (2020) 'Comparative evaluation of anti-inflammatory effect of bromelain-trypsin combination versus diclofenac sodium after surgical removal of mandibular third molar teeth', *Update Dental College Journal*, pp. 16–20. doi: 10.3329/updcj.v10i1.46687.

Jeevanandan, G. and Govindaraju, L. (2018) 'Clinical comparison of Kedo-S paediatric rotary files vs manual instrumentation for root canal preparation in primary molars: a double blinded randomised clinical trial', *European Archives of Paediatric Dentistry*, pp. 273–278. doi: 10.1007/s40368-018-0356-6.

Kavitha, M. et al. (2014) 'Solution combustion synthesis and characterization of strontium substituted hydroxyapatite nanocrystals', *Powder Technology*, 253, pp. 129–137.

Lekha, L. et al. (2014a) 'Schiff base complexes of rare earth metal ions: Synthesis, characterization and catalytic activity for the oxidation of aniline and substituted anilines', *Journal of organometallic chemistry*, 753, pp. 72–80.

Lekha, L. et al. (2014b) 'Synthesis, spectroscopic characterization and antibacterial studies of lanthanide(III) Schiff base complexes containing N, O donor atoms', *Journal of Molecular Structure*, pp. 307–313. doi: 10.1016/j.molstruc.2013.10.014.

Menon, S. et al. (2018) 'Selenium nanoparticles: A potent chemotherapeutic agent and an elucidation of its mechanism', *Colloids and surfaces. B, Biointerfaces*, 170, pp. 280–292.

Neelakantan, P. et al. (2015) 'Antibiofilm activity of three irrigation protocols activated by ultrasonic, diode laser or Er:YAG laser in vitro', *International endodontic journal*, 48(6), pp. 602–610.

Neelakantan, P. et al. (2015) 'Influence of Irrigation Sequence on the Adhesion of Root Canal Sealers to Dentin: A Fourier Transform Infrared Spectroscopy and Push-out Bond Strength Analysis', *Journal of endodontia*, 41(7), pp. 1108–1111.

Neelakantan, P., Grotra, D. and Sharma, S. (2013) 'Retreatability of 2 mineral trioxide aggregate-based root canal sealers: a cone-beam computed tomography analysis', *Journal of endodontia*, 39(7), pp. 893–896.

Parthasarathy, M. et al. (2016) 'Effect of hydrogen on ethanol-biodiesel blend on performance and emission

- characteristics of a direct injection diesel engine', *Ecotoxicology and environmental safety*, 134(Pt 2), pp. 433–439.
- Patil, S. B. et al. (2017) 'Comparison of Extended Nasolabial Flap Versus Buccal Fat Pad Graft in the Surgical Management of Oral Submucous Fibrosis: A Prospective Pilot Study', *Journal of maxillofacial and oral surgery*, 16(3), pp. 312–321.
- PradeepKumar, A. R. et al. (2016) 'Diagnosis of Vertical Root Fractures in Restored Endodontically Treated Teeth: A Time-dependent Retrospective Cohort Study', *Journal of endodontia*, 42(8), pp. 1175–1180.
- Praveen, K. et al. (2001) 'Hypotensive anaesthesia and blood loss in orthognathic surgery: a clinical study', *The British journal of oral & maxillofacial surgery*, 39(2), pp. 138–140.
- Putchala, M. C. et al. (2013) 'Ascorbic acid and its pro-oxidant activity as a therapy for tumours of oral cavity – A systematic review', *Archives of Oral Biology*, pp. 563–574. doi: 10.1016/j.archoralbio.2013.01.016.
- Rajendran, R. et al. (2019) 'Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and a Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An in Vitro Study', *Pesquisa Brasileira em Odontopediatria e Clínica Integrada*, pp. 1–10. doi: 10.4034/pboci.2019.191.61.
- Sajan, D. et al. (2011) 'Molecular structure and vibrational spectra of 2,6-bis(benzylidene)cyclohexanone: a density functional theoretical study', *Spectrochimica acta. Part A, Molecular and biomolecular spectroscopy*, 78(1), pp. 113–121.
- Santosh, P. (2015) 'Impacted mandibular third molars: Review of literature and a proposal of a combined clinical and radiological classification', *Annals of Medical and Health Sciences Research*, p. 229. doi: 10.4103/2141-9248.160177.
- Shetty, V. and Mohan, A. (2013) 'A Prospective, Randomized, Double-Blind, Placebo-Controlled Clinical Trial Comparing the Efficacy of Systemic Enzyme Therapy for Edema Control in Orthognathic Surgery Using Ultrasound Scan to Measure Facial Swelling', *Journal of Oral and Maxillofacial Surgery*, pp. 1261–1267. doi: 10.1016/j.joms.2013.01.008.
- Uthrakumar, R. et al. (2010) 'Bulk crystal growth and characterization of non-linear optical bistiourea zinc chloride single crystal by unidirectional growth method', *Current applied physics: the official journal of the Korean Physical Society*, 10(2), pp. 548–552.
- Vijayakumar, G. N. S. et al. (2010) 'Synthesis of electrospun ZnO/CuO nanocomposite fibers and their dielectric and non-linear optic studies', *Journal of alloys and compounds*, 507(1), pp. 225–229.
- Vishnu Prasad, S. et al. (2018) 'Report on oral health status and treatment needs of 5-15 years old children with sensory deficits in Chennai, India', *Special care in dentistry: official publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry*, 38(1), pp. 58–59.
- Wahab, P. U. A. et al. (2018) 'Scalpel Versus Diathermy in Wound Healing After Mucosal Incisions: A Split-Mouth Study', *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*, 76(6), pp. 1160–1164.
- Wala, D. L. J. et al. (2020) 'Clinical Evaluation of Anti- Inflammatory Properties of Combination of Bromelain, Trypsin and Rutoside with Combination of Ibuprofen, Trypsin and Chymotrypsin following third Molar Extraction– A Comparative Study', *Journal of Medical Science And clinical Research*. doi: 10.18535/jmscr/v8i2.81.
- Weber, C. R. and Griffin, J. M. (1994) 'Evaluation of dexamethasone for reducing postoperative edema and inflammatory response after orthognathic surgery', *Journal of Oral and Maxillofacial Surgery*, pp. 35–39. doi: 10.1016/0278-2391(94)90010-8.
- Website (no date). Available at: Kuldeep Govani et al (2018) 'A Prospective Study on the Effectiveness of Trypsin-Chymotrypsin and Dexamethasone in Control of Post Operative Pain, Swelling and Trismus Following Surgical Removal of Mandibular Third Molar ', *International Journal of Current Advanced Research*, 07(3), pp. 11409-11411. DOI: <http://dx.doi.org/10.24327/ijcar.2018.11411.1973> (Accessed: 14 June 2020).

## CONCLUSION

Trypsin and chymotrypsin seem reasonable to advocate the use of these drugs after surgical removal of impacted mandibular third molar for management of post-operative pain and trismus. Chymotrypsin can be used as an alternative drug to control inflammation in cases where corticosteroids are contraindicated and not feasible.

## Authors Contribution

First author (Harini G) performed analysis, and interpretation and wrote the manuscript. Second author (Dr. Dinesh Prabu) contributed to conception, data designs, analysis, interpretation and critically revised the manuscript. Third author (Dr. Bala Krishnan R N) participated in the study and revised the manuscript. All the three authors have discussed the results and contributed to the final manuscript.

**Conflict of Interest**

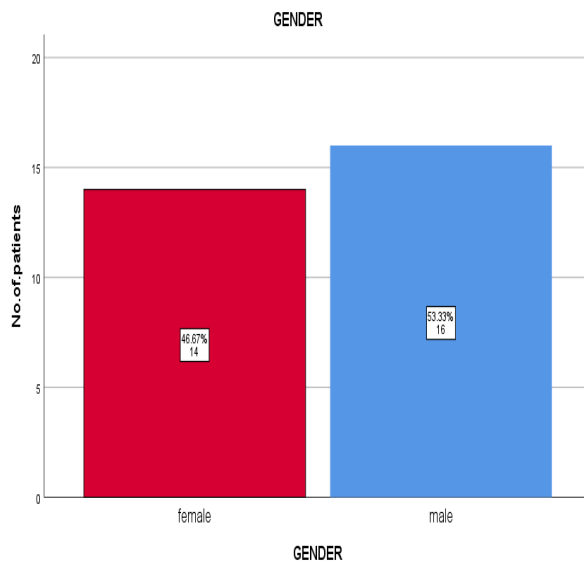
There are no conflicts of interest

**ACKNOWLEDGEMENT**

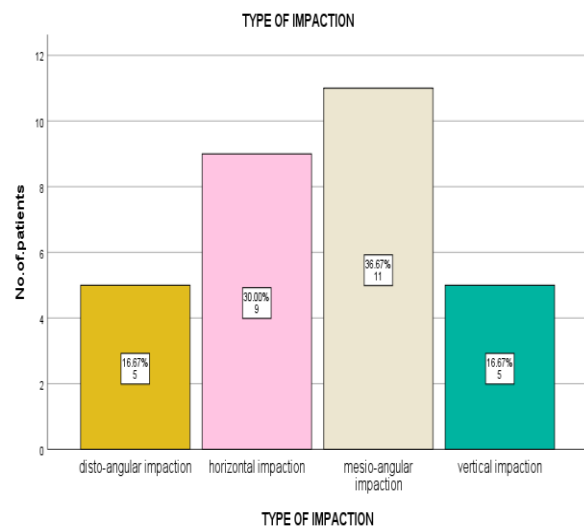
This study was supported by Saveetha institute of technical and medical sciences, Chennai.

**REFERENCES**

1. Al-Sandook, T. A., Tawk, N. O., & Qassim, D. A. (2014). Clinical evaluation of the efficacy of orthal-forte (prolytic enzymes, trypsin and chymotrypsin) on postoperative sequel following the removal of lower impacted third molar. *Int J Enhanc Res Sci Technol Eng*, 3, 169-73



**Fig.1: Gender distribution in this study. X axis denotes the number of patients and Y axis denotes the patients gender participated in this study. Male(blue) predilection was found in this study with 53.33% followed by females(pink) with 46.67%**

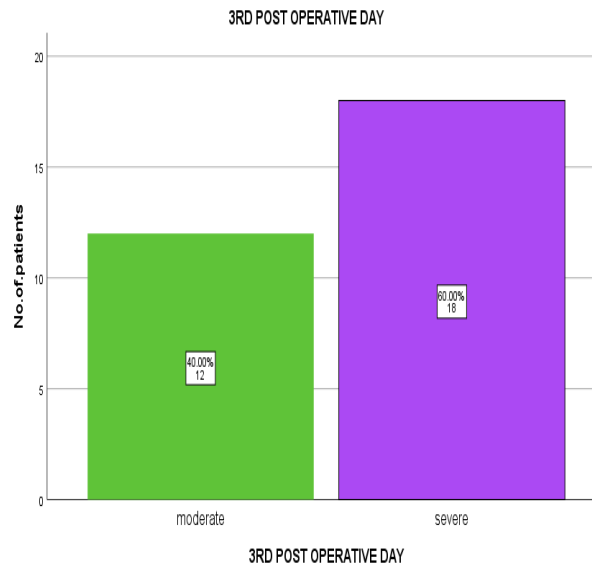


**Fig.2: Bar graph shows the type of impaction taken in this study for extraction. X-axis corresponds to the type of impaction and Y-axis corresponds to the number of patients involved in this study. The most commonly found was mesio-angular impaction (36.67%) followed by horizontal impaction (pale**

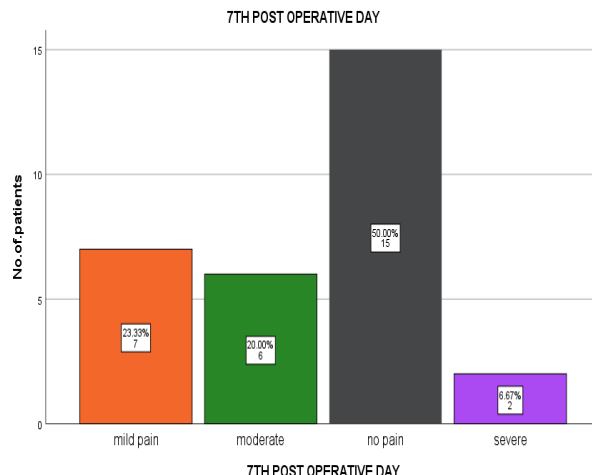
pink)-30%,disto-angular(mustard) and vertical (turquoise)impaction of 16.67% each. Mesio-angular impaction was found in predominance.

**Table 1: Comparison of pain scores(VAS) on the 3rd and 7th Postoperative day. On the third day of extraction patients experienced moderate-40% to severe pain-60%, On 7th day no pain was observed in 50% of the study population followed by mild pain- 33%,few experienced severe pain-3%,and moderate pain- 13%. In comparison about 50% experienced the reduction of pain on 7th postoperative day.**

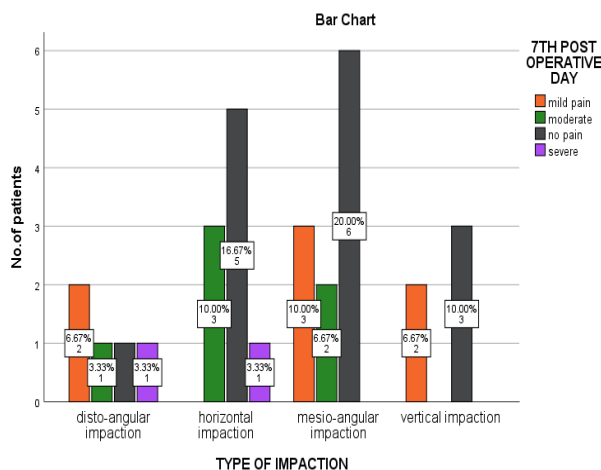
Time of surgery	Nature of pain (VAS)	Number of patients(n%)
3 <sup>rd</sup> postoperative day	No pain(score 0-)	0(0%)
	Mild pain(score 1-3)	0(0%)
	Moderate pain(score 4-6)	17(56%)
	Severe pain(score 7-9)	13(44%)
7 <sup>th</sup> postoperative day	No pain(score- 0)	15(50%)
	Mild pain(score-1-3)	10(33%)
	Moderate pain(score 4-6)	4(13%)
	Severe pain(score 6-9)	1(3%)



**Fig.3: Bar graph showing the severity of pain during 3rd postoperative day. X-axis corresponds to the severity of pain and Y-axis shows the number of patients. Severe pain(purple) was experienced by 18 patients (60%)and 12 patients(40%) experienced moderate pain(green)**



**Fig.4:** Bar graph showing the severity of pain during 7th postoperative day. X-axis corresponds to the severity of pain and Y-axis shows the number of patients. No pain(black) was experienced by 15 patients (50%) and 6 patients(40%) experienced moderate pain(green), mild pain(orange) was experienced by 7 patients(23.33%) and severe pain(purple) was experienced by 2 (6.67%) patients



**Fig.5:** Association between the type of impaction and severity of pain on 7th postoperative day was seen. X-axis corresponds to the type of impaction and Y-axis corresponds to the number of patients. Majority of patients with mesio-angular impaction(20%) experienced no pain on the seventh day followed by no pain in horizontal(16.67%)impaction and vertical impaction-10%. . Chi-square test was done and Pearson chi-square value-8.949, P-value-0.44 which was found to be statistically insignificant.