

Effects of intraoperative placement of tetracycline, tetracycline + gelatin sponge, and placebo on postoperative pain after mandibular molar extraction: A comparative prospective study

ABSTRACT

Background: Painless postoperative period is a major requisite following routine dental extractions. Reduction in the postextraction complication is beneficial to both clinician and patients. Hence, emphasis should be given to the techniques and agents that help reduce the complications for better postoperative recovery.

Materials and Methods: Three groups of 30 patients each requiring mandibular molar extractions were randomly selected with intrasocket placement of tetracycline, tetracycline plus gelatin sponge, and placebo control after extraction. A small piece of collagen membrane was used on the superior surface of the socket after the placement of the medicament in Group A and Group B. The postoperative pain scores were evaluated at 24 h, 48 h, and 7 days postoperatively.

Results: Ninety patients requiring mandibular molar teeth extraction were enrolled as the study participants. Forty-two patients (55.26%) were male and 34 (44.73%) were female. Tetracycline alone and tetracycline + gelatin sponge group shows no statistical significant difference in reducing postoperative pain after 7 days, but the pain score values were less in Tetracycline + gelatin sponge group. The comparison between tetracycline alone and control group showed no significant difference observed between the groups at 24 h but showed statistically significant difference between the groups after 48 h and 7 days, whereas comparison between tetracycline + gelatin sponge and control group showed statistically significant difference between the groups after 24 h, 48 h, and 7 days ($P = 0.009, 0.001, \text{ and } 0.017$, respectively).

Conclusion: Tetracycline and gelatin sponge intrasocket placement provides a good substitute to the prolong use of analgesics and as a good adjuvant in reducing pain in the first few days after routine dental extraction.

Keywords: Gelatin sponge, pain, postextraction, tetracycline

VINAY PATIL, P.N. RAMARAJ¹, MANDEEP SHARMA², ROHIT SINGH³, ABHIJITH GEORGE⁴, BHASKAR ROY⁵

Department of Oral and Maxillofacial Surgery, Nanded Rural Dental College and Research Center, Nanded, Maharashtra,

¹Department of Oral Surgery, KVG Dental College, Sullia,

⁴Department of Head and Neck Surgical Oncology, HCG,

Bengaluru, Karnataka, ²Department of Dentistry, Government

Medical College, Kathua, Jammu and Kashmir, ³Niharika Dental, Oral and Maxillofacial Surgery Clinic and Implant Centre, Surat,

Gujarat, ⁵GSR Hospital and Craniofacial Research Center,

Hyderabad, Telangana, India

Address for correspondence: Dr. Mandeep Sharma, Senior Resident, Department of Dentistry, GMC Kathua, Kathua, Jammu and Kashmir, India, House No. 29 Sector 5, Upper Roop Nagar, Jammu, Jammu and Kashmir - 180 013, India. E-mail: mandeep.sharma053@gmail.com

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INTRODUCTION

Exodontia is the most frequently surgical procedure performed in dentistry, and its success is equally important both to patient and the dental surgeon. For patients, the most common reason for the extraction of teeth is pain,^[1] and hence, it is important for patient as well as for the surgeon to manage the perioperative as well as postoperative pain. Researches have shown that pain, swelling, and dry

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socket are the common complications after the extraction of teeth.^[2] Dry socket is more frequently seen in mandibular molars compared to any other teeth.^[3] Alveolar osteitis more commonly known as “dry socket” is a frequent complication which occurs after extraction. This condition remains a common postoperative problem as it results in severe postoperative pain. Repeated hospital visits can also be problematic to patients with this condition. AO is known to occur between 1 and 3 day after tooth extraction and literature believes that almost 95%–100% of all the cases have reported within a week. Pathogenesis of dry socket is not very well understood in the literature. Birn’s published literature suggested that the etiology of this condition being an increase in the local fibrinolysis which further leads to disintegration of the blood clot in the socket.^[4] The pain experienced with it is debilitating and effects daily function.

Many intrasocket antibiotics have been tried in the literature to prevent or to reduce the postoperative complications after extraction. Topical tetracycline placed in the extraction socket is known to reduce postoperative pain, trismus compared to the one’s undergoing routine dental extraction without its placement.^[5]

Tetracyclines discovered in 1940s show activity against a wide variety of microorganisms including both Gram-positive and Gram-negative bacteria. Chlamydia, rickettsia, mycoplasmas, and protozoan parasites are also under its spectrum. Mechanism of action of tetracyclines is that it inhibits protein synthesis in bacteria by preventing the association of aminoacyl-tRNA with bacterial ribosome.^[6] Matrix metalloproteinases (MMPs) are a group of >20 Zn-dependent enzymes which regulate inflammation. Pathologically, the elevation of MMPs causes connective tissue and bone loss in various inflammatory diseases. Tetracyclines are effective inhibitors of mammalian MMPs. Tetracyclines can inhibit both intracellular and extracellular MMPs. Tetracycline inhibits MMPs on specific sites that has been identified as the calcium and zinc-binding site at C-11 and 12. The anti-inflammatory nature of tetracycline is utilized in the various dermatological diseases and in periodontitis too.^[7] The anti-inflammatory property of tetracyclines can be useful in the reduction of postoperative sequelae following extraction. It has also been reported that, gelatin sponge too reduces postoperative complications after oral surgical wounds. Gelatin sponge serves as a mechanical hemostatic agent which obliterates dead space which hastens healing of wound.^[8]

There is no comparative study available in the literature to evaluate the efficacy of tetracycline and tetracycline + gelatin sponge to reduce postoperative pain after extraction in

patients without any systemic antibiotic coverage. Although studies regarding the use of topical tetracycline as well as gelatin sponge independently placed in the extraction socket^[5,8] have been done but no comparative study is available in literature to evaluate their combined usage in extraction socket. This study evaluates the efficacy of tetracycline alone and tetracycline + gelatin sponge to reduce post extraction pain in patients without any systemic antibiotic coverage.

MATERIALS AND METHODS

Aims and objectives

Assessment of postextraction pain in patients after mandibular molar extraction divided into three groups (with or without intra-socket tetracycline, tetracycline + gelatin sponge).

Ninety patients requiring mandibular molar teeth extraction of the age group of 18–60 years who reported to the Department of Oral and Maxillofacial Surgery, from December 2015 to July 2017 were included in the study. Written informed consent was obtained in a given format before the treatment. Institutional ethical clearance was obtained before the study was conducted. Patients were divided into three groups in a random manner:

- Group A – Patients treated with intrasocket tetracycline alone ($n = 30$)
- Group B – Patients treated with intrasocket tetracycline + gelatin sponge ($n = 30$)
- Group C – Patients treated without any intrasocket medicaments ($n = 30$).

Patients who were immunocompromised, with acute abscess, mobile teeth, allergic to tetracycline mentally challenged patients, patients unable to communicate, who is already on systemic antibiotics for other purpose and pregnant and lactating women were excluded from the study. Teeth requiring transalveolar extractions were excluded from the study. Third molars requiring bone guttering or sectioning of the tooth were excluded too.

Preoperative analysis was done using the intraoral periapical radiograph [Figure 1]. Under strict aseptic condition, surgical procedure was carried out by the same operator. Tetracycline capsule (250 mg) was mixed with 0.5 ml of saline and placed in the socket in Group A [Figure 2], whereas in Group B, this mixture was impregnated on gelatin sponge which was cut according to the extraction socket size and was placed in the same. Group C was kept as such. Preoperative mouthwash rinsing was done with Perioguard mouthwash (1 min) and

Table 1: Pain assessment at follow-up visits

Visual Analog Scale of 10 cm score	Score after 24 h	Score after 48 h	Score after 7 days
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Figure 4: Preoperative record



Figure 5: Intra-operative procedure- tooth extraction



Figure 6: Intra-operative procedure- placement of medication and suturing of extraction socket



Figure 7: Twenty-four hours follow-up

The age of the patients included in the study was between 16 years and 60 years, out of which 50 patients (55.55%) were male and 40 (44.44%) were female [Graph 1].

The Kruskal–Wallis test [Table 2] shows statistically significant difference among three independent groups in relation to pain scale VAS ($P = 0.024, 0.003, \text{ and } 0.018$, respectively). Further statistical test (Mann–Whitney U) was applied to the same data. The Mann–Whitney U-test in between tetracycline alone and tetracycline + gelatin sponge group, which shows no statistical significant difference between them ($P = 0.069; 0.061; 1.00$, respectively), this indicates tetracycline alone and tetracycline + gelatin sponge are equally effective in reduction of pain after 7 days postoperatively [Table 3 and Graph 2]. Pain reduction after 24 h and 48 h are slightly more in

tetracycline + gelatin sponge group, but statistically results are insignificant.

Comparison between tetracycline alone and control group was done using the Mann–Whitney U-test for VAS_24, VAS_48, and VAS_7D were performed. There is no significant difference observed between the groups at 24 h ($P = 0.060$), but showed statistically significant difference between the groups after 48 h and 7 days ($P = 0.031 \text{ and } 0.017$, respectively). This indicates both the groups experienced same amount of pain at first 24 h and observed significant pain reduction in tetracycline alone group compared to the control group at 48 h and 7 days interval [Table 4 and Graph 3].

Comparison between tetracycline + gelatin sponge and control group was done using the Mann–Whitney U-test for VAS_24, VAS_48, and VAS_7D were performed. The test



Figure 8: Forty-eight hours follow-up



Figure 9: Seven days follow-up



Figure 10: Fourteen days follow-up

results showed statistically significant difference between the groups after 24 h, 48 h, and 7 days ($P = 0.009, 0.001, \text{ and } 0.017$, respectively). This indicates that tetracycline + gelatin

Table 2: Kruskal–Wallis test

Group	n	Mean rank	P
VAS_24			
Control	30	54.98	0.024*
Tetracycline alone	30	43.47	
Tetracycline + Abgel	30	38.05	
Total	90		
VAS_48			
Control	30	57.27	0.003*
Tetracycline alone	30	43.5	
Tetracycline + Abgel	30	35.73	
Total	90		
VAS_7D			
Control	30	54.77	0.018*
Tetracycline alone	30	40.87	
Tetracycline + Abgel	30	40.87	
Total	90		

*Significant association set at ≤ 0.05 . VAS: Visual Analog Scale

Table 3: Represents the Visual Analog Scale score (pain) between Group A and Group B

Pain scale	Group	n	Mean rank	P
VAS_24	Tetracycline alone	30	32.32	0.069
	Tetracycline + Abgel	30	28.62	
VAS_4s8	Tetracycline alone	30	33.15	0.061
	Tetracycline + Abgel	30	28.87	
VAS_7D	Tetracycline alone	30	25.87	1.00
	Tetracycline + Abgel	30	25.87	

*Significant association set at ≤ 0.05 . VAS: Visual Analog Scale

Table 4: Represents the Visual Analog Scale score (pain) between Group A and Group C

Pain scale	Group	n	Mean rank	P
VAS_24	Tetracycline alone	30	32.32	0.060
	Control	30	36.67	
VAS_48	Tetracycline alone	30	33.15	0.031*
	Control	30	39.62	
VAS_7D	Tetracycline alone	30	25.87	0.017*
	Control	30	35.13	

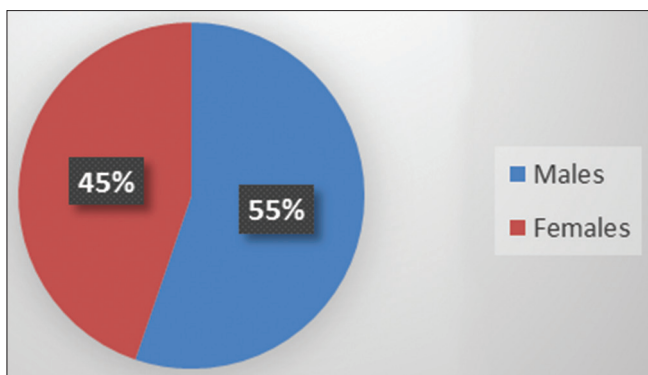
*Significant association set at ≤ 0.05 . VAS: Visual Analog Scale

Table 5: Represents the Visual Analog Scale score (pain) between Group B and Group C

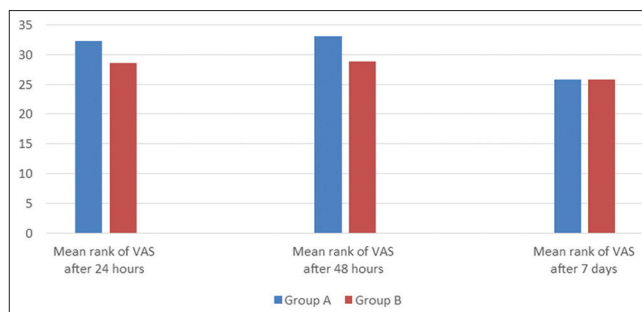
Pain scale	Group	n	Mean rank	P
VAS_24	Tetracycline + abgel	30	28.62	0.009*
	Control	30	36.67	
VAS_48	Tetracycline + Abgel	30	28.87	0.001*
	Control	30	39.62	
VAS_7D	Tetracycline + Abgel	30	25.87	0.017*
	Control	30	35.13	

*Significant association set at ≤ 0.05 . VAS: Visual Analog Scale

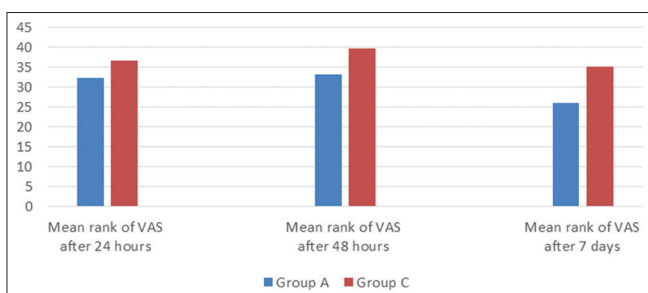
sponge group [Table 5 and Graph 4] showed better pain reduction compared to the control group at 24 h, 48 h, and 7 days interval.



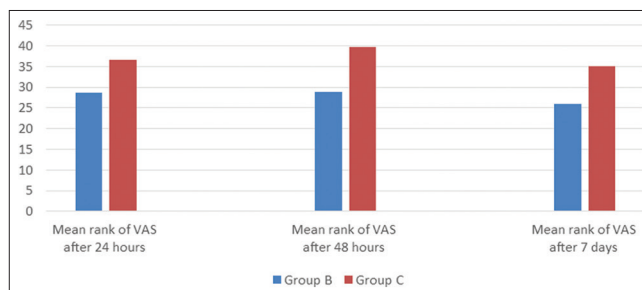
Graph 1: Gender distribution of study participants



Graph 2: Mean rank of Visual Analog Scale score in Group A and Group B at different intervals



Graph 3: Mean rank of Visual Analog Scale score in Group A and Group C at different intervals



Graph 4: Mean rank of Visual Analog Scale score in Group B and Group C at different interval

DISCUSSION

According to the International Association for the Study of Pain, pain is defined as “Unpleasant sensory and emotional experience associated with actual or potential tissue damage.” Pain after extraction is a common complication. Pain is common body response to wound anywhere in the body. Postextraction pain occurs in extraction wound as it is not different from other body wound, and this pain result from the inflammation at the site of extraction which is a part of normal wound healing.

Effort to minimize postoperative complications after the extraction of tooth is going on from long time. Maintaining asepsis, soft-tissue handling, achieving hemostasis, and proper postoperative instructions may reduce these but not completely eradicate it. The use of intrasocket placement of bioactive substances by many authors to reduce postoperative sequelae and regenerative purposes has been very well documented.

Gabler and Creamer shows that tetracycline causes the suppression of human neutrophil function,^[9] this can be on the basis for fact that intra-socket tetracycline reduces postoperative pain by reduction in the postoperative inflammation.

Tetracyclines are known to cause inhibition of MMPs which contribute to tissue destruction.^[10] Tetracyclines have the

ability to scavenge reactive oxygen species (ROS) and act as anti-inflammatory agents. Increase formation of ROS is seen in chronic inflammatory diseases and it leads to oxidative damage and also causes dysfunction of cells. Tetracyclines ability to scavenge free radicals, overcomes this oxidative stress.^[11] This anti-inflammatory action reduces the amount of pain postoperatively. The antihypnociceptive effects of tetracyclines are well documented in the literature too.^[12]

Gelatin sponge functions as a supportive and mechanical agent which provides structural support for the clot. This surface-mediated hemostatic device hastens the clot formation because of its spongy physical properties. Platelets are present blood clot and provide natural growth factors (BMP, platelet-derived growth factor, and transforming growth factor-beta) which are essential for tissue healing and regeneration.^[13]

Pain was assessed in our study on the VAS after 24 h, 48 h, and after 7 days postoperatively. The results show significant reduction in postoperative pain in tetracycline alone as well as in tetracycline + gelatin sponge groups compared to group which did not receive any intrasocket medicament. On the other hand, postoperative pain was less in tetracycline + gelatin sponge group compared to tetracycline alone group but difference was not statistically significant. According to Sanchis *et al.* also, the patients in whom intra-alveolar tetracycline was administered experienced

less pain and consumed few analgesics than compared to the patients who did not received intraalveolar tetracycline, although the results were not statistical significant.^[5]

In our results, pain was more at 24 h after extraction in all the three groups with highest pain scores for the control group and the lowest scores for group in which tetracyclines plus gelatin sponge was given. A study conducted by Hussain and Alnahr^[14] on postoperative pain after intraalveolar extraction concluded that mild pain was experienced by 38.6% cases, whereas 12.8%, 22% experienced shooting pain, constant pain at evening of extraction with 15.2% cases still suffering mild pain after 7 days too. This study also concluded that 6.8% cases used analgesics even after 7 days. In our study, tetracycline usage reduced the postoperative pain levels significantly low than the control group.

Dry socket with bone exposure, halitosis, and necrotic debris was noted in 2 out of 30 patients in Group C (control group) representing an incidence of 6.66% which is slightly higher compared to 2%–5% as mentioned in the literature for routine extraction.^[3,15] Both two cases of dry socket were noted in the region of tooth no 38; out of which one case was in 37-year-old female and other was in 48-year-old male and managed by daily socket irrigation with betadine and zinc oxide eugenol pack for 3 days.

In tetracycline alone and tetracycline + gelatin sponge group, not a single case of complicated wound healing or dry socket was found. This result is accordance with studies mentioned in literature about intrasocket tetracycline. Sanchis *et al.* show that, intra-alveolar placement of tetracycline compound after the surgical removal of impacted mandibular third molars did not affect the incidence of dry socket.^[5] Gabriela Jude Fernandes *et al.* published a case in which doxycycline/local anesthetic-soaked Gelfoam sponge was placed into the apical portion of the socket after extraction. Postoperative pain or discomfort was not reported in that case. The patient was able to carry out his normal routine activities. No evidence of dry socket was noted on follow-up of that case also. The author concluded that Doxycycline/local anesthetic/Gelfoam sponge seems to be an effective technique in the prevention of dry sockets.^[16] According to Julius *et al.*, piece of Gelfoam impregnated with 0.5 ml of Terra-Cortril which combined with oxytetracycline and hydrocortisone can be used as intrasocket medicament to reduce the incidence of localized osteitis.^[17] A double-blind study was carried out by Swanson to evaluate the effectiveness of topical tetracycline used as a suspension in a square of gelatin sponge for the prevention of dry socket in 100 impacted mandibular molars. The study results show that, the incidence of dry socket was decreased markedly in

patients who received dressing of topical tetracycline used as a suspension in a square of gelatin sponge.^[18]

As the role of dry socket in causing postextraction pain and discomfort cannot be ruled out, so efforts should be made to minimize this complication which ultimately will reduce the postoperative pain. The placement of intraalveolar tetracycline and gelatin sponge reduces the incidence of it as in our study 60 extractions were carried in Group A and B combined with no incidence of dry socket.

No other complications with the use of tetracycline and gelatin sponge were reported in our study.

CONCLUSION

The use of intraalveolar tetracycline and gelatin sponge reduces the postextraction complication of pain and dry socket. Hence, this modality of treatment should be employed following extraction, especially in the areas prone to dry socket formation as well as during traumatic extractions.

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Conflicts of interest

There are no conflicts of interest.

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