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Research Article

The Impact of the Chlorhexidine Gel (WISDOM®) on Postoperative Sequelae Associated with the Surgical Removal of Impacted Mandibular Third Molars: A Randomized Controlled Clinical Trial

Dhuha Ali, Ahmed Fadhel Al-Quisi*
Department of Oral and Maxillofacial Surgery, College of Dentistry, University of Baghdad, Baghdad, Iraq
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Abstract

Background: One of the most prevalent procedures in oral surgery is the removal of impacted mandibular third molars, typically accompanied by trismus, edema, and pain. Several methods and biomaterials were implemented to mitigate or avoid these surgical problems. ***Objectives***: To evaluate the efficiency of chlorhexidine gel (WISDOM®) in minimizing postoperative sequelae associated with the impacted mandibular third molar that will be surgically extracted and its role in promoting early soft tissue closure of the surgical site. ***Methods***: The study design was a double-masked and randomized, controlled clinical study that included healthy patients needing the removal of a mandibular third molar through surgery. The participants were randomly assigned to two groups. The extraction site of the study group was filled with a mixture of gel foam and WISDOM®. In contrast, we filled the extraction sites of the control group patients with gel foam and sutured the surgical sites for both groups. The patients were evaluated on the first, third, and seventh postoperative days for pain, swelling, trismus, and early soft tissue healing. ***Results***: Sixty eligible patients were enrolled in this study. The study group exhibited a statistically significant decrease in pain, edema, trismus, and early soft tissue healing on the first, third, and seventh postoperative days compared to the control group. ***Conclusions***: WISDOM® gel can effectively reduce postoperative pain, trismus, and swelling and promote early soft tissue healing after surgical removal of an impacted mandibular wisdom tooth.

Keywords: Biomaterials, Chlorhexidine gel, Hyaluronic acid, Impacted third molar, WISDOM® gel, Wisdom teeth.

تأثير جل صحة اللثة على نتائج ما بعد جراحة استئصال الأضراس الثالثة للفك السفلي المتأثرة: تجربة سريرية معشاة ذات شواهد

الخلاصة

الخلفية: واحدة من أكثر الإجراءات انتشارا في جراحة الفم هي إزالة الأضراس الثالثة المتأثرة بالفك السفلي، وعادة ما تكون مصحوبة بالتثلث والوذمة والألم. تم تنفيذ العديد من الطرق والمواد الحيوية للتخفيف من هذه المشاكل الجراحية أو تجنبها. **الأهداف**: تقييم كفاءة جل صحة اللثة في تقليل مشاكل ما بعد الجراحة المرتبطة بالضرس الثالث للفك السفلي المتأثر الذي سيتم استخلاصه جراحيا ودوره في تعزيز الإغلاق المبكر للأنسجة الرخوة في موقع الجراحة. **الطريقة**: دراسة سريرية مزدوجة القناع وعشوائية ومضبوطة شملت مرضى أصحاء يحتاجون إلى إزالة الضرس الثالث للفك السفلي من خلال الجراحة. تم توزيع المشاركين عشوائيا إلى مجموعتين. تم ملء موقع استخراج مجموعة الدراسة بمزيج من رغوة الجل وهلام صحة اللثة. في المقابل، قمنا بملء مواقع الاستخراج لمرضى المجموعة الضابطة برغوة الجل وخياطة المواقع الجراحية لكلا المجموعتين. تم تقييم المرضى في الأيام الأولى والثالثة والسابعة بعد الجراحة للألم والتورم والتثلث والشفاء المبكر للأنسجة الرخوة. **النتائج**: تم تسجيل ستين مريضا مؤهلا في هذه الدراسة. أظهرت مجموعة الدراسة انخفاضا ذا دلالة إحصائية في الألم والوذمة والتثلث وشفاء الأنسجة الرخوة المبكرة في الأيام الأولى والثالثة والسابعة بعد الجراحة مقارنة بالمجموعة الضابطة. **الاستنتاجات**: يمكن أن يقلل جل صحة اللثة بشكل فعال من آلام ما بعد الجراحة، والتثلث، والتورم ويعزز التئام الأنسجة الرخوة المبكرة بعد الاستئصال الجراحي لضرس العقل الفك السفلي المتأثر.

* ***Corresponding author***: Ahmed F. Al-Quisi, Department of Oral and Maxillofacial Surgery, College of Dentistry, University of Baghdad, Baghdad, Iraq; Email: ahmedquisi@gmail.com

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INTRODUCTION

Surgical extraction of the impacted mandibular third molar is the most common surgical treatment performed by oral and maxillofacial surgeons [1]. Typically, it involves surgical trauma to a highly vascularized area that is mostly composed of loose connective tissue. During the first few days following surgery, it is common to experience pain, edema, trismus, and generalized oral dysfunction as inflammatory sequelae [2]. An impacted tooth is one that, due to malposition, space constraints, or a physical obstruction in the eruption pathway, cannot erupt into the dental arch within the anticipated time frame [3]. The goal of several studies was to lower the complications following surgery on the third molar

[3,4]. The use of pharmaceuticals was the subject of several of these studies. For instance, studies have shown that using steroidal and nonsteroidal anti-inflammatory medications following surgery can help minimize the symptoms of trismus and edema [4,5]. However, these medications have a history of serious adverse effects. They are not recommended for use in certain patients due to possible side effects such as adrenal gland dysfunction, slowed wound healing, and increased susceptibility to infection [6,7]. These worries prompted scientists to look into or study the application of high-molecular-weight glycosaminoglycans, such as hyaluronic acid or hyaluronan [8,9], which is naturally found as part of the skin's extracellular matrix, vitreous humor, embryonic mesenchyme, connective tissue, synovial fluid, and mineralized hard tissues like bone and cementum, and plays a vital role in promoting wound healing and minimizing inflammatory tissue response by inducing re-epithelialization and increasing angiogenesis [9]. Many studies, on the other hand, have shown that using 0.12% chlorhexidine (CHX) before and after surgery lowers the risk of alveolar osteosis after the third molar is taken out [10]. The combined effects of 0.2% CHX and 1% hyaluronic acid in locally applied gel require further investigation to counteract the unwanted sequelae of the impacted mandibular wisdom teeth, as well as the resulting delayed healing and wound dehiscence. This study aims to assess how effective locally applied WISDOM® gel is in reducing postoperative complications linked to the surgical removal of impacted mandibular third molars. It also aims to determine the gel's role in promoting the early closure of the surgical site's soft tissue.

METHODS

Study design and setting

This study was planned and carried out as a randomized controlled clinical trial following the CONSORT (Consolidated Standards of Reporting Trials) guidelines from February 15 to May 30, 2024, at the University of Baghdad College of Dentistry, Department of Oral and Maxillofacial Surgery. The Ethics Committee at the University of Baghdad/College of Dentistry approved the study protocol on January 11, 2024, with certificate no. 894124. At the same time, this study was registered at https://register.clinicaltrials.gov/ with the identity number NCT06251141 on 8-2-2024. All participants signed informed consent after fully understanding the study's nature, the materials used, and potential complications.

Sample size calculation

G-power software (V.3.1.9.7, Kiel, Germany) was used to calculate the sample size based on the summary statistics (mean and standard deviation) of the postoperative pain for both groups obtained from the pilot study (5 patients from each group) and used to calculate the effect size, which was equal to 0.946. This value was used based on two dependent means (two-tailed) with a significance level of alpha equal to 5% and power equal to 90%. This resulted in 27 subjects for each group. We included an extra three patients to each group to prevent potential participant dropout.

Eligibility criteria and recruitment

Adult patients with no history of systemic diseases who needed surgical extraction and were willing to participate in this study were screened for eligibility. The inclusion criteria include 1) impacted mandibular third molar teeth (IMTM), which need at least flap reflection and bone removal; 2) the impacted tooth's direction should be horizontal or mesio-angular, according to Winter's classification; and 3) According to the Pell and Gregory classification, the degree of impaction should be (level A or B, class I or II).

Primary and secondary outcomes

This study evaluates the improvements in the postoperative sequelae after surgical removal of the impacted mandibular third molar, as well as the pain scores, degree of trismus, and swelling assessed at the 1st, 3rd, and 7th postoperative days. Additionally, we assessed the surgical site's healing using the early healing soft tissue score system (EHS) at the same intervals for both groups.

Randomization and blinding approach

Microsoft Excel software was used to achieve block randomization to ensure an equal number of patients placed in each group. The process of randomization was achieved by numbering the cells from 1 to 60 in the Excel sheet, representing the sequence of patients that will arrive in the clinic, then sorting random numbers in the next column by using the function (RAND). After sorting these random numbers from lowest to largest value with the expanded selection, the first 30 rows were placed in group A while the rest were placed in group B. The researchers briefed participants about the various treatments, while keeping patients blind to the assignment. The researcher established the initial diagnosis and performed the clinical and radiographic assessments. At the same time, an independent maxillofacial surgeon evaluated the pain, swelling, trismus, and EHS after surgery.

Surgical procedure

After block injection for the inferior alveolar nerve and infiltration for the lingual and long buccal nerves, an incision was made with surgical blade no. 15. Then, with the periosteal elevator, a full-thickness triangular mucoperiosteal flap was reflected. Afterwards, we exposed the cervical line of the IMTM by removing

bone as needed, using a fissure or round bur installed in a surgical straight handpiece with sufficient saline irrigation. To facilitate access and vision during the sectioning and extraction of the tooth from the bony socket, it is necessary to remove a suitable quantity of bone. Before flap suturing, all groups' sockets were irrigated with normal saline. Control group patients' sockets were filled only with gel foam, and flap replacement and suturing were performed. Study group patients' sockets were filled with 1 ml of the chlorhexidine WISDOM® gel combined with gel foam, and the flap was sutured with a black silk suture 3/0 using a basic interrupted suturing technique. The duration of the procedure was measured using a stopping timer, starting with the initial incision and ending with the final suture placement.

Postoperative assessments and follow-up

The independent oral surgeon, blind to the patient's group, conducted measurements and evaluations on the first, third, and seventh postoperative days following surgery to prevent observer bias. We used the NRS to assess the patient's pain and discomfort [11]. At the same time, the assessment of postoperative swelling was based on the scale developed according to the criteria developed by Sabur [12]. Simultaneously, we asked the patients to open their mouths to the maximum extent possible, and used a Vernier ruler to measure the distance between the maxillary and mandibular central incisors, thereby calculating mouth openness. The early wound healing was assessed using the EHS based on the scale developed by Marini *et al*. (2018) [13].

Statistics analysis

Data description, analysis, and presentation were performed using the Statistical Package for Social Science (SPSS version 21, Chicago, Illinois, USA). The Shapiro-Wilk test was utilized to check the normality distribution of quantitative variables among groups. The Wilcoxon sum rank test (WSR) compares the mean rank differences between two independent groups. The Friedman test assesses the difference in mean ranks for k-related samples. The Fishers' exact test was used to evaluates the association of distribution between two categorical variables when the expected cell count is less than 5 and exceeds 20%. On the other hand, the Chi-square test was utilized to assesses the association of distribution between two categorical variables when the expected cell count is less than 5 and below 20%. Repeated measure ANOVA was utilized for the assessment of the difference of quantitative variables among k-related times. The independent sample *t*-test is used to analyze the difference between the two independent groups. Values $p<0.05$ are considered significantly different.

RESULTS

We initially assessed 75 IMTM participants and 75 patients for eligibility in this study, excluding 15 due to their failure to meet the inclusion criteria. The flow chart (Figure 1) shows the random allocation of the remaining 60 patients into two groups, each with 30 patients.

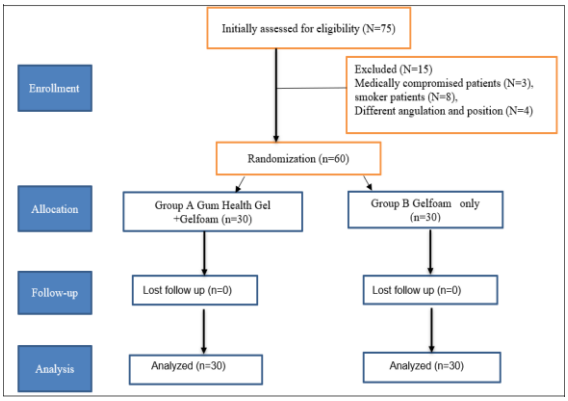

Figure 1: Flow chart of the study.

The patient's ages ranged from 18 to 39 years. The female patients represented 53.33% of the total samples. The number of impacted teeth on the right side was 35 (16 in the control group and 19 in the study group), whereas the number of impacted teeth on the left side was 25 (14 in the control group and 11 in the study group). According to winter's classification, the impacted molars were horizontal in 17 patients (28.33%) and mesioangular in 43 patients (71.67%). At the same time, according to Pell and Gregory's classification, the most commonly impacted position was CLII Level B, with 41 patients, followed by CL II Level A (only 8 patients). The least frequently impacted position was CL I Levels (A and B), with 5 patients for each level. Regarding the surgical time, it was higher in the GH gel group (33.43±12.89 min), while in control it was 32.93±11.53 min (p= 0.875). However, the statistical analysis showed no significant differences between groups regarding all these variables, as shown in Table 1. Regarding the postoperative pain assessment, the statistical analysis revealed a significant decrease in pain within each group over time, with the study group experiencing a greater decrease than the control group on all postoperative days, as presented in Table 2. For the swelling, statistical analysis showed a significant decrease inside each group within days, with a statistically significant decrease found in the study group when compared to the control groups at all-time points, as shown in Table 3. At the same time, statistical analysis revealed that the mean mouth opening during all postoperative days was higher in the study when compared to the control groups, as shown in Table 4. In terms of early wound healing, the Friedman statistical test revealed a significant increase in the EHS over time within each group. However, the study group showed the greatest improvement in soft tissue healing, with the WSR test showing a significant difference from the first postoperative day to the seventh postoperative day, as shown in Table 5.

Table 1: Distribution of study variables between groups.

Study variables		Groups		*p*-value
		Control group	Study group	
Age (year)		25.73±5.25	24.67±5.11	0.428ᵉ
Sex	Male	14(46.67)	14 (46.67)	1.0*
	Female	16(53.33)	16 (53.33)	
Impaction side	Right	16(53.33)	19(63.33)	0.432*
	Left	14(46.67)	11(36.67)	
Winter's classification	Horizontal	8(26.27)	9(30.0)	0.774*
	Mesioangular	22(73.33)	21(70.0)	
Pell and Gregory's classification	Class I level A	4(13.33)	2(6.67)	0.885*
	Class I level B	2(2.67)	3(10.0)	
	Class II level A	4(13.33)	4(13.33)	
	Class II level B	20(66.67)	21(70.0)	
Duration of operation		32.93±11.53	33.43±12.89	0.875ᵉ
Preoperative Mouth opening		46.4±3.519	43.5±2.776	0.056ᵉ

Values were expressed as frequencies, percentages, and mean±SD. ɐ: Un-paired T-test, * Chi-squared test.

Table 2: Descriptive and statistical test of pain between groups and time by using Wilcoxon sum rank and Friedman test

Groups		1-day Post-operative	3-day Post-operative	7-day Post-operative	Friedman test	*p*-value	Effect size
Control	Range	4-8	2-5	0-2	56.513	0.000	0.942
	Median	6	4	1			
	MR 1	3.00	2.00	1.00			
	MR2	42.35	41.53	40.20			
Study	Range	1-8	0-5	0-1	60	0.000	1.0
	Median	4	2	0			
	MR1	2.93	2.02	1.05			
	MR2	18.65	19.47	20.80			
WSR		5.364	4.997	4.904			
p-value		0.000	0.000	0.000			
Effect size		0.692	0.645	0.633			

Table 3: Descriptive and statistical test of swelling between groups and time by using Wilcoxon sum rank and Friedman test

Groups		1-day Post-operative	3-day Post-operative	7-day Post-operative	Friedman test	*p*-value	Effect size
Control	Range	1-2	0-2	0-1	44.345	0.000	0.739
	Median	2	1	0			
	MR 1	2.77	2.18	1.05			
	MR2	37.10	39.87	33.00			
Study	Range	0-2	0-2	0-0	53.262	0.000	0.888
	Median	1.5	0	0			
	MR1	2.78	1.88	1.33			
	MR2	23.90	21.13	28.00			
WSR		3.720	4.447	2.316			
p-value		0.000	0.000	0.021			
Effect size		0.480	0.574	0.299			

Table 4: Values of mouth opening among groups and inside each group during the follow-up time

Groups		1-day Post-operative	3-day Post-operative	7-day Post-operative	F	*p*-value	Effect size
Control	Range	13-35	15-38	22-49	50.917	0.00	0.85
	Mean±SD	23.23±4.55	29.27±5.54	35.23±6.12			
Study	Range	14-54	29-48	38-50	230.366	0.00	0.962
	Mean±SD	31.57±5.59	37.80±3.48	42.50±2.83			
Un-paired t-test		6.332	7.146	5.906			
p-value		0.0001	0.0001	0.0001			
Effect size		1.66	1.877	1.551			

Table 5: Descriptive statistics of EHS between groups during the follow-up time by

Groups		1-day post-operative	3-day post-operative	7-day post-operative	Friedman test	*p*-value	Effect size
Control	Range	0-5	1-5	1-9	54.581	0.00	0.91
	Median	1.0	4.0	6.0			
	MR1	1.05	2.0	2.9			
	MR2	18.23	Q7.33	16.83			
Study	Range	0-6	4-10	7-10	56.017	0.00	0.934
	Median	5.0	6.0	10			
	MR1	1.05	2.02	2.95			
	MR2	42.77	43.67	44.17			
WSR		5.537	5.978	6.346			
p-value		0.00	0.00	0.00			
Effect size		0.715	0.772	0.819			

DISCUSSION

One of the most frequent procedures carried out by oral and maxillofacial surgeons is the surgical extraction of IMTM, which is mostly linked to trismus, facial swelling, and postoperative pain [14]. This study utilized WISDOM® gel (1% hyaluronic acid and 0.2 chlorhexidine) as one of several approaches to enhance early wound healing and lessen the possibility of postoperative morbidities following surgical extraction of IMTM. Arakji [15] has shown a positive correlation between the emergence period of IMTM and the onset of complications associated with these teeth, suggesting their removal. The patients in this study ranged in age from 18 to 39 years, with a mean age of 25. Female patients represented 53.33% of the total samples. This finding is consistent with previous studies showing that female patients with impacted mandibular third molars are more common than male patients [16]. Males often continue to develop their jaws after the eruption of the molars, thereby increasing the area available for the eruption of the third molar. In contrast, females ordinarily cease developing at that point [17–19]. Furthermore, the distribution of patients between groups based on factors such as age, sex, the side of impaction, the duration of the operation, and the classification of teeth according to Winter's, Pell, and Gregory's classifications did not significantly influence the study's conclusions. Because of its simplicity, repeatability, and patient friendliness, the NRS was employed in this investigation to assess the degree of pain experienced following surgical IMTM extraction. The study's findings indicate that the first day following surgery was the most painful for the patients in both groups, with pain scores gradually decreasing until the seventh day. These findings are consistent with previous research indicating that pain usually increases during the first 24 hours following surgery due to the release of inflammatory mediators like prostaglandin E2 and bradykinin, and that pain starts to set in once the local anesthetic wears off [20]. However, the improvement in patients' pain scores was significantly better in the study group than in the control group. These results could be attributed to WISDOM® gel components, which contain HA. Studies have shown that applying HA to the extraction socket significantly reduces pain [21], and CHX's antiseptic properties, which reduce the number of microorganisms in the surgical site, may have an analgesic effect. This, in turn, lowers the amount of inflammatory mediators released due to bacterial activity, ultimately resulting in a reduction in pain perception [22]. Regarding the swelling, it began after the surgical removal of the IMTM and peaked on the second to third postoperative day before gradually subsiding on the fourth postoperative day. Compared to the control group, there was a significant reduction in the degree of swelling in the study group patients during the postoperative days. Researchers suggest that the anti-edematous properties of HA, its osmotic buffering capabilities, and its ability to delay leukocyte migration by adhering to the receptor CD44 are responsible for these results [23,24]. It's also worth noting that CHX is essential in reducing facial edema, particularly after third-molar surgery [25]. Trismus is a typical and expected result of surgery on the third molar. To assess the condition, the researchers measured the maximum distance between the upper and lower central incisors, both pre- and postoperatively [26]. According to Balakrishnan [27], there is a high link between trismus and postoperative pain, suggesting that discomfort is the primary factor causing limited mouth opening after IMTM removal surgery. The improvements in the study group patients' pain scores could result in a significant improvement in the degree of trismus compared to the control group. These results were consistent with research conducted by Muñoz-Cámara [28], who found that local application of HA significantly minimizes postoperative trismus after IMTM extraction. The EHS was used on the first, third, and seventh days after surgery to remove IMTM to check how well the soft tissues were healing. The study group's EHS score went up significantly compared to the control group's score. Hyaluronic acid's role in phagocytosis and the elimination of invasive bacteria components could explain these results, leading to an improved wound healing process [29]. However, this study contradicts the findings of Galli [30], who claimed that a single dosage of hyaluronic acid applied to oral cavity surgical incisions does not seem to promote wound healing. The low hyaluronic acid concentration (0.2 ml) and the method of applying it to the surgical incision after suturing could potentially lead to these poor results.

Study limitations

This study includes many limitations, such as the difficulty in standardizing the influencing factors, such as patients' varying pain thresholds and immunological characteristics, in addition to the subjective nature of some scales used in the assessment of the outcomes.

Conclusion

Intra-socket application of 1cc of WISDOM® gel can be an effective primary method to minimize postoperative discomfort, trismus, and swelling after surgical removal of the impacted mandibular third molar, with a significant improvement in early soft tissue healing compared to the control group.

Conflict of interests

No conflict of interests was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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