VOLUME - 9, ISSUE - 7, JULY - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Anaesthesiology

TO EVALUATE THE EFFECT OF COMBINED USE OF PROPHYLACTIC INTRAVENOUS DEXAMETHASONE AND BENZYDAMINE SPRAY ON POST-OPERATIVE SORE THROAT (POST) AND POST-OPERATIVE HOARSENESS (PH) AFTER INTUBATION WITH DOUBLE LUMEN TUBE

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ABSTRACT

Background and aims Post-operative sore throat and post-operative hoarseness are common after tracheal intubation. The aim of our study is to compare the effectiveness of combined use of prophylactic Intravenous dexamethasone and benzydamine hydrochloride 0.3% spray on post-operative sore throat and post-operative hoarseness after intubation with double lumen tube. **Methods** This study was conducted in 124 adult patients undergoing thoracic surgery using Double Lumen Tube intubation and patients were allocated into four groups, , Group A (Intravenous dexamethasone plus benzydamine hydrochloride 0.3% spray), Group B (Intravenous dexamethasone plus normal saline spray), and Group C (Intravenous normal saline plus benzydamine hydrochloride 0.3% spray), Group D (Intravenous normal saline plus normal saline spray). Post-operative sore throat and post-operative hoarseness were evaluated at one, six and 24h after surgery. Sore throat was evaluated using a 0-100 mm visual analogue scale. Hoarseness was defined as a change in voice quality. **Results** The incidence of post-operative sore throat and post-operative hoarseness as well as severity were significantly lower in Group A compared to other groups ($p<0.01$). The incidence of post-operative sore throat and post-operative hoarseness was significantly lower in Group B and C than Group D ($P<0.01$). However, there was no statistical difference between Group C and Group B ($P>0.005$). **Conclusions** Prophylactic application of intravenous dexamethasone and benzydamine spray to the double lumen tube cuff and oropharyngeal cavity reduces the incidence and severity of postoperative sore throat and the incidence of hoarseness associated with DLT intubation.

KEYWORDS : Benzydamine spray, Double lumen tube, Intravenous dexamethasone, Post-operative sore throat, Post-operative hoarseness.

INTRODUCTION

Postoperative sore throat (POST) and postoperative hoarseness (PH) are common following tracheal intubation, with an incidence of 14.4 - 73.9%.[1] It is considered as the eighth most undesirable outcome in the postoperative period rated by patients contributing to significant morbidity, patient discomfort and dissatisfaction in the postoperative period.[2] The double-lumen endotracheal tube (DLT) used for one lung ventilation (OLV) is more likely to cause a higher incidence of POST and PH than a single lumen endotracheal tube (ETT).[3] Various non-pharmacological methods such as, use of smaller-sized ETT, lubricating ETT with water-soluble jelly, careful airway instrumentation, gentle oropharyngeal suctioning, minimizing intracuff pressure, and extubation in deeper plane etc.[2] and pharmacological methods such as intravenous (IV) dexamethasone, beclomethasone inhalation, benzydamine hydrochloride (BH) spray, intracuff administration of alkalized lignocaine and gargling & nebulisation with ketamine, azulene sulfonate, aspirin etc[4-6] have been used but all these techniques have their own limitations and variable success rate.

Previous studies with isolated use of BH spray & IV Dexamethasone to reduce the incidence of POST & PH showed varying results. Thus, we aimed to evaluate the combined use of BH 0.3% spray to the DLT cuff & oropharyngeal cavity and IV Dexamethasone preoperatively for reducing POST and PH in patients intubated with DLT.

Materials & methods

After getting ethical committee clearance of our institution and obtaining informed written consent from the patient, this study was carried out from August 2014-September 2015. Adult patients of either sex undergoing thoracic surgery requiring DLT endotracheal intubation for one lung ventilation were enrolled in this prospective, randomized and double blind study. Patients were excluded if they had history of sore throat, hoarseness, coagulopathy, a known or predicted difficult airway, or allergy to acetylsalicylic acid or non-steroidal anti-inflammatory drugs (NSAIDs).

One hundred twenty four patients were randomly allocated in four groups, Group (A): received IV dexamethasone 8mg (2ml) plus thee puffs of BH 0.3% spray , Group (B): received IV dexamethasone 8mg (2ml) plus NS spray, Group (C): received IV NS 2ml plus thee puffs of BH 0.3% spray, Group (D): received IV normal saline (NS) 2ml plus thee puffs of NS spray . Both IV medications were given 30 minutes before intubation by a staff nurse who was blinded to the study while sprays were applied in the oropharyngeal cavity close to the vocal cords using direct laryngoscopy after induction and before intubation as well as on the tracheal cuff by another anaesthesiologist blinded to the study.

Randomization was done using a computer-generated programme with consecutively numbered opaque sealed envelopes. Colleagues not involved in the study determined the treatment allocation by opening each envelope in sequence and preparing the study drug identical in appearance and labelled with the patients' identification number.

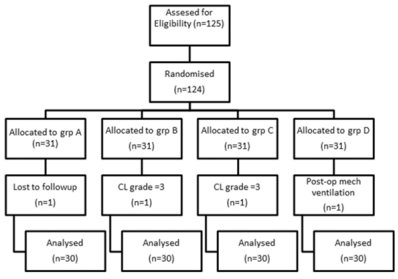

Figure 1 – Study Design

Patients were premedicated with IV midazolam 0.03mg/kg. Intraoperative monitoring included electrocardiogram, pulse oximetry, gas analyser, and non-invasive and invasive arterial pressure. An 18G epidural catheter was placed in T4-T5 space for intraoperative and postoperative analgesia. Anaesthesia was induced with IV propofol 2mg/kg titrated to effect and IV fentanyl 2μg/kg. IV vecuronium 0.1mg/kg was administered to achieve neuromuscular blockade. Tracheal intubation was subsequently performed using a DLT (Mallinckrodt Medical Inc, Athlone, Ireland) size 37 Fr for males and size 35 Fr for females. 1-2 ml of air was used to inflate distal cuff and tracheal cuff was slowly inflated to an intracuff pressure of 20

cm H2O. Anaesthesia was maintained with isoflurane (1-2%) and air/oxygen mixture (50/50) with intermittent IV fentanyl (1μg/kg) and IV vecuronium (0.02mg/kg) as and when required. Immediately following intubation and repositioning, fibreoptic bronchoscopy as well as auscultation method were used to confirm correct placement of the DLT. Intracuff pressure was monitored with a VBM handheld aneroid manometer (Sulz, Germany) every 30 min and maintained at 20 cm H2O. Neuromuscular monitoring was used to assess the degree of relaxation in all groups intraoperatively. Intraoperative analgesia was provided using 0.125% bupivacaine and 2 mcg/ml fentanyl through continuous thoracic epidural catheter. Neuromuscular block was reversed at the end of the procedure by IV neostigmine and IV glycopyrrolate IV. After gentle suctioning of oral secretions, when patients were fully recovered and were able to obey commands, tracheal extubation was carefully performed. The incidence of sore throat was scored as 'No' with a VAS of 0 or 'Yes' with all other VAS values. The severity of sore throat was assessed by visual analogue scale (VAS) 0-100 mm where 0 = no pain to 100 = worst pain imaginable. POST and PH were evaluated at one, six, and 24 h after tracheal extubation. Hoarseness was defined as a change in voice quality assessed by patients. If patients had a voice quality change during the observation period, the incidence of hoarseness was scored as 'Yes'. The side effects of the study drugs: dexamethasone (incidence of surgical site infections, hyperglycaemia) and benzydamine hydrochloride (including numbness, stinging or burning sensation, cough, dry mouth, and nausea and vomiting) were recorded. All parameters were assessed by independent Anaesthesia resident not involved in the group allocation. Patients classified as Cormack-Lehane (CL) view 3 or 4 during laryngoscopy and those who required postoperative mechanical ventilation were dropped from the study.

The primary outcome of our study was to compare the incidence of POST & PH and severity of POST. The CL view during tracheal intubation, resistance to DLT insertion (none, mild, moderate), number of intubation attempts, time to achieve intubation, time for positioning the DLT, the number of repositioning, the duration of OLV and tracheal intubation, the total amount of fentanyl administered and the side effects of the study drugs were considered as secondary outcomes.

Presuming that Group B (IV dexamethasone plus BH 0.3% spray), would improve primary outcome by 20%. By using sample size calculator with 5% alpha error, 90% power and expected standard deviation of 20% a sample size of 22 subjects per group was required. So, we included a minimum of 31 in each group to compensate for any drop out.

Demographic data were analysed using ANOVA for continuous variable & Chi square test for categorical variable. Fischer's exact test was used for inter group incidence comparison and Kruskal wallis test for inter group comparison of severity. SPSS version 16 was used for statistical analysis and $P < 0.05$ considered statistically significant.

Results:

One twenty five patients were recruited in the study out of which one patient did not meet the inclusion criteria, and the remaining 124 patients were randomized into four groups. One patient from each group was dropped from the study. Thus, 120 patients were included in the analysis. (Fig.1)

Patient characteristics were comparable in all four groups. The CL view, number of intubation attempts, resistance to DLT insertion, time for tracheal intubation and DLT positioning, number of repositioning, and the duration of OLV and tracheal intubation were similar in all groups (Table 1).

Table 1 – Patient characteristics

	A	B	C	D
Age	56	57	55.5	56
Sex	18/12	19/11	17/13	18/12
Height (cm)	165 ± 8	167 ± 9	163 ± 7	168 ± 10
Weight (kg)	60 ± 10	62 ± 9	61 ± 10	63 ± 10
Smoking (Yes/No)	15/15	14/16	16/14	14/16
Intra-op Fentanyl requirement	150 ± 18	148 ± 19	150 ± 18	148 ± 20
Surgical time	127 ± 38	129 ± 40	128 ± 40	130 ± 36
Anaesthesia time	167 ± 40	170 ± 36	168 ± 38	165 ± 42

CL Grade, number of intubation attempts, resistance to DLT insertion, time for intubation, time for DLT positioning, number of repositioning, duration of OLV and duration of intubation were comparable in all groups (Table 2).

Table 2: Factors related to tracheal intubation:

	A	B	C	D	p-value
CL Grade (1/2)	19/11	21/9	19/11	22/8	0.887
No. of intubation attempts					
1	26	25	26	27	0.8786
2	4	5	3	2	
3	0	0	1	1	
Resistance to DLT insertion					
None	22	24	23	24	0.8848
Mild	6	5	5	4	
Mod	2	1	2	2	
Time for Intubation (second)	27 ± 5.1	27 ± 4.9	26.7 ± 6.7	26.5± 5.8	0.9902
Time for DLT positioning	19.8 ± 7.5	18.3 ± 7.1	19.4 ± 7.7	18.8 ± 7.5	0.9249
Number of repositioning					
0	20	18	20	21	0.9094
1	8	10	7	6	
2	2	2	3	3	
3	1	1	0	0	
Duration of OLV (min)	115.6 ± 44	113 ± 47	114 ± 46	115 ± 45	0.9997
Duration of Intubation (min)	154.8 ± 49	154.2 ± 50	154.2 ± 52	153.9 ± 51	0.9999

A significant reduction in the incidence of POST & PH was observed at all time intervals in group A when compared to Group B, Group C and A ($p<0001$). The incidence in Group b and Group C was lower than Group D and was statistically significant at 1, 6 and 24 hs ($p<0.5$). However, the incidence was comparable between Group B and C at all time intervals. ($p>0.5$) (Table: 3, 4)

Table 3: Incidence of POST & PH

	Group A (D,BH) {n=30}	Group B (D,NS) {n=30}	Group C (BH,NS) {n=30}	Group D (NS,NS) {n=30}
Soreness				
1HR	2(6.6)	8(26.6)	9(30)	16(53.3)
6HR	1(3.3)	8(26.6)	6(20)	18(60)
24HR	0	5(25)	6(20)	14(46.6)
Hoarseness				
1HR	2(6.6)	8(26.6)	8(26.6)	11(36.6)
6HR	1(3.3)	6(20)	6(20)	13(43.33)
24HR	0	5 (25)	5 (25)	12(40)
VAS				
1 HR	10	30+10.5	30+10.8	50+15.0
6 HR	10	30+10.8	25+6.0	50+15.5

24 HR	0	20+5.5	20+6.0	40+10

Table 4: sore throat: inter group comparison

Group	1 HR	6 HR	24 HR
A vs. B	0.031	0.040	0.019
A vs. c	0.03	0.04	0.019
A vs. D	<0.001	<0.001	<0.001
B vs. C	0.999	0.999	0.999
B vs. D	0.04	0.05	0,044
C vs. D	0.04	0.05	0.044

Severity (mean VAS score) was significantly lower in Group A than in Group B, C and A at all time intervals (Figure 2).

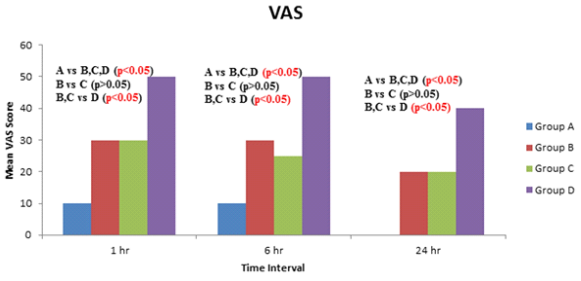

Figure 2: Showing VAS scores in all groups at various time intervals

Only one patient in Group C complained of local numbness. The incidence of dry cough were similar in all groups. 7 patients of group C had nausea/vomiting post operatively where as only 1 patient in group A , which is statistically significant. None of them had surgical site infection on follow up.

Table 5: Hoarseness: inter group comparison

Group	1 HR	6 HR	24 HR
A vs. B	0.03	0.01	0.05
A vs. c	0.019	0.04	0.04
A vs. D	< 0.001	<0.001	<0.001
B vs. C	0.77	0.541	0.738
B vs. D	0.039	0.009	0.012
C vs. D	0.05	<0.001	0.0284

Table 6: Comparisons of side effects among various groups

	Group A	B	C	D
Local numbness	0	0	1	0
Irritation/burning	0	0	0	0
Nausea, vomiting	1	0	7	0
Dry cough	2	2	3	2
Surgical site infection	0	0	0	0
Hyperglycemia	0	0	0	0

DISCUSSION:

Our findings indicate that the combined use of prophylactic BH to the DLT cuff and oropharyngeal cavity with dexamethasone given intravenously reduces the incidence and severity of postoperative sore throat and the incidence of hoarseness at one, six, and 24 h after tracheal intubation using a DLT.

DLT is commonly used for lung separation and OLV and is associated with a higher rate of laryngeal complications, such as postoperative sore throat and hoarseness, compared with single-lumen ETT. [3,7] The incidence of postoperative sore throat and hoarseness is directly correlated with the size of the ETT.[8,9] Considering the body stature of average adult Indian male and female, generally we use 37 Fr& 35 Fr DLT respectively. Similarly, single lumen ETTs of sizes 8/8.5 and 7/7.5 mm are used respectively. The outer diameter of a DLT (13-14 mm for sizes 37; 12-13 mm for size 35 Fr) is larger than that of a single lumen ETT (10.7 mm for 8.0-mm internal diameter [ID]; 10.0 mm for 7.5-mm ID; 9.5 mm for 7.0-mm ID). Moreover, DLTs typically require frequent manipulation and repositioning for optimal placement, resulting in friction between the DLT and airway that can cause airway injuries.[10] The preformed curve of the DLT may also contribute to laryngeal trauma during surgery and tracheal extubation.[7] A postoperative flexible fibrescopic assessment of vocal cord injuries revealed that the main injuries caused by DLT intubation are redness and oedema at the vocal folds.[11] The lower incidence of POST and PH in group A compared to groups B, C and D in our study may be due to the fact that we used a combination of analgesic and anti-inflammatory drugs. Benzydamine hydrochloride is a mild topical NSAID with analgesic properties whereas dexamethasone has an potent anti-inflammatory activity, which includes inhibition of leukocyte migration, maintenance of cell membrane integrity, attenuation of lysosome release, and reduction of fibroblast proliferation.[12,13] Previous studies using steroid gel applied widely over an endotracheal tube effectively mitigated POST and PH compared with application of lidocaine jelly, which does not possess any intrinsic anti-inflammatory activity.[14,15] Groups B & C, either of the drug was used and showed lower incidence and severity of POST & PH when compared to group D indicating that they are individually effective in reducing POST & PH which is in line with previous studies, but however the incidence and severity of POST & PH was higher on comparison with group A, where we found that combined use of BH & Dexamethasone resulted in much better decrease in Incidence as well as severity at 1, 6, 24hs by ~50%, thus showing a Synergistic effect. In group D, only 1 patient complained of post-operative nausea vomiting (PONV) where as it was as high as 7 in group C, whereas group A and B had no incidence of PONV. This can be explained by the fact the PONV which is a documented complication of topical benzydamine hydrochloride is negated by prior application of dexamethosone which is proved to reduce incidence of PONV.

We didn't find any side effect of dexamethasone in our study like peptic ulcer, delayed wound healing, which is in line with previous studies which states that single dose dexamethasone doesn't produce any side effect.[16,17] Potential adverse effects associated with the topical application of Benzydamine hydrochloride include local irritation, such as numbness and a burning or stinging sensation. There is discrepancy in the side effect profile with Benzydamine hydrochloride. One study showing numbness and dysgeusia in 10.5% patients who gargled with a benzydamine hydrochloride solution for 30 sec before the induction of anaesthesia [18] while in other study applying benzydamine hydrochloride to the oropharyngeal cavity immediately before intubation and reapplying regularly for 48 h after surgery produced a therapeutic effect without local or systemic side effects.[19] In our study, we hypothesize that BH 0.3% sprayed over the DLT cuff and oropharyngeal cavity after induction of anaesthesia decreased local irritation and so reduced complaints of BH 0.3% spray related adverse effects during the postoperative study period.

This study has several limitations. Although an equal dose of

BH 0.3% spray was administered to each patient, we cannot account for variable effect-site concentrations of the drug due to patient characteristics such as varied mucosal thickness in the oropharyngeal cavity or different volumes of saliva that may affect drug absorption. [17] Moreover, we did not evaluate coughing or bucking events during extubation that may have produced variable trauma and irritation. Our study did not have a large enough patient sample size to assess safety and our follow-up was for only 24 h.

To conclude, combined use of BH 0.3% spray and intravenous dexamethasone used prophylactically reduces the incidence and severity of postoperative sore throat and hoarseness at all time period after surgery without adverse effects.

Figure Legends

Figure 1: Study design.

	Group A	B	C	D
Local numbness	0	0	1	0
Irritation/burning	0	0	0	0
Nausea, vomiting	1	0	7	0
Dry cough	2	2	3	2
Surgical site infection	0	0	0	0
Hyperglycemia	0	0	0	0

Figure 2: Showing VAS scores in all groups at various time intervals.

	A	B	C	D
AGE	56	57	55.5	56
SEX	18/12	19/11	17/13	18/12
HT (CM)	165 ± 8	167 ± 9	163 ± 7	168 ± 10
WT (KG)	60 ± 10	62 ± 9	61 ± 10	63 ± 10
SMOKING (Y/N)	15/15	14/16	16/14	14/16
FENTANYL intra op	150 ± 18	148 ± 19	150 ± 18	148 ± 20
Surg time	127 ± 38	129 ± 40	128 ± 40	130 ± 36
Anaes time	167 ± 40	170 ± 36	168 ± 38	165 ± 42
Total amount of Bupivacaine used in one hour	13			

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