

CLINICAL EFFICACY OF SINGLE DOSE CHLORHEXIDINE GEL APPLICATION IN MOLARS EXTRACTIONS-A RANDOMIZED CLINICAL TRIAL



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INTRODUCTION: Alveolar osteitis (AO) is a significant post-operative complication following dental extraction. Chlorhexidine (CHX) is an antibacterial agent used in various forms for prophylaxis and treatment of various dental diseases including prevention of AO after extraction of lower 3rd molar surgeries. Few studies have been done to study the effectiveness of single dose application of 0.2% CHX gel after all molars (1st, 2nd and 3rd) in both maxilla and mandible extractions.

METHODOLOGY: A phase III, clinical trial on 253 patients was done using block randomization dividing subjects into experimental (CHX gel) and control (placebo gel) groups. The type of extraction and surgical flap design used was recorded. After 3 days post-extraction, patients were recalled and assessed for alveolar osteitis. The Chi-Square test was used to compare AO incidence in the two study groups with level of significance set at the 0.05.

RESULTS: The incidence of AO in surgical extraction cases was 38.7% (p=0.001). The group in which envelope flap with buccal releasing incision was performed had highest incidence of AO (67.74%) (p=0.001). The single dose application of CHX The Incidence of AO was 18% in the placebo gel compared to 5.4% in CHX gel group (p=0.001). No cases of hypersensitivity to intra-socket placement of CHX gel were reported in this study.

CONCLUSIONS: Within the limitation of our study, the incidence of alveolar osteitis was reduced significantly when less invasive type of extraction, less invasive flap design and single dose application of chlorhexidine gel in extraction socket was used.

KEY WORDS: Alveolar osteitis, Chlorhexidine gel, molar extraction, dry socket, flap design.

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INTRODUCTION

Alveolar osteitis (AO) is an important complication following dental extractions by general dentists and specialists alike.^{1,2} Being an inflammatory disease, it is defined as "the postoperative pain in and around the extraction site, which increases in severity at

any time between day one and day three after the extraction, accompanied by a partially or totally disintegrated blood clot within the alveolar socket with or without halitosis."³ Other names used in literature are dry socket, alveolgia, alveolitis sicca dolorosa, localized osteomyelitis, fibrinolytic or post-operative alveolitis, or septic or necrotic socket.⁴

The etiology of the disease is not clearly known⁵, but various predisposing risk factors have been identified such as smoking, use of contraceptives, pericoronitis, poor oral hygiene, bone remnants in the socket, trauma during extraction and dislodgement of blood clot from the socket⁴,⁶⁻⁸ The level of surgical skills during extraction have also been linked with AO.^{9,10} Systemic

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factors associated with AO are diabetes, vitamin C deficiency, bleeding disorders and bone diseases such as Osteosclerosis and Paget's disease etc.^{11,12} The use of systemic antibiotic prophylaxis for the prevention of AO has been reported.¹³⁻¹⁸ Various preventive local drugs, steroids and medications have been studied which includes amoxicillin paste, methylprednisolone and dexamethasone.¹⁹⁻²² Chlorhexidine (CHX) is an antibacterial agent with established efficacy in dentistry.^{13,17,23-25} Chlorhexidine is available in various concentrations and forms, such as the mouth rinse 0.12%, 0.2%, 1% and 2%; gel 0.2%.^{12,21,26} CHX has been found effective against *Staphylococcus* and *Streptococcus* species which are the major source of dental infection.²⁷ The preventive role of CHX in alveolar osteitis in 3rd mandibular molar extractions is due to decreasing the bacterial load at the wound site.^{28,29} Very little research has been done to study the effects of type of extraction and surgical flap design in generalized molars (1st, 2nd and 3rd) extractions. Although the role of CHX is beneficial in mandibular 3rd molar surgeries, but its role for prevention of AO in generalized molars extractions (1st, 2nd and 3rd) in maxilla and mandible has not been studied. Therefore, the objective of our study was to study the effect of single dose of chlorhexidine on the frequency of AO.

METHODOLOGY

Sample

After approval from the Ethical Review Committee of the institution, a phase III (A phase which is designed to assess the effectiveness of the new interventional drug for its value in clinical practice),³⁰ double-blinded randomized clinical trial was conducted at the Oral Surgery Department of the Karachi Medical & Dental College, Karachi. The data collection was done from 1st October 2013 to 31st March 2014. An informed signed consent was taken from all the patients. The sample size of 250 was calculated by using the 24 % incidence of alveolar osteitis reported previously.²⁴ Unfortunately, the trial protocol was not registered at clinical trials.gov beforehand hence the data could not be released to the registry after the conduct of the study. Inclusion criteria: Patients aged between 18-65 years visiting the outpatient department for dental extraction of 1st, 2nd and 3rd molar teeth in maxilla or mandible. Exclusion Criteria: Patients with history of bone grafts in molar region, smoking, current or past antibiotics therapy within 15 days, multiple extractions

and any systemic disease or bleeding disorder were excluded.

Grouping and Randomization

The sample was randomized using block randomization into experimental (CHX) and control groups. The study was designed to have 80% power to detect 10% relative reduction of alveolar osteitis between the two groups (experimental and controls).¹² The dental extractions were performed by a trained dentist (X) adhering to a standardized extraction protocol. The 1.8 ml cartridge of 2% lidocaine plus 1:80,000 Epinephrine was used for extractions in this study. In mandibular molars, the inferior alveolar nerve block injection technique with lingual and long buccal nerve anesthesia was used. In maxillary molars, the facial and palatal infiltration technique was used. The extractions were divided into surgical and non-surgical extractions and recorded. The surgical extractions were divided in "envelope incision flap" and "envelope incision flap with buccal releasing incision". The design of flaps used was documented by dentist X with every case. After extractions, the intervention group was applied with single dose of 10 ml quantity of 0.2% Chlorhexidine Gluconate gel (Clinica, Platinum, Pakistan) on sterile gauze. The control group received the placebo with gel consistency on the gauze. The patients were asked to bite on the gauze for 15 minutes and given standard post-operative instructions.

Alveolar Osteitis Diagnosis

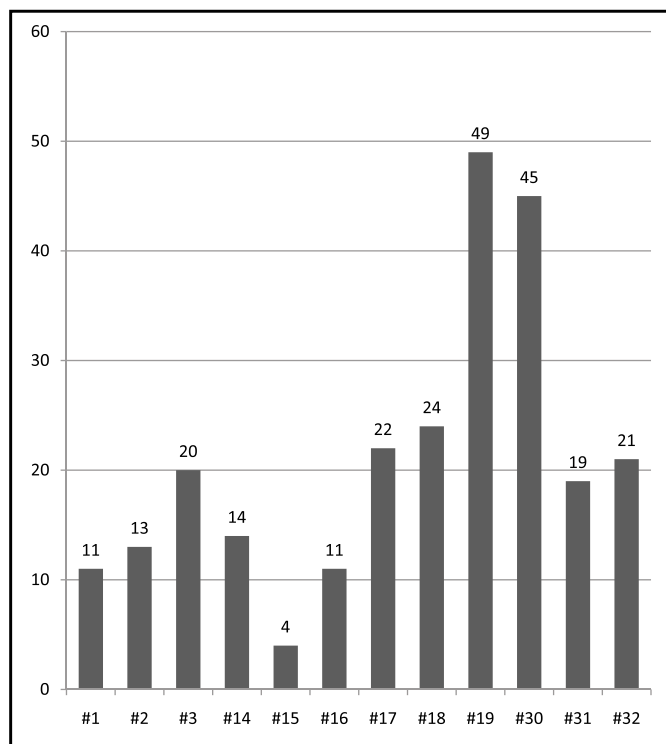
The patients were recalled on 3rd day post extraction and were assessed by a different dentist (Y). The pain was also measured on a Visual Analog Scale (VAS)¹⁹ ranging from 0-no pain to 10-worst pain imaginable. Any pain score above 5, in addition to clinical signs and symptoms based on Blum's criteria⁴ was diagnosed with Alveolar Osteitis by dentist (Y). The outcome assessor (Y) was blinded of the group allocation (CHX versus placebo) done by intervention provider (X). **Data Analysis:** The data was analyzed using SPSS 20.0 version for windows. The incidence of AO was compared with type of extraction, surgical flap design and the groups (experimental and control) using Chi-square test. Odds ratio was computed to determine the strength of association between AO and study group. The Yates corrected Chi square test was applied where the cell count in a cell was less than 5. The level of significance was set at 0.05.

RESULTS

There were a total of 253 patients; 41.9% were males and 58.1% females. The mean age of the patients was 36.65 years SD \pm 11yrs. Figure 1 represents the extraction site in Universal Tooth Numbering system. The mandibular

Figure 1

Extraction Site in Universal Tooth Numbering system



1st molars were the most common teeth to be extracted with combine incidence of left and right side teeth making 37% of the total teeth extracted. No cases of hypersensitivity to intra-socket placement of CHX gel were reported in this study.

The Table 1 represents the comparison of type of

Table 1

Association between type of extraction and alveolar osteitis

Extraction and Alveolar Osteitis		Alveolar Osteitis		Total	p-value
		yes	no		
Type of extraction	Surgical Extraction	24	38	62	0.001
	Non-surgical Extraction	6	185	191	
Total		30	223	253	

Chi square test was applied at 0.05 level of significance

extraction with incidence of alveolar osteitis. The majority of teeth were simple extractions with 75.5% of total cases. Only 24.5 % required surgical flap procedures for extractions. The surgical extractions had an incidence of 38.7% of alveolar osteitis, whereas, the simple non-surgical

extraction had only 3.1% incidence. The Chi-square test was used to establish a relationship and was found significant (p=0.001).

Table 2 and Figure 2 represent the comparison of type

Figure 2

Comparison of surgical flap for alveolar osteitis incidence

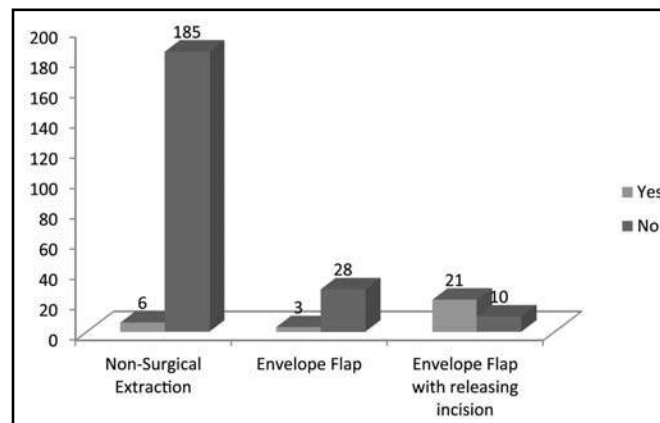


Table 2. Association between Surgical Flap and Alveolar Osteitis

Surgical Flap and Alveolar Osteitis		Alveolar Osteitis		Total	Chi-square p-value	Yates Corrected p-value
		yes	no			
Surgical Flap Used	Non-Surgical Extraction	6	185	191	0.001	0.001
	Envelope Flap	3	28	31		
	Envelope Flap with releasing incision	21	10	31		
Total		30	223	253		

Chi square test was applied at 0.05 level of significance

of surgical flap with the incidence of alveolar osteitis. The group in which envelope flap with releasing incision was performed had highest incidence of alveolar osteitis (67.74%). This decreased in envelope incision and non-surgical extractions. The Chi-square test followed by Yates correction was applied to establish a statistical relationship between the two variables and was found significant (p=0.001).

Table 3 and Figure 3 represent the comparison between **Figure 3.** Comparison of incidence of alveolar osteitis in the two study groups

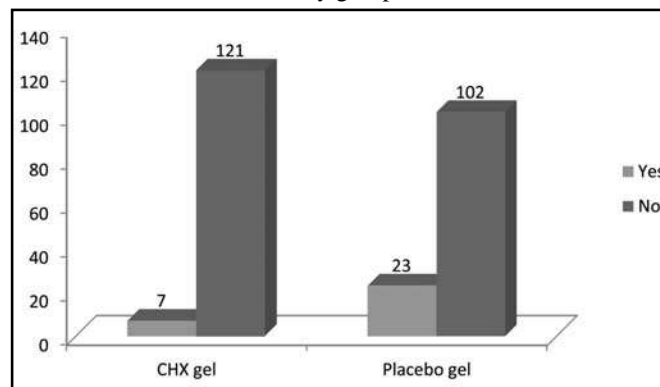


Table 3. Association between type of group and alveolar osteitis

Study group	Alveolar Osteitis		Total	OR	Chi square p-value
	yes	no			
Placebo Gel	23	102	125	3.90	0.001
CHX-Gel	7	121	128		
Total	30	223	253		

OR: Odd's ratio was calculated

CHX: Chlorhexidine Gluconate

types of gel group with the incidence of alveolar osteitis. A total of 11.9% cases were diagnosed with alveolar osteitis. The single dose application of alveolar osteitis reduced the incidence of alveolar osteitis from 18% in the control group to only 5.4% in experimental group. The Chi-Square test was applied to establish a relationship with the incidence of alveolar osteitis and was found significant ($p=0.001$).

DISCUSSION

The pain in and around the extraction site, halitosis and lack of wound healing associated with Alveolar Osteitis (AO) makes it a serious dental extraction complication.³¹ Although, it can occur at any site, but 3rd molar region had been focused predominantly in previous studies.^{28,32,33} In this study we focused on all molar extractions (1st, 2nd and 3rd) in maxilla and mandible. The level of surgical skills, trauma during extraction and invasiveness of surgical procedure for extraction has been studied to impact the incidence of AO in third molar.³⁴⁻³⁷ Malkawi et al.⁶ said the postoperative complications can be predicted with presence of pericoronitis, longer traumatic surgery and surgical flaps with releasing incisions. Haraji, et al.¹⁰ found that modified triangular flap decreases the incidence of AO and expedited healing post-surgery. Goldsmith et al.⁹ found pedicle flap had no incidence of AO, as compared to five cases in envelope flap. All the mentioned studies had relatively small sample size and focused on mandibular 3rd molar region. In this study, the incidence of AO in surgical extraction was 35.6% more than non-surgical extraction. There is a debate about the use of conservative dental extraction approach for ridge preservation which results in rapid wound healing and may be of a benefit during implant placement.³⁸⁻⁴¹ In this study, it was seen that in molar extraction cases, the surgical trauma involved with the most invasive flap design (envelope flap with buccal releasing incision) had the highest incidence of AO. The

incidence of AO was found higher in a similar invasive modified triangular flap, but this was not proven statistically significant.⁴² In another study though, the modified triangular flap design reduced the incidence of AO.¹⁰ Both studies had a small sample size of less than 50. The role of Chlorhexidine gel (CHX) has shown positive results in preventing AO, especially in the cases of impacted 3rd molars where the incidence of AO was reduced by as much as 70%.^{28,43} But the side effects of use of Chlorhexidine gel in dentistry have been questioned as well.^{16,44} Although no cases of hypersensitivity to intra-socket placement of CHX gel were reported in this study, but several case reports are now becoming available reporting both type I and type IV hypersensitivity in topically applied CHX.^{45,46} Incidence of AO in routine dental extractions varies from 0.5-5% in literature.^{11,47} In extractions of impacted 3rd molars the incidence varies from 1%-30%.^{3,48,49} In this study the incidence of alveolar osteitis was found to be 5.78% in experimental group and 22.54% in control group with a cumulative incidence of 11.85%. Several methods have been proposed to prevent AO such as intra-socket placement of antibiotics (Metronidazole, Clindamycin) in addition to topical CHX.⁵⁰

The recommended methods of use include CHX preoperative oral rinses continuing for 7 days postoperatively to single intraoral gel application; we opted for single intra-alveolar gel application rather than other topical methods in order to reduce the chance of protocol violation bias by the patients.¹³ Furthermore it has also been seen that using gel rather than CHX rinse was better in preventing AO.²⁵ Lagares et al.⁵¹ in his pilot study on third molar extractions had followed the same bioadhesive gel placement protocol as in our study and found a difference in the incidence dry socket but was not able to show statistically significant difference between the experimental and control group because of small sample size.⁵¹ In another study done in Pakistan, Babar et al. also found significant difference between control group and CHX bioadhesive gel use ($p=0.017$).⁵² In this study we found a highly significant difference in the incidence of AO between the CHX gel group and control group ($p=0.001$). The role of Chlorhexidine in the prevention of AO can be attributed to its antibacterial effect against the bacteria which causes fibrinolysis in the alveolar socket after extraction.²⁴ The use of Chlorhexidine in the prevention of Alveolar Osteitis in generalized molars (1st, 2nd and 3rd) in maxilla and mandible is emphasized. The limitation of this study is the focus on molar region

only. Further research needs to be done to address the effects of Chlorhexidine gel in all teeth extractions.

CONCLUSIONS

Within the limitations of this study, the incidence of alveolar osteitis in all molars (1st, 2nd and 3rd) extractions was relatively increased when the type of extraction was surgical, invasive flap design (p=0.001) was adopted and CHX gel was not used (odds ratio 3.9). Single application of CHX gel after molars (1st, 2nd and 3rd) extractions significantly reduces the incidence of alveolar osteitis (p=0.001). Therefore, application of chlorhexidine in generalized molars (1st, 2nd and 3rd) extraction in maxilla and mandible is recommended.

Authors' contributions:

MAK provided the intervention to the trial subjects, SB did outcome assessment of the study participants, FRK carried out statistical analysis and methodology supervision, FU critically reviewed the manuscript for publication, SMH provided clinical supervision and mentoring, TH served as data collection and entry.

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