Effects of Intra-alveolar Placement of 0.2% Chlorhexidine Bioadhesive Gel on Dry Socket Incidence and Postsurgical Pain: A Double-Blind Split-Mouth Randomized Controlled Clinical Trial

Afshin Haraji, DDS, MS
Associate Professor
Department of Oral and Maxillofacial Surgery
Faculty Principal, Dental Branch
Islamic Azad University
Tehran, Iran

Vahid Rakhshan, DDS
Scientific Faculty Member and Lecturer
Department of Dental Anatomy and Morphology
Dental Branch
Islamic Azad University
Tehran, Iran

Naiemeh Khamverdi, DDS
Dentist in private practice
Tehran, Iran

Hadiseh Khanzadeh Alishahi, DDS
Dentist in private practice
Mashhad, Iran

Correspondence to:
Dr Vahid Rakhshan
#22 Behruzi Alley
Karegar St.
PO Box 14188-36783
Tehran, Iran
Email: vahid.rakhshan@gmail.com

Aims: *To assess the effects of intra-alveolar application of chlorhexidine gel on the incidence of alveolar osteitis (dry socket) and the severity of postsurgical pain.* ***Methods:*** *A total of 160 impacted mandibular third molars were extracted in 80 patients enrolled in this trial. In each subject, a socket was randomly selected and packed to the crest of the alveolar ridge with a gelatin sponge dressing saturated in 0.2% chlorhexidine gel. The contralateral socket was packed with a dry dressing as the placebo. None of the included patients took antibiotics or analgesics. The occurrence of dry socket and patients' pain levels were assessed at the first and third postoperative days. The data were analyzed using Spearman correlation coefficient, McNemar, Wilcoxon, and chi-square tests.* ***Results:*** *Chlorhexidine gel significantly reduced dry socket incidence from 32.6% to 11.3% (*$P \leq .001$ *[McNemar and chi-square], absolute risk reduction = 21.2%, relative risk reduction = 65.4%, odds ratio = 0.263, relative risk = 0.345). It also significantly relieved postoperative pain on both sides in all the patients (*$P \leq .001$ *[Wilcoxon]) and also in the 54 subjects who did not develop dry socket (*$P \leq .001$ *[Wilcoxon]).* ***Conclusions:*** *Besides decreasing the incidence of dry socket, chlorhexidine gel can reduce postsurgical pain in patients with and without dry socket.*
J OROFAC PAIN 2013;27:256–262. doi: 10.11607/jop.1142

Key words: alveolar osteitis, chlorhexidine, dry socket, impacted teeth, postoperative pain, third molars, tooth extraction

Alveolar osteitis (also called dry socket) is a postoperative pain in and around a tooth extraction site, which intensifies at any time between the first and third postsurgical days. It accompanies a partially or totally disintegrated blood clot within the alveolar socket, with or without halitosis.[1–10] It remains the most common postextraction complication,[1–5,7,8,11–17] as removal of impacted third molars can account for 20% to 30% of dry sockets, and extraction of all teeth might lead to 0% to 70% of alveolar osteitis occurrence.[1–4,6,7,10–15,17–19] Although probably multifactorial, its etiology is not clearly understood. A cascade of fibrinolysis induced by the active role of microorganisms is suggested as a mechanism.[1–4,6–8,10,16–18,20]

Dry socket is clinically diagnosed by the presence of a denuded socket secondary to premature loss of the blood clot. It manifests as slight discomfort to the patient, followed by sudden worsening with intense or lancing pain that increases upon chewing or suction.[2–5,7,8,10,14,21] The condition usually needs many postoperative

visits for treatment—at least four appointments.[8,14] These postoperative visits along with painful accompanying symptoms[3,4,6,14] add considerably to patient morbidity and expenditures,[1–4,6,10,14] and may pose psychological distress to both patients and clinicians.[3,4,6,14]

The fundamental and perhaps the best treatment is prevention.[4,5,7,8,10,16,21] Methods advocated for this purpose include application of antibiotics (and their placement into the wound), topical antiseptic rinses, antifibrinolytic agents, saline mouthwashes, tranquilizer dressings, occlusive dressings, and polylactic acid, as well as timing of the treatment.[1,4,7–10,14,20,21] Pathological bacteria play a critical role in alveolar osteitis by preventing clot formation through fibrinolytic enzymatic activities.[1–4,6–8,10,17–20] It is probably why the most effective treatment approach has been the application of antibiotics and antiseptics,[1,4,9,19] which can enhance the healing process, particularly when used locally and prophylactically.[1,18,19,22] Concerns about the expense of antibiotics and bacterial resistance[4,7,21] justify the research on new antiseptic treatments to obtain a similar outcome with less cost and fewer adverse effects.[4,21]

Chlorhexidine is a biguanide antiseptic often used in the form of a mouthrinse and bioadhesive gel. It acts against a broad spectrum of aerobic and anaerobic oral pathogens. It is tolerated by the human immune system and does not create resistance.[19,22] It has been shown effective in the prevention of dry socket.[1–3,5–7,14,15,23] Nevertheless, several authors have found it ineffective.[3,5,6,12,19,24,25] The inconclusiveness of the results[8,9] rationalizes more assessments for this agent. The introduction of 0.2% chlorhexidine in the form of a bioadhesive gel has opened up new lines of investigation.[1–3] This gel might be more effective than the mouthwash. This is because the intra-alveolar positioning of the gel would allow more bioavailability and thus more prolonged release of the active substance and a more direct action on the alveolus.[1–4] Besides, the gel can be used immediately, unlike the chlorhexidine rinse, which should not be applied within the first 24 postsurgical hours to avoid clot detachment.[5] In addition, intra-alveolar application of chlorhexidine gel relieves the patient from the adverse effects of the rinse—ie, staining or disturbance of taste sensation.[19]

However, more evidence is still needed to prove it is effective. The literature consists of only a few controversial reports about the effects of different regimens of chlorhexidine gel application on dry socket (ie, intra-alveolar placement[1,2,4] and daily application to the wound[3]).[1–4] Hence, a definite conclusion cannot be drawn, mainly because of the small number of studies on each regimen, the debates (as two out of four studies did not report a significant effect),[1,4] and methodological drawbacks (eg, lack of any split-mouth designs). Another point entirely missing in the literature is the potential therapeutic effects of chlorhexidine on postoperative pain. The efficacy of chlorhexidine gel/solution in postsurgical pain reduction has not been assessed, except partially in a small pilot study with major flaws.[4] It is of interest to clinicians to know whether chlorhexidine can reduce postextraction pain. If so, is this effect necessarily a function of dry socket prevention, or can it appear regardless of its alveolar osteitis/infection-preventing influence?

In view of these shortcomings and disputes, the present split-mouth randomized clinical trial was conducted. Its aim was to assess the effects of intra-alveolar application of the chlorhexidine gel on the incidence of alveolar osteitis and the severity of postsurgical pain.

Materials and Methods

This study was performed on 160 extraction sites in 80 patients attending a private maxillofacial surgery clinic in Tehran, during the years 2010 and 2011. The inclusion criteria were patients being 18 to 45 years of age with an indication for bilateral extraction of impacted mandibular third molars. The surgery difficulty index needed to range preferably between 7 and 10 according to the Pederson scale (being equal on both sides).[26] The degree of difficulty was rated by an experienced maxillofacial surgeon who carried out all the preoperative patient selections.

The exclusion criteria comprised the following: unwillingness to participate or unwillingness/refusal to avoid consuming analgesics/antibiotics after surgery; failure to attend the follow-up sessions in the first or third postoperative days; presence of any systemic disease/infection; ingestion of any medications (including antibiotics and anticoagulants) during the 4 days before the operation; existence of any condition that contraindicated surgery; presence of any psychological conditions or receiving any sedatives/analgesics/psychiatric medications; presence of pain-inducing conditions such as aching teeth, recurrent aphthous stomatitis, or cheek biting; the need for antibiotic prophylaxis; pregnancy; being immunodepressed; and having allergy to any medications.[1–4]

The protocol ethics were approved by the internal review board of the university according to the Helsinki declarations. The trial and complications of surgery including the possibility of postoperative pain were thoroughly explained to the patients prior

to the study, and written consents were taken from them. The patients who were willing to participate were encouraged to avoid ingesting painkillers and antibiotics. If not possible, they would be excluded from the study and replaced by new patients. They would be offered proper treatments (including pain relief) when necessary, even after being excluded.

Surgery

The patients underwent the procedure under local anesthesia (articaine 4% with epinephrine administered to the inferior alveolar, long buccal, and lingual nerves). A mucoperiosteal pocket was cut and everted to gain access to the third molar. Osteotomy and dental sectioning were carried out when necessary. Once the tooth had been extracted, the alveolus was cleaned and the bone edges were smoothed. Both sides were operated at the same session. The order of sites to be operated was determined randomly by the surgeon, unless the patient's clinical conditions necessitated surgery of one site first, or if the patient asked so.

Intra-alveolar Chlorhexidine Gel Application. Chlorhexidine treatment was randomized in the designing stage, using the simple random sampling method of tossing a coin. The treatment was performed by the same dentist who would apply the treatment after the surgery. The surgeon was not aware of the allocations.

After the operation, the surgeon left the room temporarily. The gel was applied to one of the two same-sized dressings of gelatin sponge with colloidal silver (Gelatamp, Roeko) by the only dentist who had randomized the treatment. The dry dressing acted as the placebo. The experimental dressing was impregnated in a 0.2% chlorhexidine bioadhesive gel (1,6-bis[N-p-chlorphenyl-biguanidol hexane digluconate], Kimia). Afterwards, the dentist pushed the dressings gently into the sockets. It was made sure that they had reached the socket floors and that there was no observable excess material. Both the surgeon and patients were blinded to the assignment orders.[1]

The surgeon returned and closed the wound with simple 4/0 silk sutures.[3] After the surgery, no analgesics or antibiotics were consumed by the included patients. However, upon their request or need, proper medications would be provided (leading to their exclusion from the study).

Clinical Examination

Subjects were evaluated in the first and third postoperative days. Clinical assessments were performed by the blinded maxillofacial surgeon, according to Blum's standardized criteria.[2–4,7] Diagnosis of dry socket was regarded as positive when the patient experienced postoperative pain that intensified sometime between the first and third days, with total or partial loss of the blood clot.[7]

At each follow-up, postoperative pain was recorded using a visual analog scale (VAS). The end points were considered as "no pain" and "intolerable pain".[20,27] The results on the VAS were later converted to 10 ordered ranks (0 to 9).

Statistical Analysis

Prospective Power Calculation and Sample Size Determination. A pilot study of 45 individuals was undertaken. The proportions of dry socket in the control and experimental sides were 35.6% and 13.3%, respectively. On the basis of this pilot study, a sample size of 76 patients (76×2 sockets) was needed to obtain a 0.9 power ($\alpha = .05$, $\beta = .1$). Thus it was prospectively determined as 160 extraction sites in 80 patients to gain test powers ≥ 0.9.

Effect of Chlorhexidine on Dry Socket Occurrence. A McNemar matched-pairs test and a chi-square test of the Statistical Package for the Social Sciences (SPSS version 17, SPSS Inc) were used to compare the incidence of dry socket in both sides. A Spearman correlation coefficient was used to assess the correlation of alveolar osteitis formation between the control and experimental groups. Also, odds ratio (OR), relative risk (RR), relative risk reduction (RRR), and absolute risk reduction (ARR) were calculated. Moreover, 95% confidence intervals (CI) were estimated for the effect size measures as well as the proportions.

Effect of Chlorhexidine on Postsurgical Pain in the Sample and in Patients Without Dry Socket. After calculating descriptive statistics, a Wilcoxon matched-pairs test was used to compare pain levels between the control and experimental sides at each interval for each sex, and for the sample. It was also used to assess pain reduction over time.

The mean pain magnitudes in the patients who had not developed dry socket were also calculated. The Wilcoxon matched-pairs test was performed to assess the effect of single-dose chlorhexidine application on postoperative pain.

The level of significance for all the tests was set at $P = .05$.

Results

More than 200 patients were assessed and/or treated to include 80 subjects. The patients were mostly

Table 1 The Net (and Frequency [%]) Distributions of Subjects According to the Occurrence of Alveolar Osteitis (AO) in Their Control/Experimental Sides

	AO in experimental side					
	Males (n = 39)		Females (n = 41)		Sample (n = 80)	
AO in control side	Absent	Present	Absent	Present	Absent	Present
Absent	25 (64.1%)	0**	29 (77%)	0**	54 (67.5%)	0***
Present	8 (20.5%)	6 (15.4%)	9 (22%)	3 (7.3%)	17 (21.3%)	9 (11.3%)

** $P < .01$; *** $P < .001$.

excluded due to their refusal to avoid taking medications or their need to consume medicine. Four patients were excluded for failure to attend follow-up. The mean age of the included patients was 21.6 ± 2.5 years (range: 17 to 31 years); of them, 51.25% were females. Of the 41 females and 39 males, 19.5% and 53.8%, respectively, smoked cigarettes. Smoking was not balanced between the two sexes ($P = .001$, chi-square). Mean difficulty of tooth extraction was 7.3 ± 0.6 (range: 6 to 8).

Effect of Chlorhexidine on Dry Socket Incidence

Dry socket occurred in 14 male patients (35.9% of males, 95% CI = 22.7% to 51.6%) and 12 females (29.2%, 95% CI = 17.6% to 44.5%). Of these 26 patients (32.6% of the sample, 95% CI = 23.2% to 43.4%), 9 developed alveolar osteitis bilaterally (Table 1). When alveolar osteitis was not present on the control side, it also was absent on the experimental side (Table 1).

According to the Spearman correlation coefficient, there was a significant correlation between the occurrence of alveolar osteitis in the two sides (rho = .513, $P < .001$).

The McNemar test showed that the chlorhexidine gel had significant effects on reduction of dry socket occurrence in the males ($P = .008$), the females ($P = .004$), and the sample ($P < .001$, Table 1).

While 32.5% of the control sockets developed dry socket (95% CI = 23.2% to 43.4%), its frequency was 11.3% in the experimental side (95% CI = 6.0% to 20.0%, Fig 1). Therefore, chlorhexidine gel reduced the incidence of alveolar osteitis by 21.2% (ARR = 21.2%, 95% CI = 8.5% to 33.3%) or 65.4% compared to the control (RRR = 65.4%, 95% CI = 30.9% to 80.7%). According to the chi-square test, application of chlorhexidine was significantly associated with this reduction ($P < .001$, Fig 1). Alveolar osteitis was about 3.8-fold more likely to occur in the control side (as the reciprocal of OR = 0.263, 95% CI = 0.114 to 0.607). Avoidance of chlorhexidine gel might increase dry socket risk about 2.89 times (as the reciprocal of RR = 0.345, 95% CI = 0.173 to 0.691).

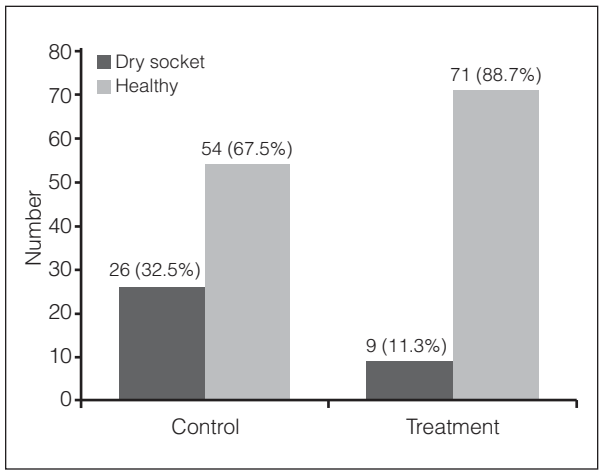

Fig 1 Number and frequency (%) distributions of dry socket on control and treatment sides among 80 × 2 extraction sites.

Effect of Chlorhexidine on Pain in the Sample

According to the Wilcoxon signed-rank test, there were significant differences between pains perceived in the control and treatment sides (Table 2, Fig 2). These differences were seen on both the first and third postsurgical days, in the men ($P_{1st} = .007$, $P_{3rd} < .001$), the women ($P_{1st} < .001$, $P_{3rd} < .001$), and the sample ($P_{1st} < .001$, $P_{3rd} < .001$). Also a significant decline was seen in pain at both the control and treatment sides over time ($P < .001$).

Effect of Chlorhexidine on Pain in the Patients Without Dry Socket

On the first postoperative day, the average pain extents for the control and experimental sides of the 54 patients without dry socket (n = 54 × 2 matched surgical areas) were 5.1 ± 1.2 and 4.5 ± 1.0, respectively. These values respectively reduced to 2.9 ± 1.2 and 2.1 ± 1.2, on the third day. At both intervals, the pain severities were significantly lower in the experimental side in comparison to the control ($P_{1st} < .001$, $P_{3rd} = .001$).

Table 2 Descriptive Statistics for Pain Severity (on a 0–9 Scale)

	Day	Side	Mean	SD	Min	Med	Max	95% CI
Males (n = 39)	1st	Control	5.51	1.37	3	5	8	5.07–5.96
		Treatment	5.05	1.28	3	5	8	4.64–5.47
	3rd	Control	3.23	1.31	0	3	5	2.81–3.65
		Treatment	2.33	1.34	0	2	5	1.90–2.77
Females (n = 41)	1st	Control	5.83	1.26	3	6	8	5.43–6.23
		Treatment	4.68	1.23	2	5	7	4.29–5.07
	3rd	Control	3.54	1.27	1	3	6	3.14–3.94
		Treatment	2.32	1.25	0	2	5	1.92–2.71
Total (n = 80)	1st	Control	5.68	1.32	3	6	8	5.38–5.97
		Treatment	4.86	1.26	2	5	8	4.58–5.14
	3rd	Control	3.39	1.29	0	3	6	3.10–3.67
		Treatment	2.33	1.29	0	2	5	2.04–2.61

SD, standard deviation; Min, minimum; Med, median; Max, maximum; CI, confidence interval for the mean.

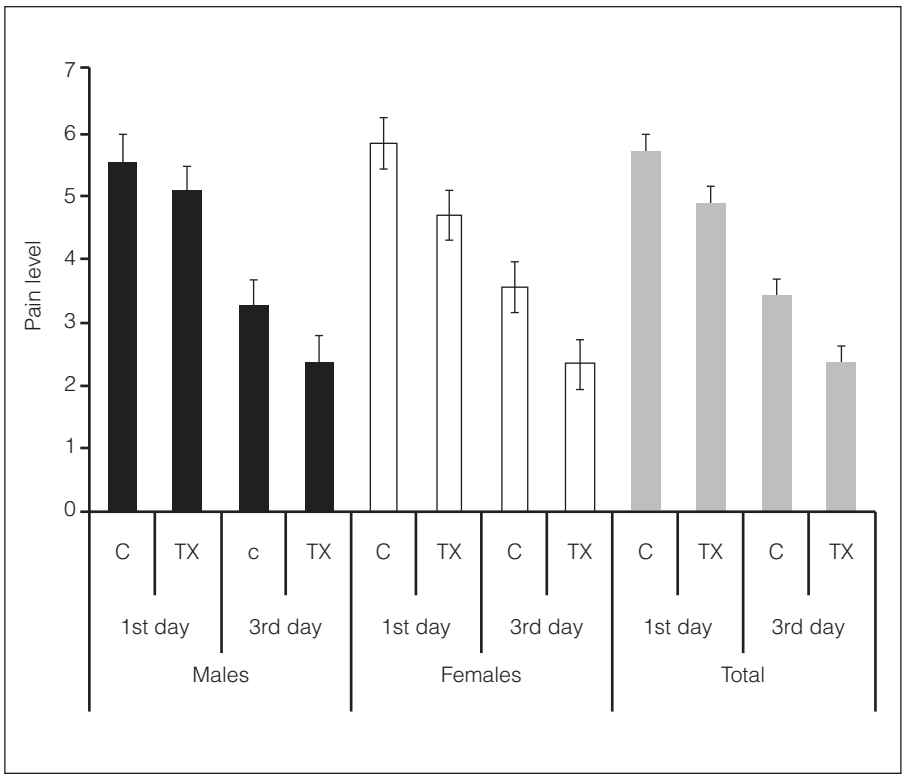

Fig 2 Mean (and 95% CI) of pain levels (on a 0–9 scale) on the control (C) and treatment (Tx) sides.

Discussion

The findings of this study revealed that chlorhexidine might reduce both dry socket frequency and postsurgical pain levels. The absolute decrease in the incidence of dry socket in this study was about 21%. This was slightly better than almost all earlier findings indicating significant absolute risk reductions such as 8%,[15] 17.5%,[11] and 10%,[28] or nonsignificant ARRs such as 8%,[25] and 3%,[19] a similar efficacy of chlorhexidine and cetylpyridium,[12] and a RRR of about one-half of control.[24] There was also one study in which the chlorhexidine rinse had been applied via intra-alveolar gelatin sponge dressings, and significant reductions had been found.[23]

The present findings also are in accord with earlier findings of reduction in alveolar osteitis by using chlorhexidine gel. The earlier findings pointed to ARRs such as a nonsignificant 13% reduction in a pilot study,[4] a nonsignificant 10% decrease in patients with bleeding disorders,[1] a significant 27.5% decrease when daily application of chlorhexidine

gel to the wound was compared with rinsing with chlorhexidine,[3] and a significant 19% reduction observed in another trial.[2] These studies as well as the present investigation suggest the efficacy of targeting microbial etiologies of dry socket.

Postoperative Pain

Pain is the most crucial symptom of dry socket.[8] Alveolar osteitis pain is attributed to the formation of kinins and plasmin in the alveolus. Kinins activate the primary afferent nerve terminations that might have been sensitized previously by other inflammatory mediators. Plasmin might convert kallikrein into kinins in the osseous alveolar marrow, causing pain and clot disintegration.[7,8] Different measures have been proposed for the prevention or alleviation of dry socket pain. These include irrigation with different agents, positioning analgesic/tranquilizer dressings, cleansing the socket, etc.[1,4,7–10,14,21] However, to the authors' knowledge, chlorhexidine has not been assessed as a medicament, apart from a pilot study reporting insignificant reductions in the treatment group.[4] The reasons for this failure to find a significant pain reduction might be the very small sample size used and the patients' consumption of painkillers, which might render the pain-related results invalid.[6]

Depending on the presence/absence of dry socket, the postsurgical pain differs in pattern. Alveolar osteitis pain intensifies between the second and fourth postsurgical days.[1–10,14,21] Nevertheless, in the absence of dry socket, a moderate pain peaks within 24 postoperative hours and then reduces rather quickly.[27] The present study indicated that an intra-alveolar dose of chlorhexidine could significantly lower the pain for about 10% of potentially tolerable maximum pain (one rank) even in patients who did not develop alveolar osteitis. Thus, chlorhexidine might be applied to reduce the dose of painkiller after surgeries. This favorable therapeutic effect seen despite the absence of dry socket might be attributable to the healing effects of chlorhexidine, which can reduce bacterial colonization and facilitate socket healing.[22]

Limitations and Strengths

The current design was constrained by some limitations. Comparable to other studies,[1–5,12,14,15,19,24] this study was single-centered, which might reduce the generalizability. Another limitation is the subjective nature of pain, which is difficult to assess. One objective approach has been assessing the number of painkiller pills taken by the patient. Nevertheless, in a split-mouth design, this method cannot be used since it reflects the total pain perceived, not the pain at each site. Furthermore, painkillers may disrupt pain perception, rendering the results questionable.

On the other hand, enrolling only patients who could tolerate postsurgical pain without analgesic consumption might also be questioned, since the results might not be generalizable to routine clinical practice. Nonetheless, it was preferable to include a narrower range of patients with clear pain, rather than attempting to include in the present study a broader range of pain tolerance at the cost of a disrupted pain sensibility due to analgesic ingestion.[6]

The placement of chlorhexidine gel by using same-sized Gelatamp blocks had the advantage of standardizing the amount of chlorhexidine administered to each surgical bed. In other studies using intra-alveolar placement of gel,[1,2,4] the amount of the gel could differ from case to case depending on the socket volume.

As another advantage, both randomization and data analysis were carried out for surgical sites (not patients). However, other than a few studies,[28] earlier investigations had assessed the incidence of dry socket among patients (not sockets), which could distort the incidences when the number of dry sockets differed from patient to patient. Some investigators analyzed the alveolar osteitis incidence among extraction sockets but randomized the patients, leading to biased findings.[9,12,15] Hence, the split-mouth randomized double-blind nature of the current study, reinforced with a large sample, could improve the reliability of the findings.

A positive feature of the present study is that all the surgeries and clinical examinations were performed by an experienced surgeon and according to standard criteria.[2–4,7] Also, smokers and contraceptive takers were not excluded. Such patients were not included in some previous studies.[4] Their exclusion together with various selection criteria and nonstandard dry socket definitions used in earlier investigations might negatively bias some previous results.[5,7,8]

The present study's sample was balanced in terms of sex, number of experimental/control surgical beds, and level of operation difficulty on the two sides (equal difficulty was part of inclusion criteria). These features were not considered in any of the previous reports. Only the equal number of male and female patients was taken into consideration in a few studies on chlorhexidine rinse,[15,19,25] but not in chlorhexidine gel experiments. Balancing the sample in terms of smoking prevalence in males and females might be advantageous. The split-mouth design adopted in this trial might control for several variables such as oral hygiene or contraceptive ingestion.

Conclusions

Single-dose intra-alveolar application of chlorhexidine bioadhesive gel can reduce dry socket incidence. It was shown for the first time that chlorhexidine could have postsurgical palliative effects as well. Interestingly, it was seen not only in the patients suffering from dry socket but also in those without it. This implied its potential influence independent of its effect on alveolar osteitis, and deserves further assessments.

Acknowledgments

The study was self-funded by the authors and their institution. The authors declare no conflict of interests.

References

1. Torres-Lagares D, Gutierrez-Perez JL, Hita-Iglesias P, et al. Randomized, double-blind study of effectiveness of intra-alveolar application of chlorhexidine gel in reducing incidence of alveolar osteitis and bleeding complications in mandibular third molar surgery in patients with bleeding disorders. J Oral Maxillofac Surg 2010;68:1322–1326.
2. Torres-Lagares D, Gutierrez-Perez JL, Infante-Cossio P, Garcia-Calderon M, Romero-Ruiz MM, Serrera-Figallo MA. Randomized, double-blind study on effectiveness of intra-alveolar chlorhexidine gel in reducing the incidence of alveolar osteitis in mandibular third molar surgery. Int J Oral Maxillofac Surg 2006;35:348–351.
3. Hita-Iglesias P, Torres-Lagares D, Flores-Ruiz R, Magallanes-Abad N, Basallote-Gonzalez M, Gutierrez-Perez JL. Effectiveness of chlorhexidine gel versus chlorhexidine rinse in reducing alveolar osteitis in mandibular third molar surgery. J Oral Maxillofac Surg 2008;66:441–445.
4. Torres-Lagares D, Infante-Cossio P, Gutierrez-Perez JL, Romero-Ruiz MM, Garcia-Calderon M, Serrera-Figallo MA. Intra-alveolar chlorhexidine gel for the prevention of dry socket in mandibular third molar surgery. A pilot study. Med Oral Patol Oral Cir Bucal 2006;11:e179–184.
5. Minguez-Serra MP, Salort-Llorca C, Silvestre-Donat FJ. Chlorhexidine in the prevention of dry socket: Effectiveness of different dosage forms and regimens. Med Oral Patol Oral Cir Bucal 2009;14:e445–449.
6. Caso A, Hung L-K, Beirne OR. Prevention of alveolar osteitis with chlorhexidine: A meta-analytic review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;99:155–159.
7. Blum IR. Contemporary views on dry socket (alveolar osteitis): A clinical appraisal of standardization, aetiopathogenesis and management: A critical review. Int J Oral Maxillofac Surg 2002;31:309–317.
8. Cardoso CL, Rodrigues MTV, Ferreira Júnior O, Garlet GP, de Carvalho PSP. Clinical concepts of dry socket. J Oral Maxillofac Surg 2010;68:1922–1932.
9. Hedström L, Sjögren P. Effect estimates and methodological quality of randomized controlled trials about prevention of alveolar osteitis following tooth extraction: A systematic review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:8–15.
10. Kolokythas A, Olech E, Miloro M. Alveolar osteitis: A comprehensive review of concepts and controversies. Int J Dent 2010:249073. Epub 2010 June 24.
11. Ragno JR Jr, Szkutnik AJ. Evaluation of 0.12% chlorhexidine rinse on the prevention of alveolar osteitis. Oral Surg Oral Med Oral Pathol 1991;72:524–526.
12. Berwick JE, Lessin ME. Effects of a chlorhexidine gluconate oral rinse on the incidence of alveolar osteitis in mandibular third molar surgery. J Oral Maxillofac Surg 1990;48:444–448.
13. Larsen PE. Alveolar osteitis after surgical removal of impacted mandibular third molars. Identification of the patient at risk. Oral Surg Oral Med Oral Pathol 1992;73:393–397.
14. Bloomer CR. Alveolar osteitis prevention by immediate placement of medicated packing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:282–284.
15. Larsen PE. The effect of a chlorhexidine rinse on the incidence of alveolar osteitis following the surgical removal of impacted mandibular third molars. J Oral Maxillofac Surg 1991;49:932–937.
16. Halabi D, Escobar J, Munoz C, Uribe S. Logistic regression analysis of risk factors for the development of alveolar osteitis. J Oral Maxillofac Surg 2012;70:1040–1044.
17. Nusair YM, Younis MH. Prevalence, clinical picture, and risk factors of dry socket in a Jordanian dental teaching center. J Contemp Dent Pract 2007;8:53–63.
18. Parthasarathi K, Smith A, Chandu A. Factors affecting incidence of dry socket: A prospective community-based study. J Oral Maxillofac Surg 2011;69:1880–1884.
19. Delilbasi C, Saracoglu U, Keskin A. Effects of 0.2% chlorhexidine gluconate and amoxicillin plus clavulanic acid on the prevention of alveolar osteitis following mandibular third molar extractions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:301–304.
20. Sridhar V, Wali GG, Shyla HN. Evaluation of the perioperative use of 0.2% chlorhexidine gluconate for the prevention of alveolar osteitis after the extraction of impacted mandibular third molars: A clinical study. J Maxillofac Oral Surg 2011; 10:101–111.
21. Noroozi A-R, Philbert RF. Modern concepts in understanding and management of the "dry socket" syndrome: Comprehensive review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:30–35.
22. Dorri M, Shahrabi S, Navabazam A. Comparing the effects of chlorhexidine and persica on alveolar bone healing following tooth extraction in rats, a randomised controlled trial. Clin Oral Investig 2012;16:25–31.
23. Fotos PG, Koorbusch GF, Sarasin DS, Kist RJ. Evaluation of intra-alveolar chlorhexidine dressings after removal of impacted mandibular third molars. Oral Surg Oral Med Oral Pathol 1992;73:383–388.
24. Bonine FL. Effect of chlorhexidine rinse on the incidence of dry socket in impacted mandibular third molar extraction sites. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:154–157.
25. Larsen PE. Use of chlorhexidine to prevent alveolar osteitis. J Oral Maxillofac Surg 1990;48:1244–1245.
26. Pederson GW. Oral Surgery. Philadelphia: WB Saunders, 1988.
27. Larrazabal C, Garcia B, Penarrocha M. Influence of oral hygiene and smoking on pain and swelling after surgical extraction of impacted mandibular third molars. J Oral Maxillofac Surg 2010;68:43–46.
28. Hermesch CB, Hilton TJ, Biesbrock AR, et al. Perioperative use of 0.12% chlorhexidine gluconate for the prevention of alveolar osteitis: Efficacy and risk factor analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:381–387.