Original Article

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Effect of Oral Prednisolone on Recovery after Tonsillectomy: A Quasi-Experimental Study

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Abstract

Background: Post-operative morbidities following tonsillectomy still remain a significant problem. Glucocorticoids might help to lessen these morbidities by decreasing inflammation at the sites of injury. The objective of this study was to assess the effect of oral prednisolone on recovery of patients after tonsillectomy.

Methods: A quasi-experimental study was conducted from August 2015 to July 2016 among 70 patients aged four years or older scheduled for elective tonsillectomy by cold steel dissection method. The experimental group received a postoperative course of prednisolone 0.5 mg/ kg/ day over seven days whereas the control group received the standard of care only. Postoperatively, all participants were assessed for pain, type of diet and activity, presence of nausea and/ or vomiting and bleeding on 1st, 2nd, 3rd, 7th and 14th day, and healing process in the tonsillectomy bed measured through the use of endoscopic photograph on 7th and 14thday.

Results: Significant reduction in pain was found in prednisolone group compared to the control group on 7th day (mean score 1.41 and 2.51 respectively, p = 0.006) and on 14th day (mean score 0.25 and 1.06 respectively, p = 0.005). Earlier return to normal diet was found on 7th day (p = 0.005) and 14th day (p = 0.02). No significant difference was found in rate of healing and other secondary outcomes. No adverse effects of prednisolone were noted.

Conclusion: Use of oral prednisolone in post-tonsillectomy patients may offer significant benefits in relieving pain and earlier returning to normal diet without any serious adverse effects.

Keywords: Pain; postoperative; Prednisolone; Tonsillectomy; Wound healing

Declarations

Ethics approval and consent to participate: This study was conducted with prior ethical approval from Institutional Review Board of BPKIHS (IRC Code: IRC/581/015). Informed consent was taken from all the adult patients and from the parents of the patients in case of children, prior to the enrollment.

Consent for publication: Informed consent was obtained from adults and from the parents of the patients in case of children for the publication of identifying features along with the manuscript.

Availability of data and materials: The full data set supporting this research will be made available upon request by the readers.

Competing interest: None

Funding: None

Authors' contributions:: PRA: Concept, design, data collection, data analysis, statistical analysis and interpretation, drafting of manuscript. STC: Concept, design, data analysis, statistical analysis and interpretation. BPS: Concept, design, data analysis, statistical analysis and interpretation. DRK: Concept, design, data analysis, statistical analysis and interpretation. All authors have read and approved the final manuscript.

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Tonsillectomy is one of the most common surgeries in otorhinolaryngology, with an estimated 100 million tonsillectomies performed globally over the last century [1]. The advances in surgical and anesthetic techniques have markedly reduced serious complications of tonsillectomy like mortality, severe hemorrhage, and pulmonary complications. However, post-operative morbidities remain a significant problem [2]. Tonsillectomy leaves an open wound in the pharynx which may be subjected to various mechanical, infectious, and inflammatory insults thereby inducing acute inflammation, nerve irritation, and spasm of superior constrictor muscle which results in post-operative pain and bleeding [3]. This oropharyngeal pain in turn causes reduced oral intake and decreased physical activity.

Glucocorticoids decrease inflammation at the sites of injury by inhibiting the production of inflammatory cell mediators such as cytokines leading to a reduction in edema and fibrosis during healing. They also block the cyclooxygenase and lipoxygenase pathways by inhibiting phospholipase enzymes which reduces prostaglandin production to relieve pain [4]. Prostaglandin antagonism, release of endorphins, and reduction of serotonin level in the gut and neural tissue are found to have antiemetic properties [5]. All these properties of steroids help to lessen the morbidities associated with tonsillectomy.

Several researches have been done on post-tonsillectomy use of intravenous steroids with conflicting results regarding their benefits during post-operative recovery [4 -10]. However, studies describing the post-tonsillectomy effects of oral steroids are limited despite their ease of administration. Hence, there arises a need for further research in this area. In this study, the effectiveness of oral prednisolone in recovery of patients after tonsillectomy has been evaluated using subjective (determined via questionnaire responses) as well as objective outcomes related to the wound healing process.

METHODS

A quasi-experimental study was conducted from August 2015 to July 2016 in the department of Otorhinolaryngology and Head and Neck Surgery, B. P. Koirala Institute of Health Sciences. Ethical clearance was obtained from the institutional review committee, BPKIHS. Well-informed, written consent in the Nepali language was taken from all the adult patients and from the parents in case of children. The sample size 70 (35 per arm) was calculated using the power analysis indicating 80% power and 5% level of significance based on the mean pain score in the study by Park et al. [11]. The sampling technique was a non-probability consecutive sampling technique.

All patients aged 4 years and older who were scheduled for elective tonsillectomy were assessed for eligibility. The patients with a diagnosis of recurrent tonsillitis who underwent tonsillectomy by cold steel dissection method were included in the study. Those who underwent tonsillectomy along with other surgical procedures such as adenoidectomy, or underwent tonsillectomy for suspected tonsillar malignancy, or patients who were known to have contraindication to steroid use were excluded from the study. The surgery was carried out either by consultant surgeons or by resident surgeons under the direct supervision of the consultant surgeons.

During intra-operative, early recovery and post-operative period, both the groups received the same treatment. The anesthetic guidelines were standardized. Intravenous steroids were not given to any patient intra or post-operatively. During early recovery, all patients were given fentanyl IV for pain control and ondansetron IV for control of post-operative nausea and vomiting (PONV). Intervention was started from 1st post-operative day where the patients in the experimental group were provided with oral prednisolone (0.5mg/ kg/ day, maximum 30mg/ day) for 7 days along with povidone iodine with hydrogen peroxide throat gargle (3:1 ratio) every 4 hours and oral analgesic, paracetamol, to control pain as necessary. The patients in the control group received only povidone iodine with hydrogen peroxide throat gargle (3:1 ratio) every 4 hours and oral paracetamol as necessary.

The pain score, the total analgesic and antiemetic requirement, presence or absence of bleeding, temperature, incidence of PONV, physical activity (none, quiet, restricted, normal), and type of diet (none, fluid, soft, normal) were recorded in the questionnaire on day 1, 2 and 3. All the patients were discharged on 4th post-operative day and were asked to follow-up on 7th and 14th post-operative day and similar records were made in the questionnaire. The estimation of healing process was done by taking endoscopic photograph of the tonsillar bed on 7th and 14th post-operative day.

The primary outcome, pain, was assessed with a simple linear analog pain scale ranging from 0 (no pain) to 10 (most severe) for patients aged more than 11 years. For patients aged 11 years or less, Oucher Faces Scale was used which consists of a series of six photographs depicting a child in various degrees of distress that correspond to a numeric scale of 0 to 10. The other primary outcome, healing process, was expressed as a percentage of re-epithelized area (area without slough) in the tonsillectomy bed, measured using endoscopic photograph. The area in the endoscopic photograph was calculated with the help of software Image J **(Fig.1).**

The data was entered and analyzed using SPSS version 11.5. The primary outcome, pain and percentage of re-

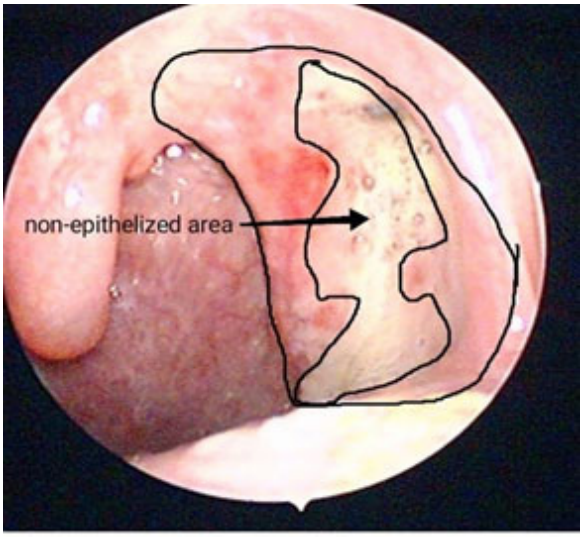

Figure 1: Calculation of area of re-epithelization of tonsillectomy bed using software Image J

epithelization were compared using Mann Whitney test and Student t test respectively. The severity of PONV, post-operative bleeding, type of diet, presence of fever and the level of activity were compared using Chi square test. The values of Fisher's exact test were considered if any cell had value less than 5. All inference tests were two-tailed at 5% level of significance.

RESULT

Of the 132 patients approached, 70 patients who met the inclusion criteria were recruited for the study. Eight subjects (4 in each group) lost to follow-up and hence only 62 subjects were followed up till the end of the study and analyzed for the primary and secondary outcomes. Out of the included samples, 8 (13%) belonged to the pediatric age group **(Fig. 2).**

The mean (SD) age was 21.90 (10.57) years and 24.0 (10.26) years in the prednisolone and control group respectively and there was slight male preponderance in both the groups. The two groups did not differ significantly in any demographic and intra-operative characteristics (operating surgeon, procedure length, intra-operative blood loss and hospital stay) **(Table 1).**

Regarding primary outcome pain, though the mean pain score was more in the control group, no significant difference was found on day 1 ($p = 0.74$), day 2 ($p = 0.07$) and day 3 ($p = 0.05$). On the other hand, a significant difference was noted in the mean pain score on 7^{th} ($p = 0.006$) and 14^{th} ($p = 0.005$) post-operative day **(Table 2).**

For another primary outcome healing process, the percentage of re-epithelized tonsillar bed was assessed on 7^{th} and 14^{th} day. Although healing was found to be slightly

Table 1: Patient Demographics and Characteristics (n = 62). Values are presented as number (%) or mean (SD)

Characteristics		Prednisolone group	Control group	*p*-value*
Number of patients		31 (50)	31 (50)	
Age (y)	**Mean (SD)**	21.90 (10.57)	24 (10.26)	0.39
Age group	Less than 12	4 (12.90)	4 (12.90)	> 0.99#
	12 and More	27 (87.10)	27 (87.10	
Sex	Male	17 (54.84)	19 (61.29)	0.79
	Female	14 (45.16)	12 (38.71)	
Residence	Urban	16 (51.61)	17 (54.84)	> 0.99
	Rural	15 (48.39)	14 (45.16)	
Caste	Janajati	18 (58.06)	16 (51.61)	0.89
	Brahmin/ Chhetri	7 (22.58)	7 (22.58)	
	Others	6 (19.35)	8 (25.80)	
Religion	Hindu	25 (80.65)	26 (83.87)	0.67
	Non Hindu	7 (19.35)	6 (16.13)	
Occupation	Student	20 (64.52)	14 (45.16)	0.30
	Housewife	4 (12.90)	6 (19.35)	
	Others	7 (22.58)	11 (35.48)	
Operating Surgeon	Consultant	14 (45.16)	16 (51.61)	0.80
	Resident	17 (54.84)	15 (48.39)	
Operative Time (min)	Mean (SD)	54.59 (26.17)	52 (25.48)	0.76
Blood Loss (ml)	Mean (SD)	31.12 (13.76)	37.41 (14.76)	0.88
Hospital Stay (days)	Mean (SD)	3.35 (0.60)	3.51 (0.81)	0.37

* Statistically significant at p-value < 0.05, # Fisher Exact Test

Table 2: Pain score of patients after tonsillectomy (n = 62)

Pain Score	Prednisolone group Mean (SD)	Control group Mean (SD)	Mann Whitney (U)	Test statistic (Z)	Effect size (r)	*p*-value##
Day 1	5.00 (1.21)	5.13 (1.74)	457.5	0.336	0.04	0.740
Day 2	3.80 (1.32)	4.52 (1.91)	352.5	1.844	0.23	0.070
Day 3	2.96 (1.4)	3.70 (1.53)	346.0	1.947	0.24	0.050
Day 7	1.42 (1.50)	2.51 (1.58)	294.0	2.738	0.34	0.006**
Day 14	0.26 (0.68)	1.06 (1.36)	321.5	2.981	0.37	0.005**

* Statistically significant at p-value <0.05 ** statistically highly significant at p-value <0.01 ## Mann- Whitney

Table 3: Percentage of area of re-epithelization of tonsillectomy bed (n = 62)

Area of Re-Epithelization	Prednisolone group Mean (SD)	Control group Mean (SD)	Mean difference (95% CI)	*p* value
7th day	50.98 (10.00)	48.44 (6.62)	2.54 (-1.76 – 6.85)	0.24
14th day	78.18 (11.58)	74.05 (9.65)	4.11 (-1.30 -9.53)	0.13

Table 4: Patient secondary outcome characteristics on day 7 and day 14

Characteristics		Prednisolone group	Control	p-value
Diet (day 7)	Liquid/soft Diet	2 (6.45)	12 (38.71)	0.005**
	Normal	29 (93.55)	19 (61.29)	
Diet (day 14)	Liquid/soft Diet	0 (0)	6 (19.35)	0.02#*
	Normal	31 (100)	25 (80.65)	
Activity (day 7)	Restricted limited activity	0 (0)	2 (6.45)	0.49#
	Normal activity	31 (100)	29 (93.55)	
Activity (day 14)	Restricted or limited activity	0 (0)	0 (0)	NA
	Normal activity	31 (100)	31 (100)	
Bleeding (day 7)	Yes	0 (0)	1 (3.23)	> 0.99
	No	31 (100)	30 (96.77)	
Bleeding (day 14)	Yes	0 (0)	1 (3.23)	> 0.99#
	No	31 (100)	30 (96.77)	

*Statistically significant at *p*-value <0.05, **Statistically highly significant at *p*-value <0.01 #Fisher Exact Test. NA: not applicable

better in patients receiving prednisolone, no significant difference was found between the two groups with p-value of 0.24 and 0.13 on day 7 and day 14 respectively **(Table 3).**

Regarding the secondary outcomes, no statistically significant differences in activity, rate of bleeding, PONV, fever, or sleep disturbance were observed on any post-operative day. However dietary intake was found to have significant difference on day 7 ($p = 0.005$) and day 14 ($p = 0.02$) **(Table 4).**

On day 1, four patients receiving prednisolone and two patients in control group had nausea, but none had vomiting episodes. On 2nd day, one child in control group had single episode of vomiting and one adult patient in control group had nausea without vomiting on 3rd day. None of the patients receiving prednisolone had PONV 2nd day onwards.

Similarly, two patients in the control group were readmitted for secondary hemorrhage, one on 7th day and other on 12th day. Both patients were managed conservatively and did not require a return to the operation theatre. None of the patients in prednisolone group had secondary hemorrhage.

DISCUSSION

It is of utmost importance that the post-tonsillectomy recovery be smooth and uncomplicated. To achieve this, steroids are being used by many otolaryngologists all over the world in various forms and dosages. Several researches have confirmed the benefits of using intravenous dexamethasone to reduce post-tonsillectomy pain, nausea and vomiting and overall morbidities without any adverse effects in both adults and pediatric population [6-8].

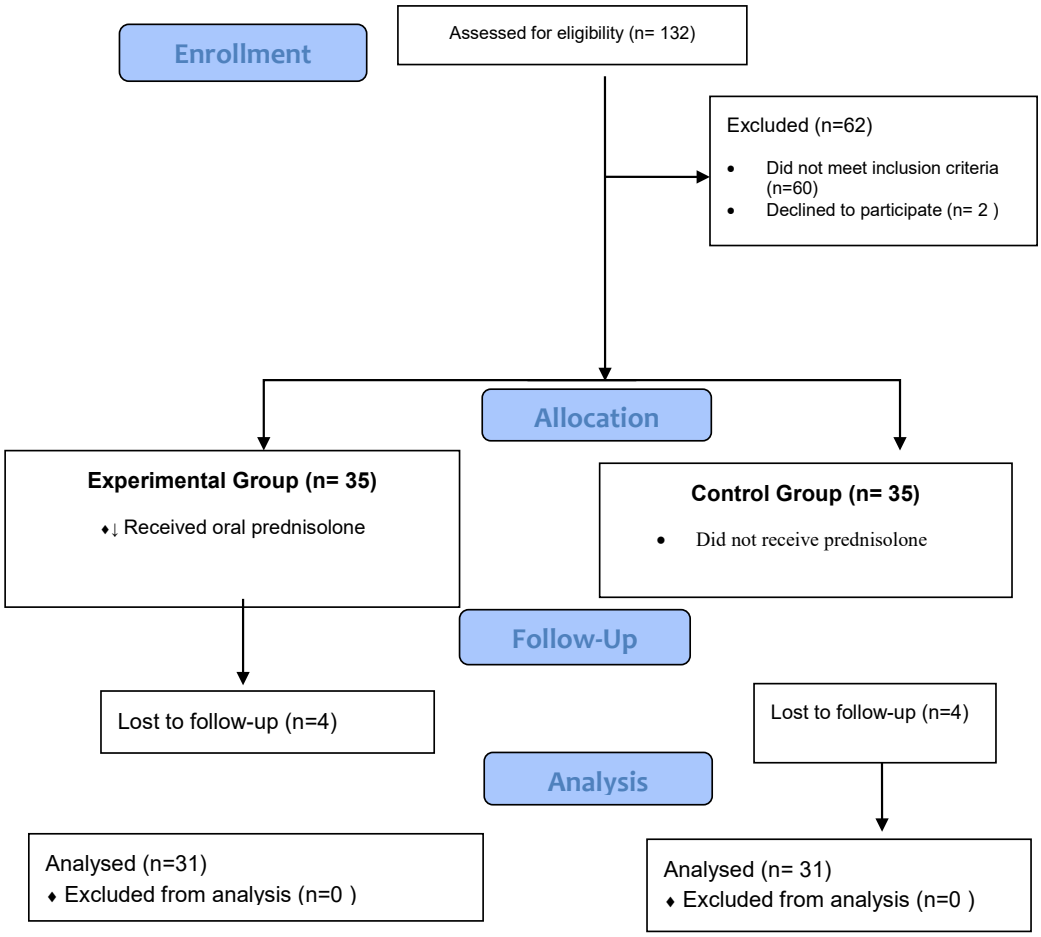

Figure 2: Conceptual framework of the study

However, other studies have shown that children receiving dexamethasone had an increased risk and severity of bleeding after tonsillectomy [9, 10].

Although the use of an oral steroid (betamethasone tablets) for recovery from tonsillectomy was first proposed by Papangelou with good results half a century ago, few studies have since then evaluated the effect of oral steroids despite being easy to administer [12]. Prednisolone, a synthetic glucocorticoid six times more potent than the endogenous hydrocortisone, has a biological half-life of 18 to 36 hours with peak effectiveness reaching around 6 to 12 hours after oral administration. It takes about 6 days for the total elimination of prednisolone from the body [13]. Prednisolone, like all steroids, has the possibility of causing sleep and behavioral changes in the short term and can rarely cause psychosis, avascular necrosis of the hip and gastric complications. In this study, only a short course of prednisolone in a low dose was used and no adverse effect was observed.

According to a study done by Issacson G, complete re-epithelization of the tonsillectomy bed occurs around 17th post-operative day [1]. Pain correlates closely with ongoing inflammation and patients may experience significant pain for 7 days and the pain may persist throughout the 2nd post-operative week after tonsillectomy [7]. In the present study, post-operative pain decreased steadily and by day 14, patients were experiencing minimal pain. Similarly, around three-fourth of the tonsillectomy bed was re-epithelized by the end of 2nd week in both the groups with slightly better healing observed in the patients receiving prednisolone but the difference was not significant ($p = 0.134$). Although few studies have shown that steroids delay healing of wound [14,15], studies specifically evaluating healing of tonsillectomy wounds have found improved healing with the use of steroids [11, 16].

In the present study, a significant reduction in pain score and earlier return to normal diet was found in patients receiving prednisolone than in the control group. This finding is in concordance with the results of Choi et al. [16]. In a study done by Palme et al., although there was no significant difference in the pain score between prednisolone and placebo group, the analgesics requirement was significantly low in patients receiving prednisolone [2]. A prospective randomized controlled trial done by Park et al. showed significant difference in pain score, dietary habit and level of activity between prednisolone and control group in the pediatric population

but not in the adult population [11]. This may be due to low dose of oral prednisolone used in that study which is half of the dose used in our study. In contrast, Macassey found no difference in pain, diet, activity, PONV in the pediatric patients even with the same dose of prednisolone as in our study [17].

There was good control of nausea and vomiting without any significant difference between the two groups in our study. The reported incidence of postoperative vomiting in children following tonsillectomy ranges from 40% to 73% [9]. The low incidence of PONV in our study may be because of use of Ondansetron in the immediate post-operative period. In contrast to the present study, several studies have found a significant difference in the control of PONV with use of steroids [6, 16, 18]. This may be due to the low number of pediatric patients in the present study. In a study by Park et al, the incidence of PONV is only about 4.5% in adults and there was no significant difference with use of prednisolone [11].

This study has a few limitations. The number of pediatric cases in this study is low probably due to the fact that most children underwent tonsillectomy along with adenoidectomy and were excluded from the study. Another limitation is that the surgical procedure was not carried out by a single surgeon. The mean area of re-epithelization was measured using gross appearance and colour which may not be accurate in determining healing process. A more objective tool to measure area of re-epithelization could verify the benefits of prednisolone.

Bias may have occurred since this study is not a randomized study. However, the two groups did not differ significantly in terms of preoperative and perioperative indices as the control group was matched with experimental group during selection and the anesthetic and surgical techniques were standardized as far as possible.

CONCLUSION

Use of oral prednisolone in post-tonsillectomy patients may offer significant benefits in terms of relieving pain and earlier returning to normal diet without any serious adverse effects.

References

1. Isaacson G. Tonsillectomy healing. Ann Otol Rhinol Laryngol. 2012;121(10):645-9. DOI: 10.1177/000348941212101004
2. Palme CE, Tomasevic P, Pohl DV. Evaluating the effects of oral prednisolone on recovery after tonsillectomy: a prospective, double blind, randomized trial. Laryngoscope. 2000;110(12):2000-4. DOI: 10.1097/00005537-200012000-00003
3. Cohen N, Sommer DD. Post-tonsillectomy pain control: consensus or controversy? Pain Manag. 2016; 6(1):31-7. DOI: 10.2217/pmt.15.58.
4. Thimmasettaiah NB, Chandrappa RG. A prospective study to compare the effects of pre, intra and post-operative steroid (dexamethasone sodium phosphate) on post tonsillectomy morbidity. J PharmacolPharmacother. 2012;3(3):254-8. DOI: 10.4103/0976-500X.99428
5. Weren M, Demeere JL. Methylprednisolone vs. dexamethasone in the prevention of post-operative nausea and vomiting: a prospective, randomised, double-blind, placebo-controlled trial. Acta Anaesthesiol Belg. 2008;1;59(1):1-5. PMID: 18468010
6. Diakos EA, Gallos ID, El Shunnar S, Clarke M, Kazi R, Mehanna H. Dexamethasone reduces pain, vomiting and overall complications following tonsillectomy in adults: a systematic review and meta-analysis of randomised controlled trials. Clin Otolaryngol. 2011;36(6):531-42. DOI: 10.1111/j.1749-4486.2011.02373.x
7. Steward DL, Grisel J, MeinzenDerr J. Steroids for improving recovery following tonsillectomy in children. Cochrane Database Syst Rev. 2011;2011(8) CD003997. DOI: 10.1002/14651858.CD003997.pub2.
8. Goldman AC, Govindaraj S, Rosenfeld RM. A meta-analysis of dexamethasone use with tonsillectomy. Otolaryngol Head Neck Surg. 2000;123(6):682-6. DOI: 10.1067/mhn.2000.111354.
9. Plante J, Turgeon AF, Zarychanski R, Lauzier F, Vigneault L, Moore L, et al. Effect of systemic steroids on post-tonsillectomy bleeding and reinterventions: systematic review and meta-analysis of randomised controlled trials. BMJ. 2012;345: e5389. DOI: 10.1136/bmj.e5389.
10. Czarnetzki C, Tramer M. How to make tonsillectomy a safer procedure: the anaesthetist's view. ORL J Otorhinolaryngol Relat Spec. 2013;75(3):144-51. DOI: 10.1159/000343706.
11. Park SK, Kim J, Kim JM, Yeon JY, Shim WS, Lee DW. Effects of oral prednisolone on recovery after tonsillectomy. Laryngoscope. 2015;125(1):111-7. DOI: 10.1002/lary.24958
12. Papangelou L. Steroid therapy in tonsillectomy. Laryngoscope. 1972;82(2):297-302. DOI:10.1288/00005537-197202000-00016
13. Tiigimae-Saar J, Leibur E, Tamme T. The effect of prednisolone on reduction of complaints after impacted third molar removal. Stomatologija. 2010;12(1):17-22. PMID: 20440092
14. deKaski MC, Rentsch R, Levi S, Hodgson HJ. Corticosteroids reduce regenerative repair of epithelium in experimental gastric ulcers. Gut. 1995;1;37(5):613-6. DOI: 10.1136/gut.37.5.613
15. Durmus M, Karaaslan E, Ozturk E, Gulec M, Iraz M, Edali N, et al.The effects of single-dose dexamethasone on wound healing in rats. Anesth Analg. 2003;97(5):1377-80. DOI: 10.1213/01.ANE.0000080611.29106.9E
16. Choi YS. Effects of oral prednisolone on recovery after tonsillectomy. Otolaryngol Head Neck Surg. 2014;151(1_suppl):148. DOI: 10.1177/0194599814541629a35
17. Macassey E, Dawes P, Taylor B, Gray A. The effect of a postoperative course of oral prednisone on postoperative morbidity following childhood tonsillectomy. Otolaryngol Head Neck Surg. 2012;147(3):551-6. DOI: 10.1177/0194599812447776
18. Steward DL, Welge JA, Myer CM. Do steroids reduce morbidity of tonsillectomy? Meta-analysis of randomized trials. Laryngoscope. 2001;111(10):1712-8. DOI: 10.1097/00005537-200110000-00008