POST-EXTUBATION SORE THROAT; HOW FAR NEBULIZED DEXAMETHASONE DECREASES ITS INCIDENCE?

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ABSTRACT:

Background: *Post-operative sore throat (POST) is a frequent complaint that occurs in 21–65% of patients receiving general anesthesia (GA) with endotracheal intubation. Effective prevention of postoperative sore throat is thus needed. The inhaled corticosteroids deliver the drug to the site of action without systemic effects. Dexamethasone is a potent synthetic glucocorticoid with anti-inflammatory effects.*

Aim of work: *To assess how far nebulized dexamethasone decreases the incidence of POST and hoarseness of voice.*

Patients and Methods: *This double blinded double armed placebo controlled randomized clinical trial was conducted on 60 people divided into 2 groups; Group D: 30 patients received dexamethasone 8 mg in 5 ml normal saline nebulized 15 minutes before general anesthesia and endotracheal intubation. Group S: 30 patients received 5 ml normal saline nebulization 15 minutes before general anesthesia and endotracheal intubation.*

Results: *Patients' characteristics (age, sex, weight, ASA and Mallampati classification), duration of surgery, type of surgery, intubation attempts and site of endotracheal tube shows non-significant difference between both groups. Peri-nebulization hemodynamics, shows non-significant difference between both groups as regards heart rate and mean arterial blood pressure at all examined timings.*

Conclusions: *In our study the incidence of POST was 2 (6.7) which mean that the pre-operative single dose of nebulized dexamethasone 8 mg effectively can attenuates the incidence and severity of POST following GA with endotracheal intubation.*

Key words: *Post-operative sore throat, General anesthesia, Nebulized dexamethasone decreases*

INTRODUCTION:

Patients undergoing general anesthesia with endotracheal intubation are suffering from postoperative sore throat (POST) which is considered minor postoperative complication **(1)**.

This complication is very annoying to the patient and may cause significant postoperative morbidity **(2)**.

Many factors leading to development of POST include trauma to Pharyngo-laryngeal mucosa from laryngoscopy, placement of a nasogastric tube, or oral suctioning. In addition, the cuff design and pressure may affect tracheal mucosal capillary perfusion, and the contact of the tracheal tube with the vocal cords and posterior pharyngeal wall may result in edema or mucosal lesions **(3)**.

We are using many measures to decrease the incidence of POST include the use of endotracheal tube with smaller size with a low cuff pressure, use of topical lidocaine and inhalation of steroids [(4)].

Steroids act as anti-inflammatory and anti-edematous drugs so that they are widely used in common practice. Dexamethasone is one of a common potent synthetic glucocorticoid; which when used in inhaled form will decrease the severity and incidence of POST and hoarseness of voice [(5)].

AIM OF THE WORK:

The purpose of this study is to assess how far nebulized dexamethasone decreases the incidence of POST and hoarseness of voice.

PATIENTS AND METHODS:

Type of Study: Double blinded double armed placebo controlled randomized clinical trial.

Study Setting: Randomized sample for population who were admitted for general anesthesia with oral endotracheal intubation in AIN-SHAMS university hospitals after Ethical Committee approval.

Study Period: From 1/2/2018 to 1/10/2019.

Study Population: Patients undergoing general anesthesia with endotracheal intubation for the following surgeries (Trabeculectomy, ureteroscope, inguinal mesh hernioplasty and knee arthroscopy).

Inclusion Criteria:

- The patient selected according to ASA status (ASA I).
- Age range between 25 till 60 years old.
- Both sexes
- Weight range between 70 to 80 kg.
- Normal blood glucose level.
- Normal blood pressure.
- Normal coagulation profile.

Exclusion Criteria:

- Patient refusal.
- If the patient has any coagulopathy disorder or receiving any anticoagulant drugs.
- Diabetic patients.
- Hypertensive patients.
- History of recent respiratory tract infection.
- Using steroids or NSAIDs on regular base.
- Nasogastric tube insertion.
- Expected difficult intubation and Mallampati scoring III or IV.

Sampling Method: Computer- generated random numbers in sealed opaque envelops.

Sample Size: 60 patients divided into 2 groups.

Ethical Considerations: Patients sign an informed consent for the study inclusion.

Study Procedures:

Pre anesthetic investigations and evaluation were done for all patients. In the preparation room under local anesthesia, an intravenous cannula was inserted, and midazolam 2 mg IV and pantoprazole 40 mg IV were given to all patients. 15 min before induction, patients were randomly allocated using computer- generated random numbers in sealed opaque envelops into one of two groups according to nebulized material; all the patients received the same amount (5ml) and the same color (crystal clear) of nebulized solution.

Group D: 30 patients received dexamethasone 8 mg (Decadron 8 mg, manufactured by Organon Laboratories Limited, Cambridge Science Park, Milton Road, Cambridge, CB4 0FL, U.K. MARKETING AUTHORISATION NUMBER(S) PL 0065/ 5013R) in 5 ml normal saline nebulized 15 minutes before general anesthesia and endotracheal intubation.

Group S: 30 patients received 5 ml normal saline nebulization 15 minutes before general anesthesia and endotracheal intubation.

After arrival in operation theatre, routine monitoring was used for all patients including noninvasive blood pressure, pulse oximetry, capnography and electrocardiography. Then lactated Ringer's solution was started 1.5 mL/kg/h. Then patients were premedicated with intravenous fentanyl 2 mic per kg body weight. Every patient was preoxygenated for 3-5 minutes before induction of anesthesia by intravenous titrated dose of propofol 2-3 mg/kg, then 0.15 mg/kg cis-atracurium was used for muscle relaxation and assisted ventilation for 3 minutes was maintained. Laryngoscopy was performed by the same anesthesiologist for all patients using a standard 3 or 4 Macintosh metal blades. Then orotracheal intubation was done using high volume low pressure single use endotracheal tube (ETT) size 7.5 mm and 7.0 mm in male and female patients respectively. ETT position was confirmed and secured. General anesthesia was maintained by oxygen, isoflurane, cis-atracurium and fentanyl as standard procedure. Mechanical ventilation was adjusted to maintain end tidal carbon dioxide between 30 and 35 mmHg, and anesthesia was maintained using isoflurane 1.2% in oxygen 100% and top up doses of cis-atracurium (maintenance dose) 0.03 mg/kg every 20 min. At the end of surgery, inhalational anesthetic was turned off, muscle relaxant was reversed by neostigmine 0.05 mg/kg and atropine 0.02mg/kg. Before extubation, pharyngeal suction was done, and the trachea was extubated when the patient was fully conscious. All patients received oxygen through face mask after operation in post anesthesia care unit (PACU).

Postoperative period:

All patients in 2 groups were examined postoperatively for the intensity of sore throat which is defined as (redness of throat and pain felt anywhere in throat especially during swallowing) by a 4-point scale (0-3): [0 = no sore throat, 1 = mild sore throat, 2 = moderate sore throat (complains of sore throat on his/her own), 3 = severe sore throat (change in voice or hoarseness, associated with throat pain)].

Measurements:

1. Patients characteristics and surgical data: age, sex, body weight, ASA-PS, Mallampati score, intubation attempts, size of ETT, duration of surgical procedure and type of surgical procedure,
2. Heart Rate (HR) and mean blood pressure (MAP) were recorded: before, during and just after nebulization.
3. All patients in 2 groups were examined postoperatively for the intensity of sore throat at 0, 1, 2, 4 hours postoperatively. Sore throat was scaled on a 4-point scale (0-3). Prevalence of sore throat was done at 4th hour postoperative (score $\geq$1).
4. Evaluation of other adverse effects, such as nausea, vomiting and cough specifically during the first postoperative four hours.

Justification of sample size:

The primary outcome measure was that the incidence and intensity of POST can be attenuated by preoperative nebulization of 8mg of dexamethasone.

The sample size calculation was performed using EpI-Info 2002 software statistical package designed by World Health Organization (WHO) and by Centers for Disease Control and Prevention (CDC).

The sample size was calculated as N $\geq$ 29 based on the following considerations: 95% level of significance, 80% power of the study, and 1:1 for each study groups to demonstrate 30% decrease in the incidence of POST with dexamethasone group compared to the control group (46% according to a previous study [(6)]. One case was added in

each group to overcome drop-out, therefore 30 patients were recruited in each group.

Table 1 shows non-significant difference between both groups as regards patients' characteristics (age, sex, weight, ASA and Mallampati classification), duration of surgery, type of surgery, intubation attempts and site of endotracheal tube (P value >0.05).

Table 1: Demographic data and patients' characteristics of both groups

		Group D (n = 30)	Group S (n = 30)	P value
Age (years)	Mean ± SD	38.87 ± 9.94	38.27 ± 9.93	0.816
	Range	26-59	25-55	
Sex	Male	16 (35.3%)	13 (34.3%)	0.438
	Female	14 (46.7%)	17 (56.7%)	
Weight (kg)	Mean ± SD	76.13 ± 3.03	75.07 ± 3.25	0.193
	Range	71-80	70-80	
Mallampati classification	MP I	18 (60%)	16 (53.3%)	0.602
	MP II	12 (40%)	14 (46.7%)	
Duration of surgery (min)	Mean ± SD	105 ± 10.09	101.33 ± 7.87	0.122
	Range	90-120	90-110	
Type of surgery	Trabeculectomy	9 (30%)	10 (33.3%)	0.552
	Ureteroscope	5 (16.7%)	7 (23.3%)	
	Inguinal mesh hernioplasty	12 (40%)	7 (23.3%)	
	Knee arthroscopy	4 (13.3%)	6 (20%)	
Intubation attempts	1	23 (76.7%)	21 (70%)	0.559
	2	7 (23.3%)	9 (30%)	
Size of endotracheal tube	7 mm	14 (46.7%)	17 (56.7%)	0.602
	7.5 mm	16 (53.3%)	13 (43.3%)	

Table 2 shows non-significant difference between both groups as regards heart rate at all examined timings (P value = 0.194, 0.288 and 0.348).

Table 2: Heart rate of both groups

		Before nebulization	During nebulization	Just after nebulization
Group D (n= 30)	Mean	86.80	87.07	87.17
	± SD	8.97	9.69	9.38
Group S (n = 30)	Mean	83.80	84.53	84.93
	±±SD	8.70	8.60	8.89
P value		0.194	0.288	0.348

Table 3 shows non-significant difference between both groups as regards Mean arterial blood pressure at all examined timings (P value = 0.201, 0.189 and 0.244).

Table 3: Mean arterial blood pressure of both groups

		Before nebulization	During nebulization	Just after nebulization
Group D (n = 30)	Mean	87.40	87.70	87.90
	± SD	8.90	9.87	10.55
Group S (n = 30)	Mean	84.43	84.23	84.93
	± SD	8.88	10.34	8.89
P value		0.201	0.189	0.244

In our study, the prevalence of sore throat at 1st, 2nd and 3rd hour postoperative was significantly decreased in group D compared to group S (13.3% vs 53.3%, P<0.001) and at 4th hour

postoperative was significantly decreased in group D compared to group S (6.7% vs 50%, P<0.001).

Table 4: Prevalence of sore throat of both groups

		Group D (n = 30)	Group S (n = 30)	P value
Sore throat	1h	4 (13.3%)	16 (53.3%)	**<0.001***
	2h	4 (13.3%)	16 (53.3%)	**<0.001***
	3h	4 (13.3%)	16 (53.3%)	**<0.001***
	4h	2 (6.7%)	15 (50%)	**<0.001***

*significant as P value < 0.05

Table 5 shows significant increase in group S than group D at all examined timings as regards intensity of sore throat (P = 0.009, 0.007, 0.008 and 0.003).

Table 5: Intensity of sore throat of both groups

		0	1 h	2 h	4 h
Group D (n = 30)	Median	0.00	0.00	0.00	0.00
	Range	0-2	0-2	0-2	0-1
Group S (n = 30)	Median	1.00	1.00	1.00	0.50
	Range	0-3	0-3	0-3	0-3
P value		**0.009***	**0.007***	**0.008***	**0.003***

*significant as P value < 0.05

DISCUSSION:

Postoperative sore throat (POST) is considered a minor postoperative complication that occurs in 21-65% of patients receiving general anesthesia with endotracheal intubation. It may be very distressing to the patient and may cause significant postoperative morbidity [(2)]. Many modalities of treatment have been tried to abolish this complication, both pharmacological and non pharmacological. Steroids have anti-inflammatory functions and are widely used in common practice. The inhaled corticosteroids deliver the drug to the site of action where it is used in patients with airway diseases without systemic effects. Dexamethasone is a potent synthetic glucocorticoid with anti-inflammatory effects [(5)].

The purpose of this study is to estimate how far nebulized dexamethasone decreases the incidence of POST and hoarseness of voice.

This double blinded double armed placebo controlled randomized clinical trial was conducted on 60 people divided into 2 groups; Group D: 30 patients received dexamethasone 8 mg in 5 ml normal saline nebulized 15 minutes before general anesthesia and endotracheal intubation. Group S: 30 patients received 5 ml normal saline nebulization 15 minutes before general anesthesia and endotracheal intubation.

As regards patients' characteristics (age, sex, weight, ASA and Mallampati classification), duration of surgery, type of surgery, intubation attempts and site of endotracheal tube shows insignificant difference between both groups.

Also, as regards Peri-nebulization hemodynamics, show insignificant difference between both groups as regards heart rate and mean arterial blood pressure at all examined timings.

As regards the prevalence and severity of sore throat at 4thhour postoperatively was significantly decreased in group D compared to group S.

Also, as regards Postoperative complications during the 1st 4hours postoperative in

both groups show insignificant difference between both groups as regard nausea, vomiting and cough.

In agreement with our results,[7] A prospective interventional study that included 80 patients. The patients were assigned to two groups, 40 patients in each group: the dexamethasone group (D) which received nebulized dexamethasone 8 mg 1 h before surgery and the control group (S) which received saline nebulizer instead. Assessment of postoperative sore throat, nausea and vomiting, odynophagia, and change of voice was used as an outcome comparative tool. They reported a significant preference of outcome values in the dexamethasone group as Sore throat mean and medians were less at all-time intervals. In that study, in the D group, the incidence of POST was 27.5% (11 out of 40 patients) compare to 72.5% (35 out of 40 patients) in the S group. While in our study the incidence was 2 (6.7%).There were no hemodynamic changes between both groups.

The results of [8] study is in accordance to ours regarding showing reduction in the incidence and severity of POST in the dexamethasone group. Group D: Patients received dexamethasone 8 mg (2 ml) with 3 ml of normal saline (total volume of 5 ml) for nebulization and Group K: Patients received ketamine (preservative free) 50 mg (1 ml) with 4 ml of normal saline (total volume of 5 ml) for nebulization. After 15 min of nebulization, induction was done, The severity of POST was graded on a 4-point scale (0–3). The incidence of POST in that study was five patients (10%) in Group D and 14 patients (28%) in Group K.

In contrast to our study [9] a prospective, study, data were collected from children (6-16 years) undergoing surgeries. The patients were allocated into 3 equivalent groups (36 patients each). Preoperative nebulization was performed for all patients. Group M received 40 mg/kg magnesium sulphate, group K received 1 mg/kg ketamine, and group D received 0.16 mg/kg dexamethasone. They concluded that Preoperative nebulization with ketamine was more effective in reducing the intensity of POST in pediatric patients postoperatively without systemic adverse effects. The controversy may be due to smaller dose 0.16 mg of received dexamethasone. In accordance with our results demonstrated that no significant differences in the MAP and HR were observed among groups of ketamine, magnesium and dexamethasone at any of the examined time points and the difference among the three groups in post-operative complications was non-significant. Number of patients with POST 15 (41.67%) in K group, 25 (69.44%) in M group and 24(66.67%) in D group. Side effects in the form of vomiting appeared more often in the magnesium group (3 cases) and ketamine group (2 cases). While on the other hand, the dexamethasone group showed no cases of vomiting (p-value= 0.238) .That was statistically non-significant although clinically significant.

In contrast to our study, [10], have reported an incidence of 27.5% of POST in the dexamethasone group in their study on nebulized dexamethasone versus MgSO4 in the prevention of POST. When compared to their study, our study showed an incidence of 6.7% in the dexamethasone group which was much lower. They found incidence of POST was 27.5% in group D and 57.5% in group M and the difference was statistically significant at all times of assessment. None of the patients in group D had postoperative hoarseness or cough or any adverse effects which were clinically and statistically not significant. No hemodynamic changes in both groups.

In agreement to our results, [11] who a studied of 120 ASA I-II patients of both sexes aged 25-60 years. Patients were randomly assigned into one of the two groups of 60 patients each: group D received dexamethasone 8 mg in 5 ml normal saline nebulization and group S (the control group) re-

ceived normal saline in 5 ml nebulization 15 min before general anesthesia and endotracheal intubation. They demonstrated that a single dose of 8 mg of nebulized dexamethasone reduced the incidence and severity of POST at 0, 2, 4, 6, and 12 h post-extubation. The incidence and severity of POST were graded using a four-point scale (0-3) and was significantly lower in group D than in group S at the following time intervals: 0 h (immediately after extubation) (P = 0.024); 2 h after extubation (P = 0.009); 4 h after extubation (P = 0.000); 8 h after extubation (P = 0.000); and 12 h after extubation (P = 0.002). However, there was no significant difference at 24 h after extubation (P = 0.513). Patients of the two groups remained hemodynamically stable with no adverse effects during the entire study period.

There are few limitations of our study. First, we were unable to measure serum concentrations of the study drugs, dexamethasone to monitor drug levels during the study period due to lack of feasibility in our institute. Second, the scale used to assess the POST score was a subjective scale and may be associated with bias. Third, the present study didn't compare the effect of different doses of dexamethasone. Lastly, Sample size was small and may need further studies with increasing sample size.

We conclude from our study that the pre-operative single dose of nebulized dexamethasone 8 mg effectively attenuates the incidence and severity of POST following GA with endotracheal intubation.

Conclusions:

We conclude from our study that the pre-operative single dose of nebulized dexamethasone 8 mg effectively attenuates the incidence and severity of POST following GA with endotracheal intubation.

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إلىأىمدىيعمل استنشاق عقارالديكساميثازون على التقليل من حدوث التهاب الحلق مابعد رفع الأنبوبة الحنجرية؟

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المستخلص

الخلفية: يعانى المرضى الخاضعون للتخديرالعام مع وضع الأنبوبة الحنجرية من التهاب الحلق بعد العملية الجراحية وهو يعتبرمن المضاعفات البسيطة. تسبب هذه المضاعفة مضايقة للمريض ويمكن أن تسبب اعتلال كبيربعد العمليات الجراحية .

الهدف:هو المساعدة فى تقدير مدى تأثير استنشاق رذاذ عقارالديكساميثازون فى تقليل قرحة الحلق وتغييرالصوت ما بعد العمليات الجراحية.

المرضى والطرق:تمت الدراسة على ٦٠ مريض تتراوح أعمارهم بين ٢٥- ٦٠ سنة خضعوا لجراحاتتحتاج الي استخدام الانبوبه الحنجرية بمستشفيات جامعه عين شمس.بعد الحصول على موافقه لجنة الجوده وأخلاقيات البحث العلمى وموافقه المرضى على المشاركه بالدراسه.تم تقسيم المرضى إلى مجموعتين متساويتين في عدد المرضى بكل منها ٣٠ مريض. المجموعة الاولى : استخدام ٨ مجم من عقار الديكسميزون في جلسه استنشاق قبل الخدوع للتخدير الكلي. المجموعة الثانية :تم استخدام محلول ملح فقط في جلسه استنشاق قبل التخدير الكلي.

النتائج والاستنتاج: لم يكن هناك فارق بين المجموعاتين فيما يتعلق بالبيانات الديموغرافية (العمر والوزن والجنس ونوعومدةالجراحه)، وكذلك لم يوجد فرق بين المجوعتين من حيث حدوث الاثار الجانبيه بعد اجراء العمليه من ترجيع وغيره حتي انه لم يوجد فرق من خلال الوظائف الحيويه ايضا فلم يحدث تغير في ضرابت القلب اومتوسط قياس الضغط وأظهرت نتائجناوجود فارق بين المجموعتين وجدنا فارق كبير بينهما فيما يتعلق بشده التهاب الحلق بعد العمليه فقد وجدنا ان اضافه امبولديكساميزازون في جلسه استنشاق قبل العمليه يقلل من التهاب الحلق بشده.