

Tonsillectomy pain control with IV dexamethasone, infiltrated dexamethasone and infiltrated bupivacaine; a randomised, double-blind, placebo controlled, prospective clinical trial

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Abstract

Objective: To compare effects of local and systemic administrations of dexamethasone and local bupivacaine on postoperative pain in patients who have had tonsillectomy.

Methods: This randomised, double-blinded, placebo-controlled and prospective clinical trial was conducted at Adana Numune Training and Research Hospital, Turkey, between April and July 2016, and comprised patients who were undergoing tonsillectomy operation due to recurrent tonsillitis, chronic tonsillitis or tonsillar hypertrophy indication. Patients were randomly assigned to 4 equal groups. Group 1 was administered 0.5 mg/kg intravenous dexamethasone. Group 2 was given 0.5mg/kg dexamethasone diluted with 10 mL saline which was infiltrated into the peritonsillar regions. Group 3 received 2.5 mL of 0.5% bupivacaine infiltration. Group 4 was the control group and received peritonsillar saline infiltration. Pain was evaluated with visual analogue scale and the data obtained was analysed with SPSS 20.

Results: Of the 60 patients, each group had 15(25%). Visual analogue scale values at the 15th minute was significantly lower in Group 1 compared to the other groups ($p<0.05$). Values of Group 4 were higher from the 1st hour through to the 24th hour compared to the other groups ($p<0.05$). Although there were no significant differences among the other groups, the lowest value of visual analogue scale was found in Group 1 in the 6th hour ($p>0.05$). Values of Group 4 at the 6th and 12th hours were significantly higher compared to Groups 1 and 2 ($p<0.05$).

Conclusion: Intravenous dexamethasone, infiltrated dexamethasone and infiltrated bupivacaine were all found to be effective on postoperative pain.

Keywords: Tonsillectomy, Pain, Dexamethasone, Bupivacaine. (JPMA 68: 1002; 2018)

Introduction

Tonsillectomy is one of the most frequently performed surgical procedures, but at the same time one of the most risky operations in terms of malpractice. Occurrence of bleeding during or following the operation is a life-threatening condition. Moreover postoperative pain significantly disrupts patient's comfort.^{1,2} Postoperatively developed pain may lead to several problems such as anxiety, nausea, vomiting, dysphagia and delayed oral intake, thus weight loss and constipation.³⁻⁵ The factors causing pain include inflammation, pharyngeal muscle spasm, venous congestion, oedema, damage to the sensory fibres, compression of the mouth opener and contact of the wound site with food.⁶⁻⁸ Numerous studies have used peritonsillar local anaesthetics, nerve blockages, dexamethasone or different surgical approaches in order to reduce pain, but there is still no consensus on this issue.^{4,9} Although opioids and non-steroids reduce post-tonsillectomy pain, these drugs are not preferred

due to their adverse effects of bleeding, vomiting, sedation and respiratory depression.^{10,11} Peritonsillar local anaesthetics are effective medicines in reduction of intraoperative bleeding and postoperative pain with minimal incidence of side effects. Bupivacaine is a preferred local anaesthetic for its long action time.¹² Similarly, dexamethasone is known for the effects of both its local infiltration and systemic applications on the reduction of postoperative pain, nausea and vomiting.¹³⁻¹⁵ However, it is still a debate that which of these drugs are more effective and therefore none of them entered into routine practice following tonsillectomy. The current study was planned to contribute to the literature by evaluating effects of the local and systemic administrations of dexamethasone and local bupivacaine on postoperative pain in adult patients undergoing tonsillectomy.

Patients and Methods

This randomised, double-blinded, placebo-controlled and prospective clinical trial was conducted at the otorhinolaryngology clinic of Adana Numune Training and Research Hospital, Turkey, between April and July 2016, and comprised patients undergoing

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tonsillectomy due to recurrent tonsillitis, chronic tonsillitis or tonsillar hypertrophy indication. Patients less than 15 and more than 45 years of age, those with upper respiratory infection, history of peritonsillar abscess, presence of analgesic use within 24 hours prior to surgery, regular use of analgesics, suspected malignant neoplasm, known hypersensitivity to bupivacaine, systemic disease, inability to understand the pain scales were excluded. Patients gave written consent and the study was approved by the institutional ethics committee.

The subjects were randomly assigned to 4 equal groups. Group 1 was administered 0.5 mg/kg intravenous (IV) dexamethasone after induction and before commencement of the operation. Group 2 was given 0.5mg/kg dexamethasone diluted with 10mL saline which was infiltrated into the upper, middle and lower peritonsillar regions. Group 3 received 2.5mL of 0.5% bupivacaine infiltration. Group 4 was the control group and received peritonsillar saline infiltration.

Standard anaesthesia protocol and standard surgical method were used in all subjects. Anaesthesia was induced by propofol 2mg/kg and rocuronium 0.6 mg/kg after obtaining an IV access. Oral endotracheal intubation was done and anaesthesia was maintained with 1.5-2 % sevoflurane. All surgical procedures were started five minutes after the peritonsillar infiltration. The injections were applied superficially and submucosally with 23-G needle. Patients were operated by the same surgeon using blunt dissection technique. Haemostasis was obtained by compression and catgut sutures, if required. The patients who received dexamethasone due to bronchospasm were not included. Patients were not given analgesics before and after the operation, unless deemed necessary. If given, their times were recorded. Operation time, amount of bleeding during the operation were noted. The amount of intraoperative bleeding was defined by the surgeon. No narcotic was used for premedication or after surgery. Postoperative pain was evaluated at

15th minute, 1st, 6th, 12th, 24th hours and 1st week with visual analogue scale (VAS) scoring. The VAS assessment was performed by another surgeon working in the clinic who was not part of the surgery and did not know in which group the patients were placed. The VAS assessment was maintained by this surgeon throughout the entire study.

Patients were questioned about whether they had additional complaints such as nausea and vomiting. All patients received oral amoxicillin-clavulanic acid twice daily for one week postoperatively. The controls and the groups were compared with each other.

At the beginning it was planned to study each group with 80% theoretical power and 0.45 effect size. As a result of the study, the effect was obtained as 0.44 and the power as 81%.

Shapiro Wilk's test was used for investigating normality of the variables due to the unit numbers. When the results were interpreted, significance level was set at 0.05.

Since the variables did not show a normal distribution, Kruskal Wallis-H Test was utilised for analysis of differences between the groups.

In the cases of significant differences obtained from Kruskal Wallis-H Test, Post-Hoc Multiple Comparison Test was used to determine the groups causing differences.

Pain was evaluated with VAS and the data obtained was analysed with SPSS 20.

Results

Of the 60 patients, each of the four groups had 15(25%). No significant difference was observed between the groups in terms of age ($p>0.05$) (Table-1). Also, there was no significant association between gender and the groups ($p>0.05$) (Table-2).

Pain evaluation of patients was carried out with VAS (Table-3) (Figure), and values at the 15th minute were significantly lower in Group 1 compared to the other

Table-1: (SD: Standard Deviation).

Group	n	Mean	Median	Age		SD	Kruskal-Wallis H test		
				Minimum	Maximum		Range	Mean	p
IV Dexa	15	25	24	17	35	6	23,8		
Local Dexa	15	30	31	18	40	8	35,2	7,05	0,071
Bupivacaine	15	30	32	22	38	6	37,6		
Control	15	25	26	17	36	6	25,4		

IV: Intravenous.

DEXA: Dexamethasone.

Table-2: Distribution of patients by gender.

	Group								Chi-square analysis	
	IV Dexta		Local Dexta		Bupivacaine		Control		Chi-squ.	p
	n	%	n	%	n	%	n	%		
Gender										
Female	9	60,0	9	60,0	9	60,0	8	53,3	2,4	0,494
Male	6	40,0	6	40,0	6	40,0	7	46,7		
Total	15	100,0	15	100,0	15	100,0	15	100,0		

IV: Intravenous.

DEXA: Dexamethasone.

Table-3: Pain evaluation of patients carried out with VAS.

		n	Mean	Group				SD	Range mean	Kruskal-Wallis H test		Two-groups comparison
				Median	Min	Max				H	P	
VAS 15th Minute	IV Dexta	15	4,7	5	2	8	2	17,1	15,7	0,001		1-2
	Local DXM	15	6,1	6	4	8	1	29,9				1-3
	Bupivacaine	15	6,5	6	4	9	1	33,6				1-4
	Control	15	7,2	7	5	9	1	41,4				
VAS 1st Hour	IV Dexta	15	3,4	4	2	4	1	16,6	26,3	0,0001		4-1
	Local DXM	15	4,3	4	2	6	1	27,1				4-2
	Bupivacaine	15	4,7	4	2	8	2	30,3				4-3
	Control	15	6,5	6	4	9	2	47,9				
VAS 6th Hour	IV Dexta	15	3,5	3	0	8	2	23,6	13,1	0,005		4-1
	Local DXM	15	3,4	3	1	6	1	22,1				4-2
	Bupivacaine	15	4,5	4	3	8	1	35,3				
	Control	15	5,1	5	3	9	2	41,1				
VAS 12th Hour	IV Dexta	15	2,3	2	0	4	1	18,5	30,5	0,0001		4-1
	Local DXM	15	2,5	2	1	4	1	18,4				4-2
	Bupivacaine	15	4,5	4	1	8	2	39,9				
	Control	15	5,1	5	3	8	2	45,3				
VAS 1st Day	IV Dexta	15	1,4	2	0	3	1	17,2	25,8	0,0001		4-1
	Local DXM	15	2,0	2	1	3	1	23,0				4-2
	Bupivacaine	15	3,1	3	1	5	1	35,9				4-3
	Control	15	4,5	5	2	9	2	45,9				
VAS 1st Week	IV Dexta	15	0,4	,0	,0	2,0	,8	30,9	0,6	0,902		-
	Local DXM	15	0,3	,0	,0	2,0	,6	31,9				
	Bupivacaine	15	0,3	,0	,0	2,0	,7	30,5				
	Control	15	0,3	,0	,0	4,0	1,0	28,6				

IV: Intravenous

DEXA: Dexamethasone

DXM: Dexamethasone

VAS: Visual analogue scale

SD: Standard Deviation.

groups ($p < 0.05$). VAS values at the 1st hour and 1st day were significantly higher in Group 4 compared to the other groups ($p < 0.05$). No statistically significant differences were observed among Groups 1, 2 and 3, but the lowest VAS scores were found in Group 1 ($p > 0.05$).

Values of Group 4 at the 6th and 12th hours were significantly higher compared to Groups 1 and 2

($p < 0.05$) but no statistically significant difference was observed between Groups 3 and 4 ($p > 0.05$). No statistically significant differences were found among the groups in terms of the VAS values at the 1st week ($p > 0.05$).

No statistically significant difference was observed between the groups in terms of bleeding amount ($p > 0.05$). Operational time was significantly shorter in

Table-4: Evaluation of the groups in terms of operational time and bleeding.

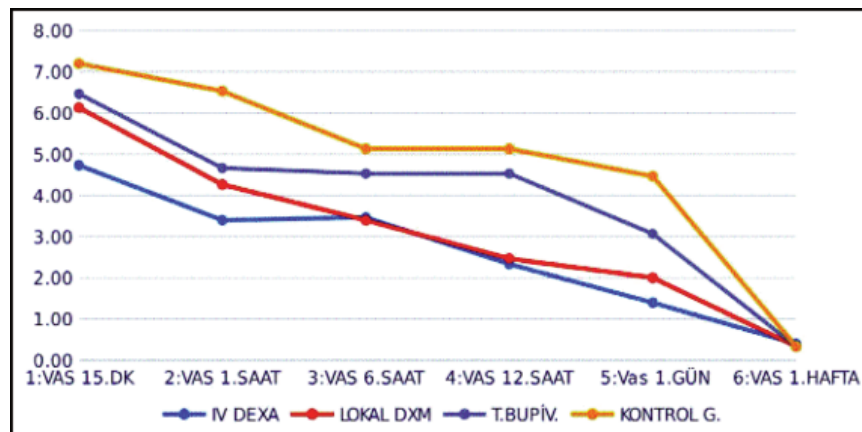
		n	Mean	Group				Kruskal-Wallis H test			Two-Groups Comparison
				Median	Minimum	Maximum	SD	Range	Mean	H	
Bleeding CC	IV Dexa	15	36,67	30,00	20,00	60,00	12,91	27,13	2,04	0,571	-
	Local DXM	15	40,67	40,00	25,00	80,00	15,91	33,03			
	Bupivacaine	15	39,00	35,00	20,00	100,00	20,28	27,63			
	Control	15	39,00	40,00	20,00	70,00	11,37	34,20			
Operational Time	IV Dexa	15	26,53	25,00	15,00	35,00	6,00	20,83	11,2	0,011	2-1
	Local DXM	15	37,33	35,00	25,00	55,00	8,21	41,70			
	Bupivacaine	15	31,67	30,00	15,00	60,00	11,44	29,10			
	Control	15	34,00	30,00	20,00	75,00	15,02	30,37			

IV: Intravenous
 DEXA: Dexamethasone
 DXM: Dexamethasone
 SD: Standard Deviation.

Table-5: Evaluation of the groups in terms of postoperative vomiting and the need for analgesics.

		Group								Chi-square analysis	
		IV DEXA		Local DEXA		Bupivacaine		Control		Chi-square	p
		n	%	n	%	n	%	n	%		
Vomiting	No	15	100,0	13	86,7	13	86,7	14	93,3	0,21	0,977
	Yes	0	0,0	2	13,3	2	13,3	1	6,7		
	Total	15	100,0	15	100,0	15	100,0	15	100,0		
Analgesics	Administered	12	20,0	10	66,7	7	46,7	4	26,7	9,8	0,019
	Not administered	3	80,0	5	33,3	8	53,3	11	73,3		
	Total	15	100,0	15	100,0	15	100,0	15	100,0		

IV: Intravenous
 DEXA: Dexamethasone.



IV: Intravenous. DEXA: Dexamethasone. DXM: Dexamethasone. VAS: Visual analogue scale. BUPIV: Bupivacaine.

Figure-1: Comparative evaluation of VAS between the groups.

Group 1 compared to Group 2 ($p < 0.05$). Although the value was higher in Group 2 than in Groups 3 and 4, the difference was not significant ($p > 0.05$) (Table-4).

No statistically significant association was observed

between the groups in terms of vomiting ($p > 0.05$). There was a significant association between the groups and the need for analgesics ($p < 0.05$) (Table-5).

Discussion

Tonsillectomy is one of the most frequently performed surgeries in otorhinolaryngology clinics. Pain reduction is crucial in order to provide patients comfort and enable them to go through this course more comfortably. Besides disruption of the quality of life, pain may also cause insufficient oral intake and dehydration, prolonging the duration of hospitalisation. From the past until today, numerous different approaches

have been attempted for this purpose. Many techniques and drugs have been used such as peritonsillar local anaesthetics, nerve blockades, dexamethasone or different surgical approaches in order to reduce pain,

but there is still no consensus about this issue. Recent electrophysiological studies have demonstrated that, a stimulus which forms due to tissue damage stimulates afferent C fibres which in turn stimulates the dorsal horn neurons, resulting in pain.^{16,17} Different surgical methods are likely to cause pain of varying severity. In a study comparing electrocautery and blunt dissection regarding pain, the use of electrocautery has been reported to create significantly greater pain.¹⁸ Similarly, in another study comparing thermal welding, electrocautery and blunt dissection, electrocautery was found to produce more severe pain.¹⁹ In our study, we performed our operations by the same surgeon using blunt dissection in order to avoid influences on postoperative pain. Haemostasis was obtained by compression and catgut sutures, if required. We did not use electrocautery.

A meta-analysis said pain is the most important cause of morbidity following tonsillectomy and that peritonsillar local anaesthetic infiltration is successful regarding this issue.²⁰ Among the most commonly used local anaesthetics are bupivacaine and its derivatives. In a study with adult patients undergoing tonsillectomy and uvulopalatopharyngoplasty (UPPP), effect of bupivacaine has been investigated and it was recommended to be used for pain reduction in intraoral surgeries.²¹ A study showed that levobupivacaine was more effective on postoperative pain and intraoperative bleeding compared to saline.²² Bupivacaine is a local anaesthetic belonging to amino amide group which inhibits access of sodium to the nerve cells, preventing depolarisation. Bupivacaine has become popular in postoperative analgesia due to its higher effect of sensory blocking rather than motor blocking. However, because of its cardiotoxic and neurotoxic impacts, levobupivacaine which is S-enantiomer of bupivacaine has been included more commonly in recent studies. Levobupivacaine can be preferred as an alternative to bupivacaine in patients with cardiac disease.²¹ It was reported in a study comparing bupivacaine and levobupivacaine that, both agents similarly reduced pain, but the effect duration of bupivacaine was slightly longer.²³ In our study, patients with cardiac disease were excluded and bupivacaine was used for its longer duration of effect. In another study performed on 60 paediatric patients undergoing tonsillectomy, bupivacaine was stated to be an effective and reliable local anaesthetic, equivalent to lidocaine.²⁴ In our study, we did not encounter any complications in our patients due to bupivacaine and found that pain reducing effect of bupivacaine was statistically significantly higher at

15th minutes, 1st hour and 1st day compared to the controls.

VAS is a reliable method used for evaluation of pain for years. It is quite important to inform patients in order to obtain true outcomes. It has been reported in the literature that a reasonable level of pain persists in 7 days after tonsillectomy; however pain is quite severe within the first 3 days and shows a progressive alleviation after the 4th day.²⁵ Therefore, early postoperative follow-up of patients is crucial for their comfort.

Dexamethasone is a synthetic glucocorticosteroid more potent than endogenous cortisol by 25 folds with anti-inflammatory effects and has a longer half-life of 36-72 hours.²⁶ In an earlier study with 41 paediatric patients, the author observed that single dose of IV dexamethasone was very effective in prevention of postoperative vomiting, but it was equivalent with placebo in terms of postoperative pain and the need for analgesics.²⁷ Similar to that study, we found the least incidences of vomiting in Group 4. However, our results related to pain are not consistent with those of the mentioned study. In another study, researchers administered single dose of IV 10 mg dexamethasone, evaluated pain every day from the 1st day until the 1st week using VAS and observed that pain was significantly low at the day of operation and at the postoperative days 4, 5, 6 and 7.²⁸ Action of single dose IV systemic dexamethasone begins in a short time because of its wide distribution, but the effect on pain may be decreased due to its lower concentration in the wound site. In another study, considering higher concentrations in the wound site researchers recommended the use of submucosal dexamethasone injection.²⁹

One of the studies compared effects of the local and IV dexamethasone on pain and found that local administration of dexamethasone was more effective within the first 16 postoperative hours.³⁰ In another study with 120 children, one group was given a combination of levobupivacaine and dexamethasone infiltration and another group was administered IV dexamethasone and levobupivacaine infiltration. They found lower VAS scores at all hours and significantly lower scores at the 2nd, 6th, 12th and 24th hour in dexamethasone infiltration group. Although VAS scores were found to be lower in the early postoperative period at the 15th and 30th minutes and in the late postoperative period after postoperative 4th day, the differences were not statistically significant.³¹ On the other hand, in a study with 62 patients undergoing tonsillectomy, effect of infiltrated dexamethasone on pain was not significant compared

to saline.³² In our study, VAS values at the 15th minute were significantly lower in Group 4, although no significant differences were observed at the other times. In the present study, we compared local and IV dexamethasone additionally with bupivacaine which has been proved in a number of studies to be an effective local anaesthetic for post tonsillectomy pain. One study compared effects of dexamethasone and levobupivacaine infiltrations on post tonsillectomy pain and reported that local dexamethasone infiltration is more effective in reduction of pain.³³ Although in our study, bupivacaine was found to be more effective in reduction of pain compared with the control group, VAS was found to be higher in this group compared to both groups of dexamethasone. This study is the first to compare these three groups together. We found significantly lower VAS scores evaluating pain in all three groups compared to the control group. While IV dexamethasone was found to be effective, this effect reached to statistical significant at the 15th minute. The least need for analgesics was also observed in this group.

The limitation of our study is that our number of patients may be more but adult tonsillectomy is fewer than children tonsillectomy in our clinic. Similarly larger series are needed to confirm this result. Secondly, though the VAS is a simple, valid and reliable method used for many years, a wide degree of inter-patient variability exists.

Conclusion

IV dexamethasone, infiltrated dexamethasone and infiltrated bupivacaine were all effective on postoperative pain compared to the control group. However, single dose IV dexamethasone was found to be more effective, especially in the reduction of pain in the early period. It can be preferred in patients undergoing tonsillectomy because it is safe, inexpensive and easily applicable. Nevertheless, similar larger series are needed to confirm this result.

Disclaimer: Due to non-existence of RCT registration authority in Turkey. Hence RCT Trial Number has not been allotted. The approval to conduct the study has been taken from local IRB.

Conflict of Interest: None.

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