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Original Research

Nasal Sprays Containing Mometasone Furoate for Relief of Post-Adenotonsillectomy Pain in Children: A Prospective Controlled Study

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Abstract

Objectives: Adenotonsillectomy is one of most common surgeries performed in childhood. Post-operative pain associated particularly with tonsillectomy is still a problem for many physicians. Despite advances in surgical techniques, analgesics, or anti-inflammatory drugs, no unique strategy for post-tonsillectomy pain management has been suggested. The aim of this study is to investigate the analgesic effect of steroid containing nasal spray applied to tonsillar region after tonsillectomy.

Methods: Eighty-two patients were assigned into two groups as study and control. In study group, nasal spray containing steroid was applied to each tonsillar region after surgery for 5 days. Post-operative pain of all patients was assessed using a visual analog scale and results were compared.

Results: Pain decreased gradually over time in both the study and control groups. Although the pain scores from 4 h post-surgery to post-operative day 5 were not found to significantly decrease in children that used nasal spray containing steroid, these patients developed less pain on post-operative day 5,with statistical significance ($p<0.05$).

Conclusion: Post-tonsillectomy pain was reported to increase around post-operative day 5, which coincides with the time of intense wound inflammation. Therefore, significant pain reduction on post-operative day 5 observed in children that used nasal spray with steroid may have clinical importance for overcoming this problem.

Keywords: Mometasone furoate, nasal spray, pain relief, steroid, tonsillectomy, visual analogue scale

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Adenotonsillectomy is a widely performed procedure in otorhinolaryngology, and tonsillectomy alone has been reported to be the second most common surgery in pediatrics.[1] Although there has been a focus on post-tonsillectomy pain management for decades, most children who have undergone tonsillectomy with or without adenoidectomy still experience severe pain. Post-tonsillectomy pain is also an important cause of concern for the patient, the clinician, and the patient's family.[2] Inadequate pain control may lead to dehydration, insufficient oral intake, nausea, respiratory problems, and bleeding, which all cause re-hospitalization, parental anxiety, or repeated vis-

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its to the emergency department.[3,4]

To diminish the morbidity rate after tonsillectomy, various medications have been suggested, including paracetamol, nonsteroidal anti-inflammatory drugs, anesthetics, opioids, and steroids.[5-9] Recently, the use of steroids has been encouraged to reduce post-tonsillectomy pain and morbidity. Steroids are thought to contribute to post-tonsillectomy pain relief through inhibition of fibrin accumulation, vasodilatation, edema formation, and leukocyte infiltration.[10] Several studies have demonstrated that a single intravenous dose of dexamethasone reduces post-tonsillectomy pain, nausea, and vomiting.[11-13] Other researchers have also reported reduced post-tonsillectomy pain, nausea, and vomiting, and decreased analgesic consumption after local infiltration of steroids to the tonsillar region preoperatively.[14-16] However, systemic administration and local infiltration of steroids are invasive interventions, and they need to be performed in a hospital. Moreover, they provide no repeatable application at home. Therefore, we aimed to investigate the postoperative analgesic effect of a synthetic steroid (mometasone furoate) by applying to the tonsillar region using its nasal spray form, which may offer patients a non-invasive and repeatable opportunity for pain relief.

Methods

Between June 2016 and September 2017, 82 patients (49 males and 33 females), ranging in age from 3 to 13, scheduled for adenotonsillectomy were included in the study, which was conducted in the otorhinolaryngology clinic of a tertiary education and research hospital. This study was approved by the Institution's Ethics Committee (approval number of 1201/24 May, 2016). After informed consent was obtained from the patients' parents, patients admitted to the clinic for adenotonsillectomy were selected and assigned to the study and control groups. Recurrent or chronic tonsillitis with adenoidal hypertrophy or chronic adenoiditis and adenotonsillar hypertrophy leading to obstructive symptoms were indications for adenotonsillectomy. The exclusion criteria included bleeding disorders, having severe chronic or systemic diseases (i.e., diabetes, pulmonary, and cardiac diseases) or mental disorders and syndromes, acute infection, synchronous surgery in addition to adenotonsillectomy, or receiving anticoagulant therapy or any analgesic and steroid within 24 h of surgery. Patients were scheduled for surgery during the morning hours of the day in which the operation took place, usually at 8.30 a.m., 9.00 a.m., or 9.30 a.m. The patients received a standard anesthetic, which was administered by the same consulting anesthesiologist. The anesthesia was induced by propofol, fentanyl, and atracurium, and it was maintained with sevoflurane and remifentanil without any premedication. All the adenotonsillectomies were performed by a senior surgeon. Adenoidal curettes in appropriate size were used for adenoidectomy. After curettage of adenoid tissue, a round gauze swap was placed in nasopharynx for homeostasis and was left there during tonsillectomy. The standard dissection and snare method with cold instruments were preferred for the tonsillectomy. No partial tonsillectomy was performed. After bleeding was controlled with bi-polar cautery and irrigation with saline, each tonsillar fossa of the patients in the study group was gently dabbed with a gauze swap, and mometasone furoate (Nasonex Aqueous 50 mcg nasal spray, Merc & Co., Inc., Kenilworth, NJ, USA) was sprayed on each dried tonsillectomy region once (50 mcg) for patients younger than 12 and twice (100 mcg) for patients 12 and older. After waiting for 15 min, the operation was completed and the patients were awakened and transferred to the post-operative care unit. When the children were stable and completely awake, they were sent to the clinic. During adenotonsillectomies, none of the patients received additional analgesic. No antibiotics were given during or after surgery.

First oral intake was allowed 4 h after surgery, if the patients were free of post-operative nausea and vomiting (PONV). Post-operative feeding was started with water and maintained with clear fluids, including apple juice and sherbet as much as the patient could take. Popsicles and ice cream were also allowed. In the presence of PONV, the patients were given intravenous metoclopramide (0.1 mg/kg for patients younger than 6 and 2.5–5 mg/kg for patients 6 and older).

The post-operative analgesia protocol was started simultaneously with the first oral intake. Paracetamol at 15 mg/kg/dose, perorally, was given to all patients included in the study every 6 h during hospitalization. This protocol was maintained at home until the first post-operative visit. On post-operative day 6, patients returned to the hospital for first control examination. The children who had bleeding and needed intervention in the operating room or who were re-admitted to the hospital for severe pain and had received additional analgesics, such as nonsteroidal anti-inflammatory drugs and opioids, or who had infection and were given antibiotics during follow-up, were excluded from the study.

The pain of all patients included in the study was assessed using a visual analogue scale (Wong - Baker FACES pain rating scale) validated in children (Fig. 1).[17] The faces on the pain scale were explained to the patients, and they were asked to select a face that illustrated the pain they were experiencing. The scale was also explained to the parents. Thus, at 4, 8, and 12 h postoperatively, the patients selected the faces and a senior surgeon of the clinic marked the results on the scale near the parents; in this way, the scores

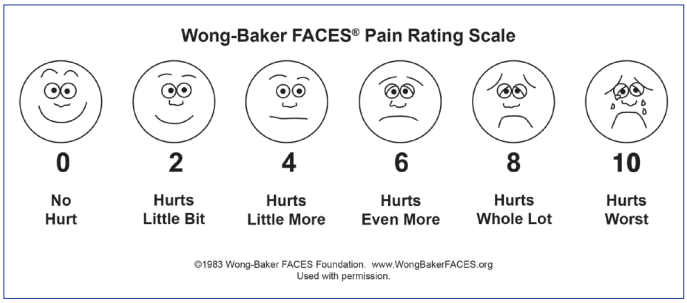

Figure 1. Wong Baker® FACES scale used to assess the post-operative pain of children.

were recorded. On the 1st day morning, after surgery (24 h post-surgery) mometasone furoate was sprayed on the tonsillar region of each of the patients in the study group at determined doses (mentioned above) before oral intake. After waiting for 15 min, the patients were asked to select the face on the pain scale that represented their level of pain, and the score was recorded. The patients in the control group who received only paracetamol after surgery were also assessed using the same pain scale method, and the scores were also recorded.

If the patients were awake, stable vitally, had no bleeding, and could take soft foods and enough water, they were allowed to go home on the 1st day after surgery. They were advised to take liquids, including water and apple juice, and sherbet as much as they could tolerate, and soft cold/warm foods, such as custard, chicken broth, potato puree, and vegetable meals. They were warned to avoid citric foods and drinks. In the case of any bleeding, severe nausea and vomiting, severe pain limiting oral intake substantially, or fever leading to any concern, the parents were warned to return the hospital. The parents of the patients in the study group were also given four copies of the pain scale on which the post-operative dates were written to be marked every morning at the same hour, 15 min after the nasal spray was applied. The nasal spray applied in the hospital (Nasonex Aqueous 50 mcg nasal spray, Merc & Co., Inc., Kenilworth, NJ, USA) was prescribed for the patients in the study group before discharge.

At the first follow-up, the tonsillar regions were examined carefully by a senior surgeon who was blinded to the patients. The findings, including infectious signs and coagulum, were recorded. The parents were also asked about minor bleeding, fever, and nausea/vomiting during the post-operative period at home. The completed pain scales were collected from the parents, and the pain scores from days 2, 3, 4, and 5 were also recorded. The data from each patient were transferred to a computer file using Excel 2010 software for Windows (Microsoft Corporation, Redmond, WA, USA).

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 15.0 for Windows (SPSS, Inc., Chicago, IL, USA). Descriptive statistics for the categorical variables were expressed as mean, standard deviation, and interquartile range. The Mann–Whitney U-test was used to compare the numerical variables between independent groups due to the absence of normal distribution. The ratio of the categorical variables between groups was analyzed using the Chi-square test. Statistical significance was defined as $p<0.05$.

Results

Ninety-nine children scheduled for adenotonsillectomy were initially included in the study. Fifty-two patients were selected for the study group and 47 patients were selected for the control group. Eleven patients in the study group were excluded during the follow-up because the pain scales of four patients were filled out incompletely despite using the nasal spray every day at home, two patients did not use the nasal spray every day, two patients were readmitted to the hospital and needed bleeding control in the operating room, two patients were given antibiotics for infection, and one patient had severe pain with poor oral intake and received additional analgesics in the hospital.

Six patients in the control group were also excluded from the study because one patient had bleeding and needed surgical intervention, one patient had severe pain with poor oral intake and was given additional analgesics in hospital, the pain scales of two patients were marked incompletely, one patient received antibiotic for infection, and one patient was given additional analgesic (ibuprofen) by her parent at home during the week after discharge. Thus, the study group consisted of 41 patients (25 males and 16 females) and the control group consisted of 41 patients (24 males and 17 females).

The demographic data between the patients in the study (n=41) and control groups (n=41) were compared. No significant difference was found between the groups in terms of gender and age ($p>0.05$) (Table 1).

Table 1. Demographic data, including the age and sex of the children in the study and control groups

	Control group Mean±SD (Median)	Study group Mean±SD (Median)	p
Age	7.0±2.7 (6)	6.6±2.1 (6)	0.619
Gender			
Male	24 (58.5)	25 (61.0)	1.000
Female	17 (41.5)	16 (39.0)	

SD: Standard deviation.

The pain scores of the patients in the study and control groups were comparatively analyzed. The scores obtained at 4, 8, 12, and 24 h postoperatively showed no statistically significant difference between the study and control groups (p>0.05) (Table 2 and Fig. 2). The scores after discharge on post-operative days 2, 3, and 4 also revealed no statistically significant difference when the groups were compared (p>0.05) (Table 2 and Fig. 2). However, the pain scores in the study group on post-operative day 5 were found to be lower than the scores in the control group on the same day with a statistically significant difference (p=0.033) (Table 2).

When complications, including minor bleeding, fever, nausea, and vomiting that did not required any intervention or additional medication, were compared between the groups, no statistically significant difference was found (p>0.05) (Table 3). The occurrence of minor bleeding seemed to be slightly higher in the study group (n=4) than the control group (n=0); however, this difference was not statistically significant.

No side effects from the steroid application that would lead the parents to be concerned were noticed. The parents of three patients in the study group reported a burning sensation after spraying mometasone furoate, but this did not cause them to suspend the steroid usage.

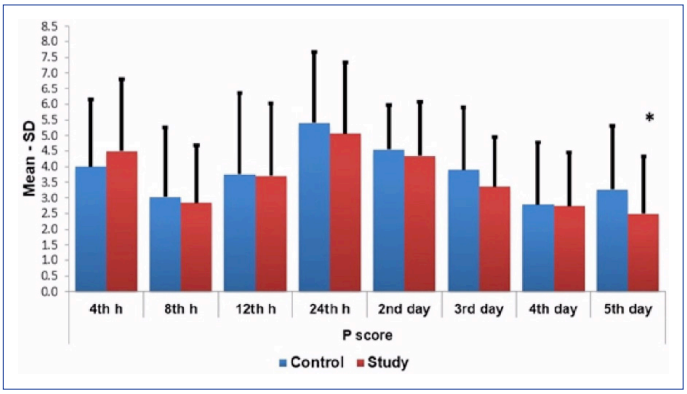

Figure 2. Demonstration of the mean pain scores in the study and control groups based on the post-operative time. The post-operative day 5 scores were statistically significant between the groups. Patients that used steroid spray had less pain on post-operative day 5 than patients that were only given paracetamol. P score: Pain score; *Statistical significance (p=0.033).

Discussion

Tonsillectomy with or without adenoidectomy is one of the most widely performed surgeries in pediatric otorhinolaryngology. However, pain relief after tonsillectomy is still a problem for many clinicians dealing with this surgery, and it has been supported by a large number of studies about this topic. The clinical importance of post-tonsillectomy pain control is based on the undesirable consequences related to the pain, including poor oral intake, dehydration, re-admission to the hospital, bleeding, sleep problems, or behavioral changes.[18]

After tonsillectomy, pain stems from inflammation, nerve irritation, and spasms in the pharyngeal muscles. Local trauma in the oropharynx from this surgery causes the release of chemokines, substance P, pro-inflammatory factors, and vasoactive intestinal peptides, all of which induce vasodilatation, tissue edema, and pain.[19]

In the past, several surgical techniques such as cold dissection or hot dissection of tonsils,[20] anti-inflammatory drugs, including salicylates,[21] or various anesthetics for local infiltration to the surgical field[22-24] have been investigated for pain relief after tonsillectomy. Recently, corticosteroids have become the drugs of interest for many researchers and clinicians to reduce post-tonsillectomy pain and related morbidities by decreasing local inflammation by blocking the chemical mediators of inflammation.

Table 2. Comparison of the mean pain scores of the patients in the study and control groups over time. Except the post-operative 5th day, no statistically significant difference between groups was observed

Time	Control group		Study group		p
Mean VAS sores	Mean±SD	Min–Max	Mean±SD	Min–Max	
4th h	4.00±2.14	4 (2–6)	4.49±2.31	4 (3–6)	0.303
8th h	3.02±2.24	2 (2–4)	2.83±1.84	2 (2–4)	0.851
12th h	3.76±2.58	4 (2–4)	3.71±2.30	4 (2–6)	0.904
24th h	5.41±2.25	6 (4–7)	5.07±2.28	6 (4–6)	0.545
2nd d	4.54±1.42	4 (4–6)	4.34±1.73	4 (4–6)	0.342
3rd d	3.90±2.00	4 (2–6)	3.37±1.58	4 (2–4)	0.298
4th d	2.78±1.99	2 (2–4)	2.73±1.72	2 (2–4)	0.937
5th d	3.27±2.04	4 (2–4)	2.49±1.83	2 (2–3)	0.033

VAS: Visual analog scale; SD: Standard deviation; h: Hour; d: Day.

Table 3. Comparison of morbidity between the study and control groups after discharge. Minor bleeding seems to be slightly higher in steroid group but it was not statistically significant

	Study group		Control group		p
	n	%	n	%	
Morbidity	5	12.2	3	7.3	0.712
Fever	0	0.0	2	4.9	0.085
Minor bleeding	4	9.8	0	0.0	
Nausea/vomiting	1	2.4	1	2.4	
None	36	87.8	38	92.7	

It has been reported that patients treated with antibiotics alone had more pain than patients given both oral corticosteroids and antibiotics for the first 4 days after undergoing tonsillectomy.[25] A single dose of intravenous dexamethasone administered before surgery was reported to provide no notable decrease in pain after tonsillectomy;[26,27] however, Lachance et al.[28] and Hermans et al.[29] suggested this medication to decrease post-tonsillectomy pain and analgesic consumption. According to Gao et al.,[15] the concentration of dexamethasone at the surgical site diminishes after a single dose intravenous administration of this drug because of its broad distribution. Therefore, pre-operative infiltration of low-dose dexamethasone to the surgical area was proposed to achieve a higher regional steroid level by preventing the loss of the drug due to its distribution and elimination in the body's systemic circulation.[14,15] However, steroid infiltration to the surgical site is an invasive intervention that can only be performed under hospital conditions; unfortunately, it does not allow for repeated doses after discharge. Thus, we hypothesized that topical oropharyngeal use of nasal sprays containing steroids may contribute to pain relief after tonsillectomies, and it may provide repeated application to each tonsillar fossa every day at home until the first follow-up. To the best of our knowledge, no prior study has investigated the oropharyngeal use of nasal steroids for post-tonsillectomy pain relief.

Nasal sprays containing mometasone furoate, which is a synthetic steroid that acts to reduce inflammation and congestion in the nose, are widely used to treat allergic rhinitis. The mometasone furoate particles directly infiltrate the nasal mucosal cells and are absorbed in small quantities into the systemic circulation. The steroid particles crossing the cell membrane bind to specific cytoplasmic receptors with high affinity. This decelerates or inhibits the inflammation cascade. We supposed that the mechanism of action of mometasone furoate may serve to provide pain relief after tonsillectomy by reducing local inflammation. In the present study, the doses recommended for nasal application of mometasone furoate were used in the tonsillar region.

The results of this study revealed no statistically significant difference between the study and control groups in terms of pain scores, except the scores on postoperative day 5. Between the first 4 and 24 h and on the days up to post-operative day 5, this medication appeared not to be sufficient for reducing post-tonsillectomy pain. Pain was at its highest level on the 1st day in both groups. It gradually decreased between post-operative day 1 and day 4, but it showed an increase on postoperative day 5 in the control group. However, in the study group, pain continued to decrease on post-operative day 5. As reported in the literature, the pain scores after tonsillectomy decrease gradually from post-operative day 1 to post-operative day 10, and this improvement was often interrupted by an increment in pain on day 4 to day 5 in patients that were only treated with paracetamol.[30] This increase in pain was attributed to the maximum wound inflammation and fibrin deposition that was reported to be around post-operative day 5 from the onset.[31] The pain increase observed on post-operative day 5 in our control group may be correlated with this peak time of wound inflammation.[31] Correspondingly, in our study, the children that used the mometasone furoate nasal spray (study group) had less pain on postoperative day 5 than the children that were only treated with paracetamol (control group). Probably, the anti-inflammatory effect of mometasone furoate became more noticeable on post-operative day 5, when the wound inflammation after surgery is most intense.[31,32] Therefore, this study's finding of the pain decrease on post-operative day 5 in the study group may be clinically important.

The present study has some limitations. The first limitation is that it did not include a larger cohort. Seventeen patients were excluded from the study during follow-up. Six of them marked the scale incompletely, and two patients did not use the steroid spray every day. Second, it should also be considered that the mometasone furoate dose recommended for intranasal application might be quantitatively inadequate for oropharyngeal application because many of the drug's particles are swallowed or eliminated before reaching the targeted area. Presumably, higher drug doses may be more effective in reducing post-tonsillectomy pain.

Conclusion

Although the literature reports on various oral, parenteral, or infiltrative medications, and many kinds of surgical techniques such as cold dissection, coblation or partial tonsillectomy, for reducing post-tonsillectomy pain, no unique treatment modality has yet been suggested.[33] The present study revealed that topical application of mometasone furoate to the surgical field provided a significant decrease in pain scores on post-operative day 5, which coincides with the time of intense wound inflammation. This finding may be clinically relevant in terms of effective pain control during the profound inflammation stage of tonsillectomies. In fact, this issue may deserve to be studied in larger cohorts.

Disclosures

Ethics Committee Approval: The study was approved by the Şişli Hamidiye Etfal Training and Research Hospital's local Ethics Committee (approval number of 1201 / 24.05.2016).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – O.U., M.A., G.B., P.S, M.E., B.T., B.U.C.; Design – O.U., M.A., G.B., P.S, M.E., B.T., B.U.C.; Supervision – O.U., M.A., G.B., P.S, M.E., B.T., B.U.C.; Materials – O.U., G.B., P.S, M.E., B.T.; Data collection &/or processing – O.U., P.S, M.E., B.T.; Analysis and/or interpretation – G.B., P.S, M.E. ; Literature search – O.U., G.B., P.S.; Writing – O.U., M.A., G.B., B.T.; Critical review – O.U., M.A., B.U.C.

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