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The Effect of Topical Dexamethasone on Postoperative Pain Intensity in Patients Undergoing Dacryocystorhinostomy Procedure

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ABSTRACT

Background and Objective: It is very important and necessary to use certain methods in order to prevent or reduce the intensity of pain after surgery. Of all known methods, those that avoid the dangerous side effects of opioids or nonsteroidal anti-inflammatory drugs (NSAIDs) can be useful. The present study was conducted with the aim of investigating the effect of topical dexamethasone on postoperative pain intensity in patients undergoing dacryocystorhinostomy (DCR).

Methods: This double-blind randomized clinical trial was conducted on 80 patients aged 18-75 who were candidates for DCR and referred to Khatam Al-Anbia Hospital in Mashhad. Patients were randomly divided into control and intervention (dexamethasone) groups. In the intervention group, at the end of the procedure, a tampon impregnated with dexamethasone was placed in the upper part of the middle concha. In the control group, a tampon washed in distilled water was placed in the same place. Pain intensity was recorded on a verbal rating scale (VRS) 0, 3, 6, 12, 18 and 24 hours after the operation.

Findings: There was no significant difference in pain intensity at different time points in the two groups of intervention and control; the frequency of severe pain during recovery was equal to 22.5% and 15.7%, within 3 hours after the operation was equal to 17.5% and 10.0%, within 6 hours after the operation was equal to 12.5% and 0.5%, within 12 hours after the operation was equal to 12.5% and 2.5%, within 18 hours after the operation was equal to 0% and 2.5% and within 24 hours after the operation was equal to 0% and 0%, respectively. There was no significant difference in the process of changes in pain intensity during the 24 hours of the study based on the follow-up test.

Conclusion: The results of the study showed that topical use of a single dose of dexamethasone (8 mg) could not reduce postoperative pain as well as the need for opioids in DCR surgery.

Keywords: *Dacryocystorhinostomy, Dexamethasone, Pain, Randomized Clinical Trial, Verbal Rating Scale.*

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Introduction

Pain specialists have made great efforts to control acute postoperative pain, but it remains a serious clinical problem. Several studies have expressed the negative effects of intractable pain with the greatest physiological effects on different parts of the body. Adrenal sympathetic hyperactivity, coronary artery ischemia, deep vein thrombosis, inappropriate breathing depth, atelectasis, tachycardia, high blood pressure, etc. are some of these complications. Despite many efforts to reduce the need for opioid drugs in the treatment of postoperative pain by providing other drugs or using alternative methods, opioids are currently the main options for postoperative pain control despite their known negative effects. The ultimate goal is to discover non-opioid drugs with affordable prices, fewer side effects, and longer lifespans (1, 2).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat pain after eye surgery, but these drugs have adverse effects on the kidneys and digestive system. It seems that other drugs can be used instead of NSAIDs to treat postoperative pain (3).

Steroids are widely used to treat inflammation, autoimmune disorders, and cancer (4). Many studies have shown the role of steroids in pain control as an adjunctive analgesic. Dexamethasone is the most common corticosteroid drug that has been studied as a pain reliever after various surgeries including total hip arthroplasty or mandibular surgery, tonsillectomy, knee arthroplasty, and breast cancer surgery (5-9). Glucocorticoids inhibit the synthesis of prostaglandins and reduce vascular permeability, which reduce inflammation and edema and ultimately reduce pain. They also stimulate lipocortin synthesis, which results in blocking the production of eicosanoids (10).

In general, both NSAIDs and steroids provide the same analgesic and anti-inflammatory effects at similar therapeutic doses. However, the use of NSAIDs poses a significant risk to the gastrointestinal system (11, 12).

Various studies have reported the effects of local anesthetics and dexamethasone compounds by injection for nasal surgery (13). However, no previous studies have used dexamethasone for nasal packing in endoscopic nasal surgery. The aim of this study is to investigate the local effects of dexamethasone on pain after dacryocystorhinostomy (DCR) surgery.

Methods

After approval by the Ethics Committee of Mashhad University of Medical Sciences with the code IR.MUMS.MEDICAL.REC.1399.517 and registered in the Iranian Clinical Trials System with the code IRCT20210113050021N1, this randomized controlled double-blind clinical trial was conducted on patients referred to Khatam Al-Anbia Hospital in Mashhad who were candidate for DCR surgery from 2011 to 2020. All patients were informed and the study protocol was explained and written consent was obtained. Patients aged between 18 and 75 years and able to speak Farsi, candidates for DCR surgery and patients in anesthesia class I and II (ASA: normal and healthy patients, patients with mild systemic disease) were included in the study. Patients with a history of uncontrolled systemic hypertension, known and confirmed mental illness, history of seizures, patients with a history of alcohol and drug use (all based on the patient's own report), patients taking any painkiller in the 24 hours before surgery, allergic to dexamethasone and patients with any unusual complications during surgery were excluded from the study.

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Randomization was done using PASS statistical software. The studied groups (coded) and the number of patients in each group were entered into the software and a random sequence was created. The sequences were generated and placed in sealed envelopes so that the contents of the envelopes could not be seen from the outside. The envelopes were numbered. For each patient admitted in the study, an envelope was opened and based on the contents of the envelope, they were placed in one of two study groups. Both groups included 40 patients. In the dexamethasone group, a tampon impregnated with 8 mg (2 ml) of dexamethasone was placed in the upper part of the middle concha immediately after the end of the operation by the surgeon without identifying it. In the control group, a tampon soaked in distilled water was rubbed in the same place. Tampons were removed 2 to 4 hours after surgery. All operations were performed by one surgeon. The pain intensity of the patients was evaluated for 24 hours after the surgery using the numerical verbal response score (VRS). There are different VRS lists. Based on NHS Trust in the University Hospital of Wales, the pain intensity of the patients was assessed on a 4-point scale: no pain= 0, mild= 1, moderate= 2 or severe= 3. Patients were evaluated 0 (immediately after entering the recovery department), 3, 6, 12, 18 and 24 hours after the operation. If the patient's pain was moderate or severe, rescue pain treatment was available according to the protocol.

The sample size in this study was calculated based on the mean pain score of the patients using topical dexamethasone compared to the control group in the first 12 hours after surgery, and considering 5% dropout, 56 people were in each group and a total of 112 people. Finally, out of 112 patients who met the inclusion criteria, according to the power analysis and due to the corona pandemic, the sample size was changed to 80 people. 40 people were included in the intervention group and 40 were considered as controls.

SPSS 16.0 software (SPSS Inc./IBM Corp., Chicago, IL, USA) was used for statistical analysis. The Kolmogorov-Smirnov test was used to evaluate the normality of data distribution. The results were expressed as mean±standard deviation for continuous variables and number (percentage) for categorical variables. Data were analyzed using chi-square test, independent sample t-test or non-parametric equivalent, and $p<0.05$ was considered significant.

Results

In this study, 80 DCR candidates were examined in two groups of dexamethasone and control group (40 subjects in each group). There was no significant difference between the groups in terms of basic characteristics such as gender, age and weight (Table 1).

In most of the patients in both intervention and control groups (33 [82.5%] and 29 [72.5%] patients, respectively), silicone tubes were not used during surgery and there was no significant difference between the groups in terms of silicone tube use. In the two intervention and control groups, the frequency of cases of needing post-operative pain relief was 70% and 72.5%, respectively, which was similar in the two groups. Based on the time of taking painkillers in 24 hours after the operation, the intervention group needed painkillers earlier than the control group, but this difference was not significant between the two groups.

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Table 1. Characteristics of study patients

Index	Intervention group Number(%) or Mean±SD	Control group Number(%) or Mean±SD	p-value*
Gender			
Woman	28(70.7)	29(72.5)	0.805
Man	12(30.0)	11(27.5)	
Age (year)	56.28±14.18	52.43±14.92	0.241
Weight (kg)	66.87±13.20	68.81±15.93	0.555
Use of silicone tube			
Yes	11(27.5)	7(17.5)	0.284
No	29(72.5)	33(82.5)	
Use of painkillers during 24 hours after the operation			
Yes	29(72.5)	28(70.0)	0.805
No	11(27.5)	12(30.0)	
Period until the first administration of painkillers 24 hours after the operation	8.50±3.07	7.12±4.00	0.369

***The results were analyzed using chi-square or independent t tests.**

No significant difference was observed between the two groups regarding the mean pain score at different time points from the time of entering recovery to 24 hours after the operation (Table 2). Based on the analysis of the changes in pain intensity, no difference was observed in the changes in the pain score during the 24 hours of follow-up of the patients (p=0.456) (Figure 1).

Table 2. Postoperative pain intensity based on VRS at different times of the study in the intervention and control groups

Group and intensity of pain	Recovery Number(%)	3 hours Number(%)	6 hours Number(%)	12 hours Number(%)	18 hours Number(%)	24 hours Number(%)
Intervention						
No	11(27.5)	15(37.5)	16(40.0)	21(52.5)	26(65.0)	29(72.5)
Mild	9(22.5)	9(22.5)	13(32.5)	14(35.0)	10(25.0)	8(20.0)
Moderate	11(27.5)	9(22.5)	6(15.0)	3(7.5)	4(10.0)	3(7.5)
Severe	9(22.5)	7(17.5)	5(12.5)	2(12.5)	0(0.0)	0(0.0)
Control						
No	11(27.5)	13(32.5)	16(40.0)	24(60.0)	24(60.0)	23(57.5)
Mild	13(32.5)	16(40.0)	14(35.0)	12(30.0)	13(32.5)	16(40.0)
Moderate	9(22.5)	7(17.5)	8(20.0)	3(7.5)	2(5.0)	1(2.5)
Severe	7(17.5)	4(10.0)	2(5.0)	1(2.5)	1(2.5)	0(0.0)
p-value*	0.785	0.366	0.657	0.876	0.544	0.113

***The results were analyzed using chi-square tests.**

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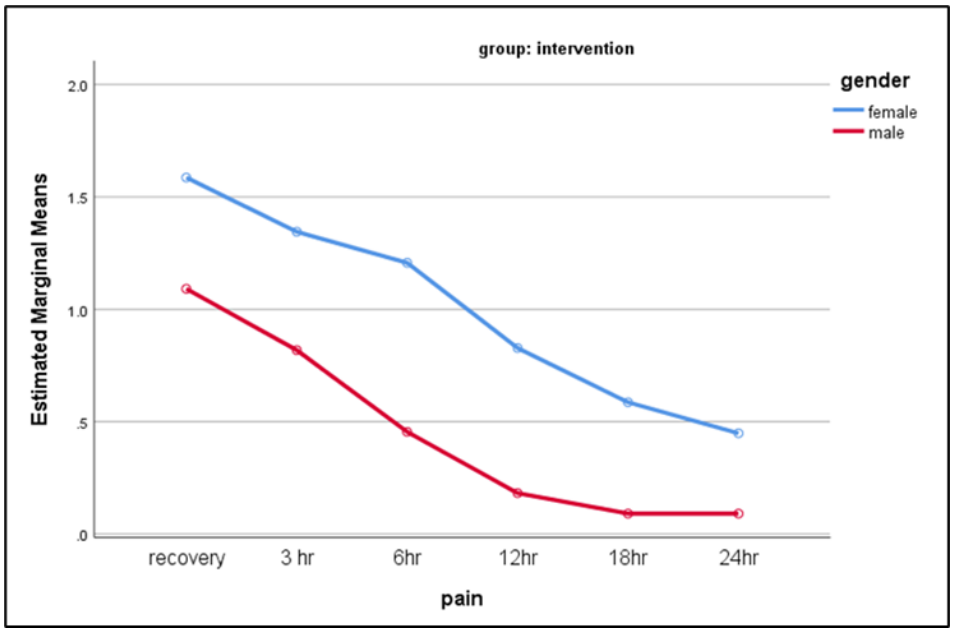

Figure 1. Changes in pain intensity (based on VRS) in patients under study within 24 hours after surgery

The lack of difference between the pain scores between the two groups at different time points was completely independent of the effect of patient gender (Tables 3 and 4). Furthermore, the trend of pain score changes in both intervention and control groups based on the gender of the patients did not show any significant difference (Figure 2 and 3).

Table 3. Intensity of postoperative pain according to gender in the intervention group

Group and intensity of pain	Recovery Number(%)	3 Hours Number(%)	6 Hours Number(%)	12 Hours Number(%)	18 Hours Number(%)	24 Hours Number(%)
Woman (n=29)						
No	6(20.7)	9(31.0)	9(31.0)	12(41.4)	16(55.2)	19(65.5)
Mild	7(24.1)	7(24.1)	10(34.5)	12(41.4)	9(31.0)	7(24.1)
Moderate	9(31.0)	7(24.1)	5(17.2)	3(10.3)	4(13.8)	3(10.3)
Severe	7(24.1)	6(20.7)	5(17.2)	2(6.9)	0(0.0)	0(0.0)
Man (n=11)						
No	5(45.5)	6(54.5)	7(63.6)	9(81.8)	10(90.9)	10(90.9)
Mild	2(18.2)	2(18.2)	3(27.3)	2(18.2)	1(9.1)	1(9.1)
Moderate	2(18.2)	2(18.2)	1(9.1)	0(0.0)	0(0.0)	0(0.0)
Severe	2(18.2)	1(9.1)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
p-value*	0.474	0.564	0.213	0.132	0.099	0.233

***The results were analyzed using chi-square tests.**

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Table 4. Intensity of postoperative pain according to gender in the control group

Group and intensity of pain	Recovery Number(%)	3 Hours Number(%)	6 Hours Number(%)	12 Hours Number(%)	18 Hours Number(%)	24 Hours Number(%)
Woman (n=29)						
No	7(25.0)	8(28.6)	8(28.6)	14(50.0)	14(50.0)	13(46.4)
Mild	8(28.6)	11(39.3)	11(39.3)	10(35.7)	11(93.3)	14(50.0)
Moderate	7(25.0)	6(21.4)	7(25.0)	3(10.7)	2(7.1)	1(3.6)
Severe	6(21.4)	3(10.7)	2(7.1)	1(3.6)	1(3.6)	0(0.0)
Man (n=11)						
No	4(31.3)	5(41.7)	8(66.5)	10(83.3)	10(83.3)	10(83.3)
Mild	5(41.7)	5(41.7)	3(25.0)	2(16.7)	2(16.7)	2(16.7)
Moderate	2(16.7)	1(8.3)	1(8.3)	0(0.0)	0(0.0)	0(0.0)
Severe	1(8.3)	1(8.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
p-value*	0.629	0.723	0.135	0.232	0.244	0.093

***The results were analyzed using chi-square tests.**

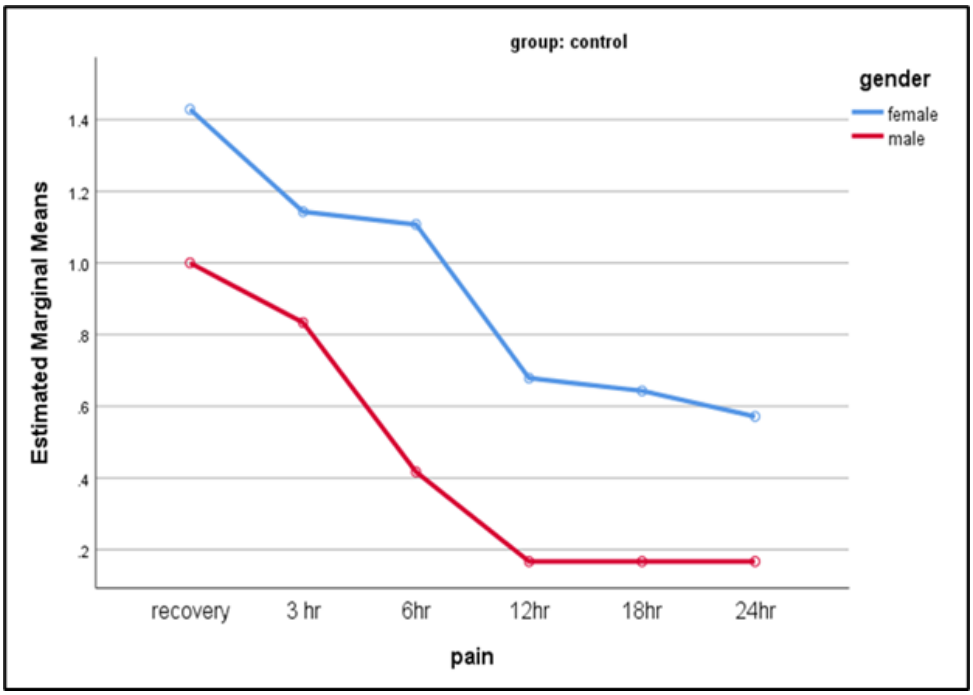

Figure 2. Comparison of pain intensity within 24 hours after the operation between men and women in the intervention group

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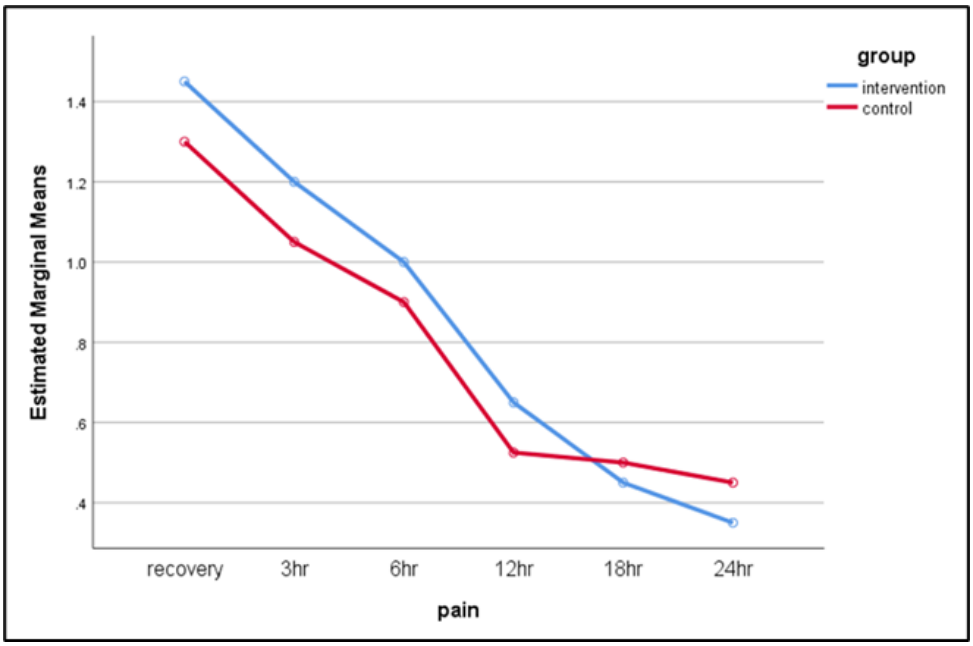

Figure 3. Comparison of pain intensity within 24 hours after the operation between men and women in the control group

Discussion

In this study, topical dexamethasone 8 mg (2 ml) had no effect on the pain score and the patients' need for opioids after DCR compared to the control group. Consistent with our results, the study by Mathiesen et al. showed that the combination of pregabalin and dexamethasone had no effect on pain intensity or opioid requirement compared to pregabalin alone (14). In another similar study, the effect of IV dexamethasone on postoperative pain was reported to be minimal (15). In addition, Lovich-Sapola et al. suggested that a single dose of dexamethasone (10 mg) has no analgesic effect and is unable to reduce the incidence of postoperative nausea and vomiting (PONV) after intrathecal injection of tetracaine and neostigmine (16).

Many studies have confirmed the role of dexamethasone in prolonging analgesia with the addition of some local anesthetics. Yayik et al. showed that the combination of topical dexamethasone with bupivacaine using a wet tampon reduced pain scores in the postoperative period and during tampon removal and also reduced the need for analgesia in endoscopic nasal surgery (17). Some studies have shown that the mechanism of action of dexamethasone when used as an adjunct to local anesthetics is due to its inhibitory effect on nerve signaling. However, others have suggested that dexamethasone increases the duration of local anesthesia through vasoconstriction in the injection area or by increasing the activity of inhibitory potassium channels on C-fibers of pain, reducing their activity and prolonging sensory and motor block (18).

Dexamethasone also inhibits the release of inflammatory mediators such as interleukins and cytokines. All these dynamics lead to the reduction of postoperative pain (19, 20). In a study by Desmet et al., it was found that both perineural and systemic forms of dexamethasone administration prolonged the blocking effect of local anesthetics almost equally, suggesting that dexamethasone, administered via the neural route,

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brings long-term blockade by entering the systemic circulation with its anti-inflammatory effects (21). The results of our study are in contrast with many studies that have confirmed the role of dexamethasone in reducing postoperative pain, which could be due to differences in dosage, methods of administration, form of application of the drug (solution vs. ointment) and other characteristics in each procedure. The dose and type (solution vs. ointment) of dexamethasone can influence the results of the study.

The limitation of the present study was that the tampon was removed 2 to 4 hours after surgery to prevent dexamethasone complications (infection) in patients, which seems to be a short time.

The results of this study showed that there is no significant difference in the intensity of postoperative pain between the two dexamethasone and control groups. The present study also showed that the use of topical dexamethasone 24 hours after surgery compared to the control group does not affect the demand of patients for pain relief, and a topical dose of dexamethasone (8 mg) cannot reduce postoperative pain and the need for opioids in DCR surgery compared to the control group.

Conflict of interest: The authors declare no conflict of interest.

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