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Oral Health-Related Quality of Life and the Use of Oral and Topical Nonsteroidal Anti-Inflammatory Drugs for Pericoronitis

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Background: Pericoronitis is inflammation of the tissue surrounding a third molar, or wisdom tooth. This study aimed to evaluate the effects of oral and topical analgesic nonsteroidal anti-inflammatory drugs (NSAIDs) on oral health-related quality of life (OHQoL), in terms of oral health and lifestyle, in patients with symptomatic pericoronitis.

Material/Methods: The study included 60 patients who presented with pericoronitis and who did not undergo surgery within the following seven days. The patients were randomly assigned to three groups and were treated with oral diclofenac (N=20), oral flurbiprofen (N=20), and topical benzydamine (N=20). OHQoL was assessed for all study participants with a self-reported eight-item scale that was developed to evaluate pericoronitis. The total OHQoL scores were calculated for each day during the seven-day study period.

Results: The study group treated with topical benzydamine had a significantly greater improvement in the OHQoL scores compared with the oral diclofenac and oral flurbiprofen groups on the first four days. Comparison of patients treated with diclofenac and flurbiprofen showed no significant differences for all seven days. A significant initial improvement in OHQoL was found on day 1 for the benzydamine group, on day 2 for the flurbiprofen group, and day 3 for the diclofenac group.

Conclusions: In this study, topical benzydamine was found to be a more effective alternative to oral NSAID analgesics, diclofenac and flurbiprofen, in improving OHQoL in patients with pericoronitis.

MeSH Keywords: Analgesics • Pericoronitis • Quality of Life

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Background

Oral health-related quality of life (OHQoL) is assessed by methods that measure the degree of ease of performing daily activities such as eating, speaking, socializing, and sleeping associated with an oral health condition [1]. The findings from the assessment of OHQoL may help clinicians to make treatment decisions that improve daily life for patients [2]. Pericoronitis is inflammation of the tissue surrounding the third molar and is a painful condition that can affect the quality of life [3,4]. Pericoronitis is most commonly associated with mandibular third molars, or wisdom teeth [3,5]. Symptoms of pericoronitis may range from mild to severe, with severe cases resulting in a fever, dysphagia, facial swelling or cellulitis, trismus, and enlarged lymph nodes [3]. However, even in cases of mild pericoronitis, patients may also experience severe pain [6].

Pericoronitis is usually treated by extraction of the semi-impacted molar tooth, which results in the complete resolution of the condition [4]. Mild cases of pericoronitis without infection do not usually require antibiotic treatment [7,8]. Nonsurgical treatment of pericoronitis has the aim of reducing the symptoms associated with inflammation [9], but the possibility of future recurrence remains a significant problem. However, third molar surgery can result in functional limitations and discomfort due to postoperative complications that include pain, swelling, and trismus. Previously published studies have shown that surgical removal of the third molar can reduce the quality of life in the immediate postoperative period [10–12]. Although patients are informed that medically-treated pericoronitis is likely to recur in the future, patients may elect not to undergo surgical treatment because of special events such as holidays, vacations, examinations, and work projects [6]. Also, patients who are given the option of third molar retention may decide to postpone surgical treatment until they develop recurrent pericoronitis [13]. In these cases, patients usually require medication for short-term pain relief with the hope that they will feel better and be able to return their daily routine.

Because pericoronitis is an inflammatory condition, nonsteroidal anti-inflammatory drugs (NSAIDs) have been the analgesics of choice. However, there have been no previous studies to compare the effects of oral and topical NSAIDs on the quality of life of patients with symptomatic pericoronitis. Diclofenac and flurbiprofen are the most frequently prescribed systemic NSAIDs in our clinic. Benzydamine is a topical NSAID that is used to relieve inflammatory conditions of the mouth [14]. Oral administration of NSAIDs is known to cause gastrointestinal complications, which is an important factor that limits their use [15]. However, the use of topical NSAIDs has the advantage of a lower risk of gastrointestinal toxicity and other undesirable side effects [16]. Although it would seem preferable to prescribe a topical NSAID for patients with symptomatic pericoronitis, there have been no previous studies to compare the effects with orally administered NSAIDs on OHQoL.

Therefore, this study aimed to evaluate the effects of oral and topical analgesic NSAIDs, including topical benzydamine and oral diclofenac and flurbiprofen, on OHQoL in terms of oral health and lifestyle, in patients with symptomatic pericoronitis.

Material and Methods

Patients

This study was undertaken in the Department of Oral and Maxillofacial Surgery of the Near East University. The Medical Ethics Committee of the Near East University approved the study (Ref. YDU/201747-417). The study participants were consecutively enrolled and included 60 individuals who presented with pericoronitis and who did not wish to undergo third molar surgery within the following seven days. The study inclusion criteria required that subjects were young adults aged 18 years or more, who were healthy with an American Society of Anesthesiologists (ASA) physical class status of 1, who were diagnosed with mild pericoronitis affecting one semi-impacted mandibular third molar, with spontaneous pain and localized swelling. Exclusion criteria were a history of smoking, allergy to nonsteroidal anti-inflammatory drugs (NSAIDs), including diclofenac, flurbiprofen, and benzydamine, or who had used systemic antibiotics or analgesic drugs within the previous three days before admission. Patients who had symptoms of severe pericoronitis, such as fever with a temperature >101°F (>38.3°C), dysphagia, trismus, or facial swelling, were also excluded. All patients who volunteered to participate in the study were verbally informed of the purpose and the details of the study, and signed an informed consent to participate before enrollment.

Patient groups and the three NSAID treatments

Patients who met the inclusion criteria were randomly assigned to three groups: the diclofenac group (N=20), treated with diclofenac 50 mg capsules (Cataflam, Novartis Sağlık, Gıda ve Tarım Ürünleri San. Tic. A.Ş., İstanbul, Turkey) and placebo spray; the flurbiprofen group (N=20), treated with flurbiprofen 100 mg capsules (Majezik, Sanovel İlaç San. ve Tic. A.Ş., İstanbul, Turkey) and placebo spray; and the benzydamine group (N=20), who received topical benzydamine 0.045 g, 30 mL oral spray (Tantum Verde, Angelini İlaç San. ve Tic. A.Ş, İstanbul, Turkey) and placebo capsules. All patients were instructed to take one capsule orally every eight hours and apply the spray four times to the area of pericoronitis every four hours for seven days, commencing immediately after the initial clinical examination.

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The dose of the active medications used in this study was based on the maximum daily dose recommended by the manufacturers. The study medications were provided to the patients by the same clinic nurse, and the patients and the researchers were blinded to the study medication allocation. A pharmacist prepared the diclofenac, flurbiprofen, and placebo capsules.

Controls used in the study

Placebo capsules contained starch, and placebo sprays consisted of normal saline solution with a peppermint flavor. All capsules were identical in size, shape, and color. The benzydamine solution and the control saline solutions were put into identical 30 mL spray containers without any label or brand name. A controlled study was conducted, as each patient received both a capsule and a spray container. Written treatment dosing and administration instructions were also included in the boxes, with a contact telephone number. Patients were instructed to contact the clinic in case of any adverse events or if they had any questions.

Evaluation of oral health-related quality of life (OHQoL)

The impact of pericoronitis on patient quality of life was evaluated each day for one week using the self-reported oral health-related quality of life (OHQoL) questionnaire. The OHQoL questionnaire evaluated oral function and lifestyle subscales using the quality of life instrument developed by Shugars et al. [17], in which the participants were asked to rate how much difficulty they experienced with eating, chewing, talking, mouth opening, sleeping, and participating in social life, sports, and hobbies. Responses were given on a five-point Likert-type scale in which each item was scored from 1 (none) to 5 (severe). A total score for each OHQoL questionnaire was calculated by combining the responses to the eight individual items, ranging from 8–40; the higher scores indicated a worse quality of life.

Determination of the study sample size

The minimum study sample size was determined from the findings of a pilot study. The pilot study included a sample of 15 patients. The effect size of the pilot study was calculated using G*Power software version 3.1.9.2 (Franz Faul, Universitat Kiel, Germany) based on a pooled standard deviation (SD) of 3.8. The minimum required sample size to detect an effect size of 0.472 with 80% power and a two-sided significance level set at 0.05 was calculated as 59. Therefore, 60 patients were included in this study, with 20 patients in each group.

Statistical analysis

Data were expressed as the mean±standard deviation (SD). The Shapiro-Wilk test was used to identify the normal distribution of the data for each variable. Age and gender differences between the treatment groups were assessed with one-way analysis of variance (ANOVA) and the chi-squared (χ^2) test. Two-way ANOVA followed by a post hoc Tukey's test were used to analyze the differences in outcome variables at different time points between the groups. Statistical analysis was performed using GraphPad Prism software version 7 (GraphPad Software Inc., La Jolla, CA, USA). A P-value <0.05 was considered to be statistically significant.

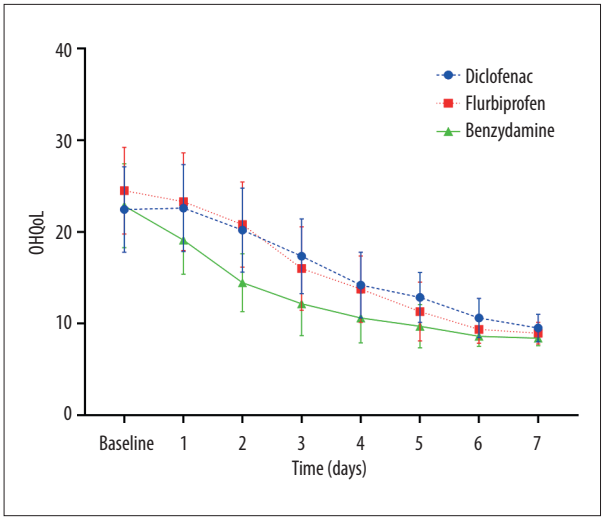

Figure 1. Changes in the mean oral health-related quality of life (OHQoL) scores during the study period in patients with pericoronitis treated with diclofenac (DCF), flurbiprofen (FBP), and benzydamine (BNZ).

Results

Study participants and adverse events

Initially, 181 patients were assessed for eligibility for this study, of whom 121 were excluded because they did not meet the study criteria (Figure 1). Patients were randomly assigned to three groups and were treated with the three nonsteroidal anti-inflammatory drug (NSAID) formulations, oral diclofenac (N=20), oral flurbiprofen (N=20), and topical benzydamine (N=20). The study participants included 29 men (48.3%) and 31 women (51.7%) with a mean age of 21.03±1.99 years (range, 18–25 years). There were no significant differences between the groups for age (P=0.052) or gender (χ^2=1.74; P=0.419). All patients were university students, no participant left the study, and there was no missing data. There were six patients, four in the flurbiprofen group and two in the diclofenac group, who reported adverse events, all of which were gastrointestinal symptoms, including heartburn, abdominal pain, and nausea. These symptoms were well controlled following treatment with proton pump inhibitors. Eleven patients

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Table 1. Mean oral health-related quality of life (OHQoL) values for the patients with pericoronitis treated with diclofenac (DCF), flurbiprofen (FBP), and benzydamine (BNZ).

Day/OHQoL	DCF group	FBP group	BNZ group
	Mean (±SD)	Mean (±SD)	Mean (±SD)
Baseline	22.45±4.66	24.50±4.73	22.85±4.58
Day 1	22.60±4.74	23.30±5.32	19.10±3.73
Day 2	20.20±4.58	20.80±4.64	14.45±3.15
Day 3	17.35±4.08	16.00±4.55	12.15±3.47
Day 4	14.20±3.57	13.75±3.61	10.60±2.72
Day 5	12.85±2.72	11.30±3.21	9.70±2.36
Day 6	10.60±2.13	9.35±1.50	8.60±1.09
Day 7	9.5±1.50	8.95±1.19	8.40±0.82

OHQoL – oral health-related quality of life; DCF – diclofenac; BNZ – benzydamine; FBP – flurbiprofen.

Table 2. P-values for intergroup comparisons between the patients with pericoronitis treated with diclofenac (DCF), flurbiprofen (FBP), and benzydamine (BNZ).

Day/OHQoL	DCF *vs.* BNZ	FBP *vs.* BNZ	DCF *vs.* FBP
Baseline	0.9406	0.3554	0.2037
Day 1	0.0105*	0.0015*	0.8292
Day 2	<0.0001*	<0.0001*	0.8714
Day 3	<0.0001*	0.0042*	.4995
Day 4	0.0040*	0.0141*	0.9148
Day 5	0.0246*	0.3779	0.4010
Day 6	0.1750	0.7810	0.5041
Day 7	0.6303	0.8908	0.8908

OHQoL – oral health-related quality of life; DCF – diclofenac; BNZ – benzydamine; FBP – flurbiprofen. * Statistically significant (P<0.05).

in the benzydamine group reported minor side effects that included oral numbness and taste alterations.

Oral health-related quality of life (OHQoL) scores

Baseline OHQoL scores were similar between the three treatment groups. Concerning the mean OHQoL scores, the benzydamine group showed improvement in the OHQoL scores when compared with the other two groups at all time points (Table 1), but these differences were statistically significant only during the first four days of treatment. Also, on the fifth day, the benzydamine group showed a greater decrease in OHQoL scores compared with the diclofenac group. On the sixth and seventh days of the treatment, there was no significant difference between the three groups in mean OHQoL scores (Table 2). The comparison of the diclofenac and flurbiprofen groups showed no significant difference in the OHQoL scores for all seven days (Figure 1). The first significant improvement in OHQoL was observed on the first day for the benzydamine group, on the second day for the flurbiprofen group, and on the third day for the diclofenac group. The flurbiprofen group and the benzydamine group showed significantly improved OHQoL scores with each successive day, from day 1 to day 3. The diclofenac group showed significantly improved OHQoL scores with each successive day, from day 1 to day 4. Analysis of each item in the questionnaire showed that the items that made the most significant contributions to the change in OHQoL scores, following treatment, were eating and talking (P<0.0001).

Discussion

For patients with symptomatic pericoronitis, pain relief is essential to improve their quality of life [3,4]. Surgical removal of the affected third molar is the most reliable treatment for pericoronitis, which may explain why there have been no previously reported studies to evaluate pharmacological treatments

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for the symptoms of pericoronitis. Shahakbari et al. compared the efficacy of green tea mouthwash with chlorhexidine to reduce pain and trismus and found that green tea showed better results than chlorhexidine [18]. Other nonsurgical treatments include low-level laser therapy and photodynamic therapy, both of which have beneficial effects in reducing the symptoms of pericoronitis [9,19].

Patients with pericoronitis may refuse or postpone third molar surgery for personal reasons. In a study by Tang et al., patients who presented with symptoms of pericoronitis underwent surgery by an average of 2.5 months after initial diagnosis [6]. Also, even for patients who choose molar extraction, surgery is not always possible in the acute phase of pericoronitis [19]. Therefore, effective management of the symptoms of pericoronitis is essential to maintain the quality of life for patients. However, no previously published data were available in the literature about the potential improvement in the quality of life achieved by symptomatic treatment with analgesics. Debridement and irrigation with antimicrobials have been recommended to eliminate the acute symptoms of inflammation [9,18]. In this study, these procedures were not performed, as the aim was to assess the sole analgesic effects of nonsteroidal anti-inflammatory drug (NSAID) regimens.

The majority of patients in this study described their pain as severe at the time of diagnosis, and analgesic medications were required. Therefore, a placebo-only control group was not undertaken for ethical reasons. However, because the pharmaceutical forms of the active medications used in capsules and sprays were different in appearance, patients who received oral NSAIDs (diclofenac or flurbiprofen capsules) also received placebo spray, and the patients who received benzydamine spray also received placebo capsules. The two most commonly prescribed oral NSAIDs in our clinic are diclofenac and flurbiprofen, which explains the choice of these two analgesics. There is evidence in the literature that both diclofenac and flurbiprofen provide sufficient analgesia after third molar surgery [20,21]. It is possible that this analgesic effect also applies to patients with pericoronitis because both conditions affect the same tissues. Mild pericoronitis could also be a potential indication for the use of topical NSAIDs, considering that the inflammation is typically localized to the gingiva and oral mucosa covering the tooth. In addition to its anti-inflammatory effect, benzydamine has an additional local anesthetic effect.

Oral NSAIDs (diclofenac and flurbiprofen) produce a systemic anti-inflammatory effect by the inhibition of the cyclooxygenase enzyme [22]. Topical application of benzydamine may affect the formation of thromboxanes and alter the biosynthesis of prostaglandin, which modifies tissue biochemistry that is relevant to local mechanisms of inflammation and pain. Benzydamine also has a stabilizing effect on cell membranes [23]. The depth of diffusion of the drug into the oral tissues is unknown, but the surface concentrations of benzydamine have been estimated to exceed 100 mmol/l [24]. In this study, the maximum recommended doses of the study medications were used to ensure the best possible analgesic effect. The costs of the three study medications were similar. In Turkey, the current cost of 15 tablets of flurbiprofen (100 mg) is $2.20, the cost of 20 tablets of diclofenac (50 mg) is $2.70, and the cost of the 30 mL spray of benzydamine is $3.00.

To our knowledge, this is the first study to investigate the change in oral health-related quality of life (OHQoL) outcomes during the administration of oral and topical NSAIDs in patients with pericoronitis. The OHQoL instrument, developed by Shugars et al., was used in this study, because it focussed specifically on the impact of third molar problems during a short timeframe [4]. The OHQoL self-reported eight-item scale was previously used to assess the impact of pericoronitis on lifestyle and oral function [3,4], the effect of quality of life on the decision to undergo third molar removal [6], and the degree of improvement in quality of life obtained following third molar removal [25]. In these previous studies, pericoronitis had adverse effects on the OHQoL results. One study reported that the OHQoL results for symptomatic pericoronitis were significantly associated with the decision made by the patient for early third molar surgery [6]. In another study, removal of the third molar was shown to improve the OHQoL results three months after surgery [25].

In the present study, the patient group treated with topical benzydamine showed the most significant improvements in OHQoL scores, which were significantly improved during the first four days of the study. At the end of the study, all the groups showed similar results for the OHQoL scores. However, the results of the OHQoL assessment did not show a significant difference in oral function and lifestyle between the patients taking diclofenac and flurbiprofen at all times. The most rapid improvement in OHQoL was achieved with the use of topical benzydamine, with the diclofenac group being the slowest to achieve a significant improvement. These findings may indicate that the use of topical benzydamine results in more rapid analgesia than the use of the oral NSAIDs used in this study. A statistically significant gradual decrease in OHQoL scores, which is indicative of the positive quality of life changes, was noted starting from day one and lasted for at least two days in all the groups. This favorable early response to analgesic treatment can be attributed to the administration of maximum doses of study medications. However, the significant favorable response disappeared after the fourth day. These results indicate that the use of topical benzydamine may be more beneficial in improving quality of life than the use of oral diclofenac and flurbiprofen for symptomatic treatment of pericoronitis.

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A common side effect associated with the use of systemic NSAIDs is gastrointestinal symptoms [22]. However, topical NSAIDs are associated with a significantly reduced risk of adverse gastrointestinal events due to the reduced plasma concentrations of the medication [15,16]. In this study, six patients who received oral NSAIDs (diclofenac and flurbiprofen) experienced gastrointestinal symptoms, whereas none of the patients had gastrointestinal complications in the group treated with benzydamine spray. However, more than half of the patients in the benzydamine group experienced only minor side effects, including oral numbness, a tingling sensation, and taste alterations. The incidence of side effects was highest (55%) in the benzydamine group, lower (20%) in the flurbiprofen group, and lowest (10%) in the diclofenac group. When comparing the incidence of side effects between the oral NSAIDs and topical benzydamine, oral NSAIDs groups (15%) had a lower incidence. Although the benzydamine group showed the greatest and most rapid improvements in OHQoL scores, the highest incidence of side effects was also seen in this group. Conversely, the diclofenac group showed the slowest improvements in OHQoL but the lowest incidence of side effects. Considering the severity of the side effects, these were less severe when topical benzydamine was used when compared with the use of oral NSAIDs.

This study had several limitations. All the study subjects were healthy young university students, which might not be representative of the general population. However, pericoronitis is more common in young adults, and this age group was representative of the condition. Patients with severe pericoronitis that would necessitate the use of antibiotics were excluded from the study to avoid the potential confounding effects of concomitant medications. The absence of severe cases of pericoronitis may have affected the results of quality of life assessments. Further limitations were the small sample size used in this study and the short study duration.

Conclusions

The aim of this study was to evaluate the effects of oral and topical analgesic nonsteroidal anti-inflammatory drugs (NSAIDs), including topical benzydamine and oral diclofenac and flurbiprofen, on oral health-related quality of life (OHQoL) in terms of oral health and lifestyle, in patients with symptomatic pericoronitis. The findings showed that topical benzydamine was a more effective alternative to oral NSAID analgesics, diclofenac and flurbiprofen, in improving OHQoL in patients with pericoronitis. However, the use of topical benzydamine spray was associated with side effects in more than half of the participants in this study, and clinicians should prescribe this medication with caution.

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