Nebulizatin Methylprednisolone, Racemic Epinephrine and Lidocaine in minor Pediatric Laryngeal Surgery
By

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Abstract

Objectives: **The main objectives of anesthesia for laryngeal surgery are to provide immobile field, enough space for the rigid laryngoscope, secured airway and ventilation, hemodynamic stability and of the same importance is the uneventful recovery (suggest to cancel)** . The aim of this study is to compare the effects of three different drugs given by nebulizing techniques. We compared methylprednisolone, racemic epinephrine and lidocaine effects on postoperative respiratory complications after short-term laryngeal surgery

Materials & Methods: **Sixty ASA I & II children admitted for minor laryngeal surgery were included in this prospective**, placebo-controlled, randomized, and double-blinded study. Patients were randomly allocated into four even groups, 15 each: 0.9% Normal Saline (group I) control group, Methylprednisolone 3.0 mg/kg (group II), Racemic Epinephrine 2.25 % 0.005 ml/kg (group III) and Lidocaine 1.0 mg/kg (group IV). All the drugs were prepared in 5 ml solution and given over 10 min periods by nenulizer in the recovery area before shifting the patient to the OR. Postoperative respiratory complications were assesed using Postoperative Respiratory System Evaluation Scoring (PRSES).

Results: Patients of Lidocaine and R-Epinephrine groups showed better recovery criteria as regard incidence of respiratory complications compared to Methylprednisolone and Saline groups. All the drug groups **showed** significant difference compared to the saline group.

Conclusions: Lidocaine and R-Epinephrine administration by nebulizatin in the immediate preoperative period is very effective in reducing postoperative respiratory complications after short-term laryngeal surgery by way of rigid laryngoscope. Methylprednisolone is less effective.

Key Words: Nebulizatin, Racemic-Epinephrine, Methylprednisolone, Lidocaine; minor laryngeal surgical procedures; laryngoscopy; Postoperative Respiratory System Evaluation Scoring (PRSES).

INTRODUCTION

Many different anesthesia techniques can be applied in endoscopic laryngeal surgery. The main objectives of these techniques is to provide the surgeon with a clear view, immobile field, and a sufficient area to work in, and the anesthesiologist with minimal homodynamic changes related to laryngoscopy and surgery, to protect the trachea, to ensure ventilation and oxygenation, and to promote rapid awakening and return of protective airway reflexes (1). It is also important to prevent possible respiratory complications such as cough, stridor, and laryngospasm caused by laryngoscopic laryngeal surgery for postoperative security and comfort of the patients (2).

To achieve these goals, some adjuvant drugs in addition to conventional balanced general anesthesia have been tried. Intravenous lidocaine, Methylprednisolone, esmolol and others have been studied, but there is still confusion with regard to this topic (3, 4). On the other hand, the effects of nebulizatin lidocaine, Methylprednisolone and racemic epinephrine have not been investigated in endoscopic laryngeal surgery by way of rigid laryngoscope under general anesthesia. Topical Lidocaine anesthesia of the mucosa of the upper airway is effective as a means of ameliorating postoperative coughing, sore throat, stridor, and laryngospasm related to the upper airway (5). Racemic epinephrine has been used in postextubation laryngeal edema in pediatrics and adults' .Its effectiveness is due to the Levo-isomers in the molecule (6).Corticosteroids decrease the risk of postextubation stridor in children by approximately 40% (7). It has been shown that patients who received topical Methylprednisolone yield slightly better scores of sore throat and cough 1 hour after surgery as compared with patients who have been administered lidocaine (8).

To our knowledge this is the first study that compares the effects of nebulised lidocaine, Methylprednisolone and racemic epinephrine on postoperative respiratory complications caused by short-term laryngeal surgery by way of rigid laryngoscope under conventional balanced general anesthesia.

MATERIALS AND METHODS

The Ethics Committee of King Khaled University Hospital (KKUH), Riyadh, KSA approved the study design. The study was a prospective, controlled, and double-blinded study using a random selection of ASA I & II children admitted for **management of minor laryngeal lesions (nodules, cysts, polyps and localized papillomas)**. Written consent was obtained from all patients. Exclusion criteria were history of allergy to the drugs used, moderate or severe respiratory diseases or bronchial asthma, diseases related to endogenous steroid secretion or deficiency, use of drugs that affect respiratory, circulatory, or endocrine system, anesthesia duration over than 30 minutes, and unplanned surgery outside the larynx . **cases with intraoperative injection of vocal cords were were excluded, as the injection itself might induce laryngeal swelling ,edema and postoperative stridor. All patients have been assessed in the ENT clinics. Fibroptic endoscopy assessment and recording was documented.**

Sixty patients who underwent elective direct laryngoscopic surgeries between September 2004 and March 2006 have been included. Patients were randomly allocated into four equal groups, 15 each:
Normal **S**aline 0.9% (**group I**) as a control group;
Methylprednisolone 3.0mg/kg (**group II**),
Racemic **E**pinephrine 2.25% 0.005 ml/kg (**group III**),
Lidocaine 1.0 mg/kg (group IV).
All drugs have been given by ultrasonic nenulizer in the recovery area before shifting the patient to the operating theatre, Drugs was prepared by the pharmacy in a 5 ml syringes and given by a nurse who is blind about the protocol.Nebulization was given over a period of 10 min.

Anesthesia was inhalationally induced in all groups with sevoflurane.Immediately ,after securing the IV line and primary laryngoscopic evaluation of the larynx, fentanyl 2.0 ug/kg followed by continuous infusion of propofol as 10 mg/kg/hr for the first 10min, then 8.0 mg for the second 10 min and then 6.0 mg. No muscle relaxation was needed to get vocal cord immobilization. **Intravenous Dexamethazone** was routinely used as surgeon orders immediately after induction of anesthesia in all cases in a dose of 0.2 mg/kg. After fulfilling the citeria of surgical plane of anesthesia (central pupils, automatic breathing and BiSpectral Index (BIS) of 40% which we use in our hospital), **we allowed the surgeon to start the procedure utilizing different types of operating laryngoscope. Laryngeal surgeries involved cold dissection, microdebrider, or the use of CO_2 laser**. We did not intubate the patients, we used ventilating laryngoscope with periods of intermittent controlled ventilation .In all times we did not allow the oxygen saturation to come down bellow 94%. Increments of sevoflurane have been used to control the depth of anesthesia and fluctuation of hemodynamics which is characteristic to laryngeal surgery.

Surgical excision of polyposis were performed by way of rigid direct laryngoscope (Karl Storz, 8590 J, Tutlingen, Germany) by the same ENT surgeon **(suggest to cancel**). At end of the surgery, anesthetics were interrupted, and the patients were ventilated with oxygen 100% and gave him the chance to breathe spontaneously and recovered fully

The time interval between interruption of anesthetics and full recovery was recorded (open eyes on command) as "recovery time" .Postoperative Respiratory System Evaluation Scoring (PRSES), was applied for evaluation of postoperative respiratory complications (Table I)(9). PRSESs were recorded at the first, fifth, and 10th minute after full recovery by the same anesthetist.PRSESs were carried out inside the theatre, and patients shifted to the Post Anesthesia Care Unit after securing airway completely.

Complications such as postoperative nausea and vomiting (PONV), sore throat, swallow difficulty, pain, irritability and shivering which occurred in the operating room and post anesthesia care unit, were recorded.

***TABLE I*: Postoperative Respiratory System Evaluation Scoring (PRSES) (9).**

PRSES-1: Normal respiratory pattern, deep enough.
PRSES-2: Cough reflex 3 times without pause or 5 times /min
PRSES-3: Spasmodic respiratory pattern, extension of exprium (with retching sound, strain, or short duration of apnea)
PRSES-4: Partial laryngospasm,, severe respiratory stridor (which can be treated by positive ventilation with oxygen)
PRSES-5: Complete laryngospasm, no air exchange (which needs muscle relaxation with succinylcholine for ventilation).

Statistical analysis was performed with SPSS 10.0 (SPSS, Inc., Chicago, IL).Numerical data were analyzed between groups using analysis of variance; Leven's test of equality of error variances; Tukey HSD, and Bonferroni's post hoc tests were performed where appropriate. Categorical data were analyzed using cross-tabulation and Pearson chi-square test. Data are presented as mean +/- sd or percentage of frequency when appropriate. $P<0.05$ considered as significant.

- **There is no inclusion of the statistical values in the results**

RESULTS

60 patients were enrolled in the study. All groups were similar with regard to the numbers of cases, type of surgery, ages of patients, duration of anesthesia, history of bronchial asthma, and hoarseness (Table II). Recovery time was insignificantly longer in Methylprednisolone group II compaired to the other group

***TABLE II*: Demographic and Physical Data and Recovery Time (mean +/- Standard deviation or number and percentage of frequency).**

Variables	Group I (Saline,control)	Group II (Methylprednisolone)	Group III (R-Epinephrine)	Group IV (Lidocaine)
Cases: N.	15	15	15	15
Age's :y	3.93±1.62	3.50±1.52	3.73±1.66	3.81±1.72
B.WT : kg	12.08±2.68	12.28±2.88	11.98±3.04	12.14±2.92
Hoarseness	11	12	11	11
History of Bronh.Asthma	3	2	3	3
Previous Cortisone	15	15	15	15
Anesthesia Time (min)	21.76±5.67	20.97±5.66	21.16±5.40	20.86±5.57
Recovery time (min)	7.48±2.38	8.18±3.51	7.51±3.11	7.39±2.55
Grade of laryngeal Stenosis (suggest to cancel)				

PRSESs in all evaluation times were better in groups III and IV than in group I and II. During the all evaluation periods, PRSES scores were insignificantly better in Lidocaine group IV compaired to R-Epinephrine group III. The PRSES-1 was more frequent in groups III and IV than group I and II at the first minute after full recovery (Table III).

***TABLE III*: PRSES** at **First Minute** after full recovery (n, percentage of frequency).

Groups	PRSES -1	PRSES -2	PRSES -3	PRSES -4	PRSES -5
GI: Normal Saline	**8 (%)**	**4 (%)**	**2 (%)**	**1 (%)**	**-**
GII: Methylprednisolone	**9 (%)**	**3 (%)**	**2 (%)**	**1 (%)**	**-**
GIII:R-Epinephrine	**11 (%)**	**3 (%)**	**1 (%)**	**-**	**-**
GIV:Lidocaine	**12 (%)**	**2 (%)**	**1 (%)**	**-**	**-**

The PRSES-1 was more frequent in groups III and IV than group I and II at the fifth minute after full recovery (Table III).

TABLE IV: **PRSESs** at **Fifth Minute** after full recovery (n, percentage of frequency).

Groups	PRSES -1	PRSES -2	PRSES -3	PRSES -4	PRSES -5
GI: Normal Saline	**9 (%)**	**3 (%)**	**2 (%)**	**1 (%)**	**-**
GII: Methylprednisolone	**11 (%)**	**2 (%)**	**1 (%)**	**1 (%)**	**-**
GIII: R-Epinephrine	**13 (%)**	**1 (%)**	**1 (%)**	**-**	**-**
GIV :Lidocaine	**13 (%)**	**2 (%)**	**-**	**-**	**-**

The PRSES-1 was more frequent in groups III and IV than group I and II at the 10th minute after full recovery (Table III).

TABLE V: **PRSESs** at **the 10th Minute after** full recovery (n, percentage of frequency).

Groups	PRSES -1	PRSES -2	PRSES -3	PRSES -4	PRSES -5
GI: Normal Saline	**10 (%)**	**2 (%)**	**2 (%)**	**1 (%)**	**-**
GII: Methylprednisolone	**11 (%)**	**3 (%)**	**1 (%)**	**-**	**-**
GIII: R-Epinephrine	**13 (%)**	**1 (%)**	**1 (%)**	**-**	**-**
GIV :Lidocaine	**14 (%)**	**1 (%)**	**-**	**-**	**-**

Generally, postoperative respiratory complications were more frequent in groups I and II (Saline and Methylprednisolone groups) than groups III and IV (R Epinephrine and lidocaine groups) at all evaluation times. In addition, results of group IV (lidocaine group) were better than group III (R-Epinephrine group) at the first, fifth, and 10th minute after full recovery (Fig. 1).Early postoperative complications except respiratory problems are shown in Table VI

***Fig.* 1: Number of cases that were evaluated as Postoperative Respiratory System Evaluation Scoring (PRSES) at 1, 5, and 10 minutes postoperative in the study groups. PRSES-1 was more frequent in groups III and IV than group I and II at all times. Frequency of PRSES-1 in group IV was insignificantly higher than group III.**

***TABLE VI*: Early Postoperative Complications Except Respiratory Problems (number, percentage of frequency)**

Complications	Group I (Saline)	Group II (Methylprednisolone)	Group III (R-Epinephrine)	Group IV (Lidocaine)
PONV	2	1	2	2
Sore throat	3	2	1	-
Shivering	2	1	2	1
Pain *(repetition*)	1	-	-	-
Irritability	1	1	3	1

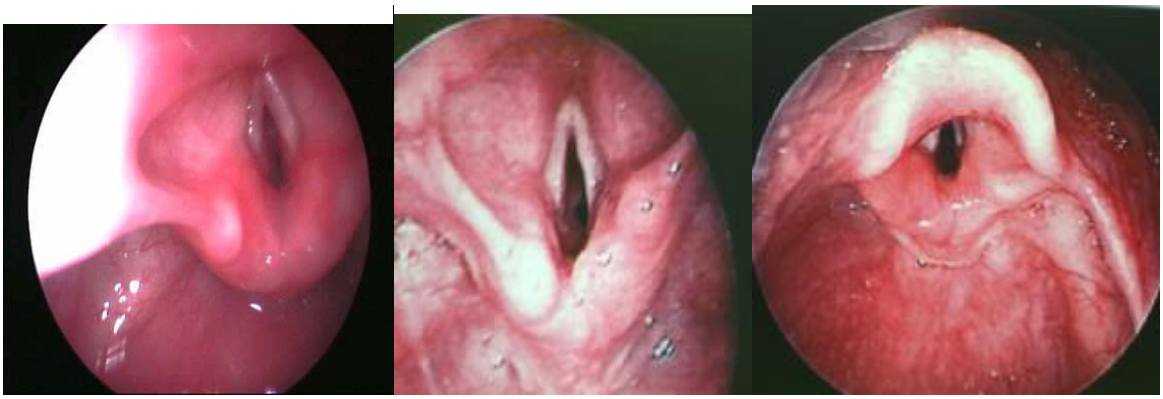

***Fig* 1** .Patient developed edema

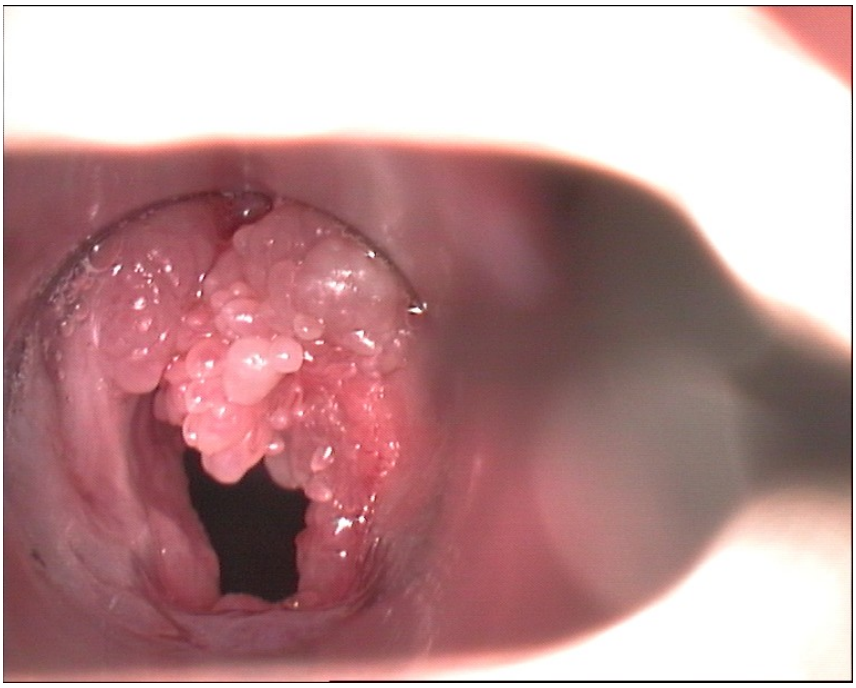

***Fig* 2**. Advanced cases of viral Polyposis

DISCUSSION

Anesthesia for patient with laryngeal pathology, even minor, and operated upon with rigid laryngoscopy is challenging for the anesthetist and ENT surgeon. Prerequisites for anesthesia and surgery are well established (10, 11,12). Rapid recovery and criteria of recovery from anesthesia are of paramount importance for the security of airway. In the present study, recovery time was insignificantly longer in the Methylprednisolone group II compared to other groups. This effect of Methylprednisolone could be explained by the fact that acute cortisol administration (group II patients were treated by intravenous dexamethazone plus nenulizer metylprednisolone) increases slow-wave sleep, probably because of feedback inhibition of corticotrophin releasing hormone CRH and Corticotrophin releasing hormone (CRH) found to impair sleep and enhances vigilance (12).R-Epinephrine group should recovery pattern comparable to groups I and IV and better than III. Although Lidocaine found to prolong recovery time when used as an adjunct to general anesthesia, the results of the present study did not show any prolongation in the recovery time for patients of group IV.This is because Lidocaine in therapeutic doses did not cause toxic plasma levels and did not affect recovery time (13).

PRSESs were better in R-Epinephrine group III and Lidocaine group IV compaired to group I and II. R-Epinephrine exerts its effects by causing constriction of the precapillary arterioles via stimulation of α-receptors and thereby decreases capillary hydrostatic pressure. The final result is fluid resorption from the interstitial space instead of capillary leakage and resolution of the laryngeal mucosal edema (14). Soltani and Aghadavoudi (15) compared six different applications of lidocaine during general anesthesia and the researchers found that the time from the conclusion of surgery to removal of the ETT (recovery time) was longest (10 +/- 0.2 min) in the group that received additional IV lidocaine 1.5 mg.kg-1 at the end of surgery, whereas recovery time in the group that received additional sprayed topical lidocaine to the laryngopharyngeal structures near the inlet of the larynx during laryngoscopy was 7 +/- 0.2 minutes. Their result with topical lidocaine was consistent with our group IV results, where our mean recovery time was 7.39±2.55 min.

The second most important aspects to consider during laryngeal surgery are the Prevention of postoperative respiratory complications to ensure airway security and the patient's comfort during the postoperative period. In this aspect, the best scores of postoperative respiratory evaluation (PRSESs) were observed in the Aerosolized Lidocaine group IV and R-Epinephrine group III respectively. Kocamanoglu and colleagues (16) used topical Lidocaine as seven puffs of aerosol applied to the orapharyngolaryngeal structures (1 puff each to hard palate, oropharyngeal wall, root of tongue; 2 puffs each to vallecula and larynx) of the patients with the help of a laryngoscope and his results with consistent to ours. Topical lidocaine proved to be very effective in prevention of postoperative coughing, sore throat, stridor, and laryngospasm (2, 9, 11).

The present study has shown that the use of Aerosolized Methylprednisolone has little preventive effect on the development of mucosal edema of orolaryngeal structures that usually takes place during laryngoscopic surgery and its results is not superior to normal saline used in group It has

been shown that patients who received topical Methylprednisolone yield slightly better scores of sore throat and cough 1 hour after surgery (Table V) as compared with patients who have been administered normal saline.

In the present study we revised our routine use of IV dexamethazone with the induction of anesthesia. Still there is a big debate regarding its use. While, it has been asserted in some studies that corticosteroids do not significantly reduce the incidence of postextubation laryngeal edema or stridor (16). Still, postoperative stridor in a critically ill patient was successfully treated with intravenous cortisone (17). Meade and colleagues (18) have reported a meta-analysis on the topic of corticosteroids to prevent postextubation airway complications and claimed that IV corticosteroids decrease the risk of postextubation stridor in children by approximately 40%. Moreover patients who received topical Methylprednisolone yield slightly better scores of sore throat and cough 1 hour after surgery as compared with patients who have been administered lidocaine (19,20). On the other hand, Hoing and colleagues (17) compared the effects of administering 250 mg Methylprednisolone or NaCl 0.9% IV to patients who underwent direct laryngoscopy under general anesthesia with regard to edema and the size of redness of certain anatomic structures of the larynx and hypopharynx and found no statistically significant differences between the two groups. They asserted that routine prescription of cortisone before microlaryngoscopy was not necessary but was recommended when the operation was expected to take more than 30 minutes to give chance to metylprednisolone to show its effects. The last recommendation of Hoing (17) is consistent with our results in control group, where the routine use of IV dexamethazone did not prevent the occurrences of postoperative respiratory complications which is significantly high in the control group and metylprednisolone group. The time interval between the injection of Methylprednisolone and evaluation of the respiratory system is important because this interval was approximately 40 to 55 minutes (operation time of 28 minutes + recovery time of 10 minutes + evaluation time of 10 minutes), and this time might be not enough for the peak effect of Methylprednisolone on the respiratory system, or IV Methylprednisolone might be ineffective in the prevention of postoperative respiratory complications caused by laryngeal surgery and this observation might need further investigation.

In the present study, R-Epinephrine was used according to the British dosage recommendations which tend to be more conservative compared to American. We used 0.4 ml/kg of 1 mg/ml solution, which showed effective results on the prevention of postoperative respiratory complications. Results of R-Epinephrine was insignificantly less than Lidocaine effects and better than either Saline or Methylprednisolone. This result is consistent to the results of Nutman , Orlicek and Waston and their colleges (14, 21, 22).

In our study, sore throat was observed in 3 patients of the control group I and 2 patients of Methylprednisolone group II groups (20% and 13.6%, respectively). Difficult swallow was seen only in 2 patients of Lidocaine group (13.6%) whose duration of anesthesia was shorter than 15 minutes and expected that lidocaine is still effective (23).

CONCLUSION

In conclusion, lidocaine IV or topical administration was effective in reducing postoperative respiratory complications after short-term laryngeal surgery by way of rigid laryngoscope under general anesthesia. Methylprednisolone prolonged recovery time from anesthesia, and it did not yield a significant positive effect on the prevention of postoperative respiratory complications after endoscopic short-term laryngeal surgery.

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