ORIGINAL ARTICLE

Comparison of Two Different Doses of Nalbuphine for Postoperative Tonsillectomy Pain in Children

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ABSTRACT

Aim: Tonsillectomy has a high incidence of postoperative pain. We studied 0.25 mg kg^{-1} nalbuphine at the time of induction of general anaesthesia to assess the effectiveness of analgesia in postoperative period and compare it to 0.1 mg kg^{-1}.

Study design: Comparative interventional.

Place and duration of study: This study was conducted at the Paediatric ENT department of the Children Hospital and the Institute of Child Health Lahore from 2007 to 2010.

Methodology: Sixty ASA physical status one patients, aged 5-12 years scheduled for tonsillectomy were included in this study. Patients were divided randomly into two groups of 30 each. Group A received 0.25mg kg^{-1} Nalbuphine and group B received 0.1 mg kg^{-1} Nalbuphine at induction of anaesthesia. General anaesthesia was induced and maintained with standard technique. All patients were monitored throughout the surgery and postoperatively in recovery room. The children's Hospital of Eastern Ontario pain scale (CHEOPS) was used to evaluate pain objectively in post op period.

Results: There was significant reduced requirement of analgesia in immediate recovery room in group A. CHEOPS score was 4±0.18 (P value=0.001). Side effects especially PONV were similar in two groups. Mild sedation was noted in 73% in group A and 76% in group B.

Conclusion: We conclude that Nalbuphine in therapeutic doses of 0.25mg kg^{-1} at the time of induction of general anaesthesia is effective dose to keep the pain free wake up and recovery room stay for children of 5 to 12 years for tonsillectomy without the comorbidities as OSAS (Obstructive Sleep Apnea Syndrome), airways anomalies. It provides child centered approach to post operative analgesia for tonsillectomy without significant side effects.

Keywords: Nalbuphine, Children, Tonsillectomy, postop analgesia

INTRODUCTION

Patients undergoing tonsillectomy have high incidence of postoperative pain[1,2]. Post operative pain is a complication of surgery similar to infection and hydroelectric imbalance, and likewise it must be treated. Pain therapy can be more effective with pain measurement using pain scales. Severe pain is reported in 25 to 50% of children[3,4]. Pain has traditionally been treated with Morphine sulphate resulting in high incidence of postoperative nausea and vomiting (PONV) compared with other forms of analgesia[5,6] . Respiratory depression and sedation from Morphine sulphate may also be hazardous after pharyngeal surgery when a prompt return of airway reflexes are required[7,8]. In view of these side effects, alternative analgesic strategies have been suggested. NSAIDS have been shown to be as effective as opioids for tonsillectomy pain and are opioid sparing in the recovery period[8]. They also reduce the incidence of post operative nausea and vomiting[4,6,9,10]. But there are concerns that they may predispose to postoperative hemorrhage[11,12]. Paracetamol is a safe and effective analgesic but if used alone often provides insufficient analgesic effect[4,6]. We reviewed analgesics used for tosillectomy pain in our set up. The concept of "on demand analgesia" in children is a challenge to child behavior to his /her illness. This study was conducted to achieve the effectiveness of Nalbuphine dosages and minimal side effects for post op tonsillectomy analgesia.

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METHODOLOGY

Sixty children of ASA physical status I, aged 5 to 12 years, and scheduled for tonsillectomy were included in study. Exclusion criteria were bleeding diathesis, renal or hepatic impairment, cardiorespiratory disease, neuromuscular disease, neurological disorder, parental language barrier, mental retardation and cognitive impairment in child, history of chronic pain or analgesic drug use, history of severe obstructive sleep apnea syndrome, patients with airway anomalies and Down's syndrome. Children were randomly selected at the preoperative anaesthetic evaluation done the day before surgery,

using sealed envelope to be opened by anaesthesia resident at the time of induction of anaesthesia.

Written informed consent was obtained from parent/guardian of each child and approved by the hospital ethical committee. All patients were fasted 6 to 8 hours pre operatively. After taking intravenous line, lactated Ringer' solution started and monitors (NIBP, ECG , Pulse oximeter and temperature probe) were applied .General anaesthesia was induced with intravenous Propofol 2mgkg^{-1}, Atracurium 0.5mgkg^{-1}, Nalbuphine 0.25mgkg^{-1} in group A and Nalbuphine 0.1mgkg^{-1} in group B, maintenance of anaesthesia with Sevoflurane and Nitrous oxide with Oxygen. Intraoperative monitoring was heart rate, NIBP, ECG, SpO_2 and temperature. Intravenous Dexamethasone 0.1mgkg^{-1} given to all patients intraoperatively. After operation, neuromuscular blockade was reversed with intravenous Neostigmine (0.04mgkg^{-1}) and atropine (0.02mgkg^{-1}). After tracheal extubation done in lateral position on awakening. Patients were transferred to the recovery room. In recovery room assessment of postoperative pain was performed by an observer, who was blinded to group allocation at the induction of anaesthesia. Postoperative pain was assessed by using Children Hospital of Eastern Ontario Pain Scale (CHEOPS). In the recovery room, non invasive BP, ECG, heart rate, SpO_2 was monitored for 50 to 90 minutes. and assessment of pain score was assessed at 5, 15, 30, 45, 60, 75 and 90 minutes using the (CHEOPS) established by McGrath et al[13] . Postoperative complications like nausea, vomiting, were observed and recorded. Patients with postoperative CHEOPS score of more than 5 were given intravenous Nalbuphine 0.05 mg kg^{-1} to 0.1 mg kg^{-1}. Recovery times were defined as time from when the patient entered the recovery room to when they were cleared consciousness, stability of vital signs and absence of side effects. Grading of pain intensity using CHEOPS SCORE was as: Mild pain < 6, moderate pain from 6 to 8 and severe pain > 8 (CHEOPS scale- Table 1).

The sample size was calculated by using Prevalence of rescue analgesia in Group A is 10% and 39.4% in Group B, 80% power of study and 95% confidence level with 5% margin of type –I error using following formula (using WHO Formula):

$$n = \frac{\left\{ z_{1-\alpha}\sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)} \right\}^2}{(P_1-P_2)^2}$$

With the following assumptions:

A significance criterion of 0.05 (5%) and a with 95% confidence level. i.e., Use α = 0.05

A 95% degree confidence corresponds to $\alpha = 0.05$.

So, $\alpha/2 = 0.025$. In the Table of the Standard Normal (z) Distribution, the critical value is therefore $z_{\alpha/2} = 1.96$.

Zcrit = 1.96 at α = 0.05 (Two-tailed test).

n= Estimated Sample Size for each group (No. of cases in each group)

P1=Prevalence of 10% in Group A is 72%

P2=Prevalence of 39.4% in Group B is 32%

Z1-α=Standardized value of Z at Alpha (α)=5%

Z1-β= Standardized value of Z at 1-β = 80%

Solving the Above equation for sample size n,

We get, n=60 patients (30 patients in each group).

Study groups

Group A: In this group patients were treated with 0.25 mg kg^{-1}

Group B: In this group patients were treated with 0.1 mg kg^{-1}

Sampling Technique: Non Probability, Purposive Sampling.

RESULTS

Patients were analysed using Numerical data like patient age, weight, duration of surgery and measurement of post op pain score in children by using CHEOPS score and compared by using student 't' test. Data of 60 children were analysed. 30 children in group A and 30 children in group B, there was no significant difference in patients age, weight and duration of surgery in two groups. (Table 2)

There was a significant reduced requirement of analgesia in immediate recovery of group A, CHEOPS score was 4±0.18 (P value=0.001) and this was effective analgesia as CHEOPS score measured till 50 to 90 minutes (Table 3) (Fig 1). In group B, CHEOPS score was significantly high indicating the additional doses of Nalbuphine just after extubation and in Immediate recovery as CHEOPS (5.33±1.8 to 4.2±6.1 P value=0.07). Side effects, especially PONV were similar in two groups as 4% presented with moderate nausea and 11% mild nausea, 5 % presented with vomiting .Mild sedation was noted in 73% (Table 4)

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Table: 1: Children's Hospital of Eastern Ontario Pain Scale (CHEOPS)

Item	Behavior	Score	Definition
Cry	No cry	1	Child is not crying
	Moaning	2	Child is moaning or quietly vocalizing, silent cry
	Crying	2	Child is crying but the cry is gentle or whimpering.
	Scream	3	Child is in full-lunged cry; sobbing: may be scored with complaint or without complaint
Facial	Composed	1	Neutral facial expression
	Grimace	2	Score only if definite negative facial expression
	Smiling	0	Score only if definite negative expression
	None	1	Child is not taking
Child verbal	Other complaints	1	Child complaints but not about pain, e.g., "I want to see my mommy," or "I am thirsty."
	Pain complaints	2	Child complaints about pain.
	Both complaints	2	Child complaints about pain and about other things, e.g., "It hurts; I want my mommy."
	Positive	0	Child makes any positive statement or talk about things without complaints
Torso	Neutral	1	Body (not limbs) is at rest; torso is inactive.
	Shifting	2	Body is in motion in a shifting or serpentine fashion.
	Tense	2	Body is arched or rigid
	Shivering	2	Body is shuddering or shaking involuntarily.
	Upright	2	Child is vertical or in upright position
	Restrained	2	Body is restrained
Touch	Not touching	1	Child is not touching or grabbing at wound.
	Reach	2	Child is reaching for but not touching wound.
	Touch	2	Child is gently touching wound or wound area.
	Grab	2	Child is grabbing vigorously at wound.
	Restrained	2	Child's arms are restrained.
Leg	Neutral;	1	Legs may be in any position but are relaxed; includes gentle swimming or serpentine-like movements.
	Squirming / kicking	2	Definitive uneasy or restless movements in the legs and/or swimming or serpentine-like movements.
	Drawn up / tensed	2	Legs tensed and/or pulled up tightly to body and kept there striking out with foot or feet.
	Drawn up/tensed	2	Legs tensed and/or pulled up tightly to body and kept there
	Standing	2	Standing, crouching, or kneeling.
	Restrained	2	Child's legs are being held down.

From McGrath P, Johnson G, et al.: CHEOPS: A behavioral scale for rating postoperative pain in children. In Fields H, editor: Advances in pain research and therapy. New York, 1985, Raven Press, pp 395-404

Table 2: A comparison of patients and surgical characteristics

Variable	Group A	Group B	Significance
Age Years (Mean)	7.72 ± 1.85	7.73 ± 1-99	P value = 0.974
Weight kg (mean)	28 ± 5.05	26.1 ± 5.96	P value =0.154
Duration of surgery min (mean)	49.53 ± 5.75	49 ± 5.58	P value =0.71

Table 3: A comparison of CHEOPS score in postoperative time between Group A and B

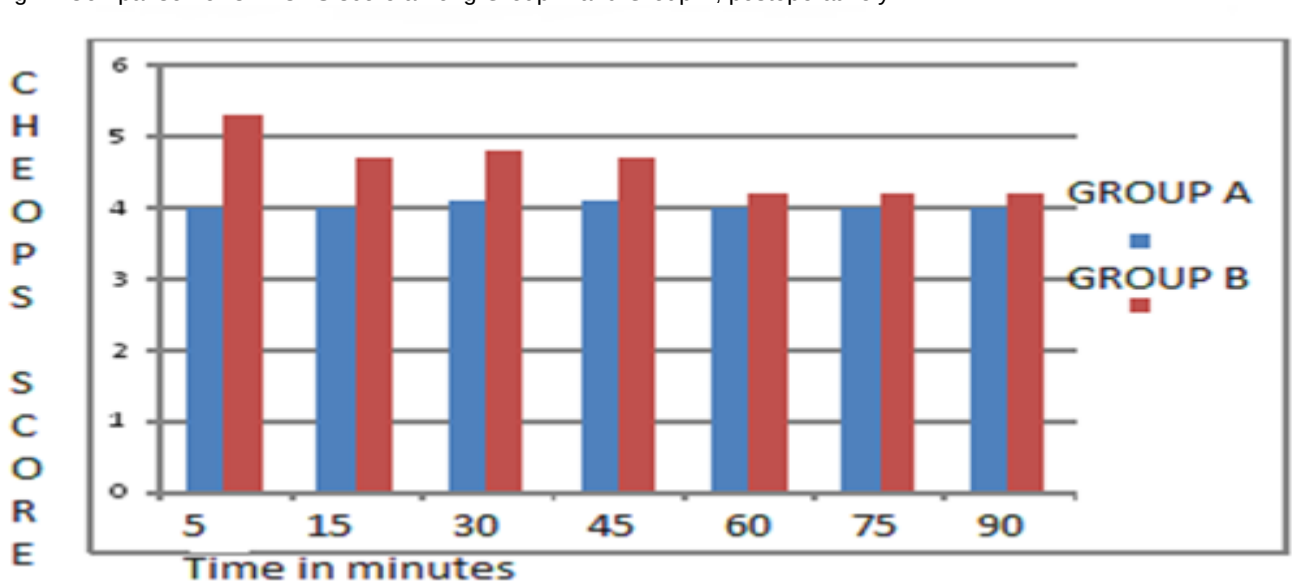
Time (Min)	Mean CHEOPS Score Group A	Mean CHEOPS score Group B	Significance
5	4 ± 0.18	5.33 ± 1.8	P value = 0.001
15	4± 0.18	4.7 ± 1.5	P value = 0.02
30	4.1± 0.4	4.8±1.6	P value = 0.02
45	4.17±0.5	4.7±1.5	P value =0.07
60	4.07±0.36	4.23±0.62	P value=0.21
75	4± 0.01	4.4±0.6	P value =0.07
90	4.0±0.01	4.2±0.61	P value =0.07

Overall Mean CHEOPS Group A = 4.05 ± 0.30
Overall Mean CHEOPS Group B = 4.59 ± 1.33
P value = ≤ 0.05

Table: 4: Patients exhibiting side effects

Side effects	None		Mild		Moderate		Severe	
	A(n=30)	B(n=30)	A(n=30)	B(n=30)	A(n=30)	B(n=30)	A(n=30)	B(n=30)
Sedation	8(26.6%)	7(23.3%)	22(73.6%)	23(76.7%)	none	None	None	none
Nausea	26(86.6%)	24(80%)	3(10%)	3(10%)	1(3.33%)	3(10%)	none	none
Vomiting	28(93.3%)	27(90%)	1(3.33%)	1(3.33%)	1(3.3%)	2(6.66%)	none	none
Blurred vision	26(86.6%)	24(80%)	4(13.3%)	6(20%)	None	none	none	none

Fig. 1: Comparison of CHEOPS score among Group A and Group B, postoperatively



DISCUSSION

In this study, we observed the effective post op analgesia with the use of 0.25 mg kg^{-1} Nalbuphine as compared to 0.1 mg kg^{-1} of Nalbuphine at induction. It has advantage of greater acceptability and predicatability of clinical effectiveness of the two recommended doses. Many approaches to analgesia have been proposed to minimize the morbidity of posttonsillectomy pain. The importance of effective and safe post op analgesia of paediatric tonsillectomy is a demanding task for the anaesthetist. The objective to achieve pain free tracheal extubation and wake up makes easier to keep clear airway, oxygenation and co-operative child. There were certain risks if moderate to severe post op pain of tonsillectomy treated with Morphine sulphate resulting in an acceptable high incidence of PONV unless antiemetics are used[5,6]. Safety was also unpredictable due to risks of respiratory depression of Morphine[14]. Post tonsillectomy, upper airway obstruction was reported where oral Midazolam was used as premedication in combination with morphine for post op analgesia[15]. NSAIDS are effective analgesic but due to risk of hemostasis derangement caused by the inhibition of thromboxane A_2 and the consequent decrease in platelets function. The NSAIDS increased the risks of reoperation for haemostasis after tonsillectomy[16]. Paracetamol is a safe analgesic, if used alone, often provides unsatisfactory analgesia[17]. Ketamine peritonsillar infiltration reduces PACU time and early (6 to 24 hours) pain intensity and reduces PACU analgesic requirement[18]. In our study, we administered semisynthetic agonist antagonist analgesic Nalbuphine with therapeutic dose 0.25 mg kg^{-1} at the time of induction of general anaestheia and analgesic effectiveness and safe convenience was observed in post op period. In immediate recovery from general anaesthesia, children not only cry but often become wild, thrash if analgesia is inadequate and can result in postoperative bleeding of tonsillectomy. It has been studied that children have consistently been offered/or received fewer, smaller and less frequent doses of opioids analgesics. Mukherjee K et al studied Fentanyl instead of morphine as it has rapid onset and less PONV than morphine sulphate although the incidence is not clear[19]. But fentanyl was not available in our set up. Limitation of post op pain management in our set up is due to lack of organized post op pain services. One of the goals of surgery is the provision of pain free PACU outcome. Recent survey in the United states and Europe by Apfelbum

and Benhamou D has emphasized the insufficient quality of post operative pain management and need for further improvement[20,21]. Opioid analgesics produce inadequate analgesia due to improper dosages or improper dosages schedules .

Nalbuphine hydrochloride [(-)-17 (cyclobutylmethyl)-4, 5α- epoxymorphinan-3,6α,14-trial hydrochloride] is a synthetic narcotic agoinst-antagonist analgesic[22]. It is structurally related to narcotic antagonist, naloxone, and to the potent narcotic analgesic, oxymorphone. In regard to morphine, nalbuphine could induce less respiratory depression at high dose and less effect on arterial pressure[23]. When it is used in increasing dosages, respiratory depression reaches a ceiling effect, unlike the reaction that occurs with morphine and meperidine that increases respiratory depression with increasing dosages[24]. In our study, we observed this significant effect of nalbuphine. Nalbuphine is effective analgesic and recommended initial pharmacological dose is (0.3 mg kg^{-1}) (I/M, I/V, S/C) in children[24]. Jailon and colleagues[25] have shown that the elimination half life of nalbuphine is shorter in infants of 1.5–5 year than in those of 5 – 8.5 year and that systemic clearance per kilogram of body weight decreased with age. Studies of different doses of nalbuphine to compare the analgesic efficacy are few. A study by F. Bressolle, S. Khier, A. Rochette, et al[26], used allometric power model for dose adjustment. Patients who completed the study received administered doses of nalbuphine ranging from 1–1.4 mg-kg^{-1} day^{-1} (mean, 1.12 mg kg^{-1} day^{-1}) including one to four additional bolus doses required in 14 children to maintain adequate pain relief in children undergoing laparascopic fundoplication for gastro oesophagcal reflux aged 1–11 year. The bolus dose at the initiation of treatment ranged between 0.18 and 0.21 mg kg^{-1} (mean, 0.2mg kg^{-1}), the maintenance dose ranged between 0.73 and 0.83 mg kg^{-1} (mean, 0.8 mg kg^{1}). The maximum dose of 1.4 mg kg^{1} day^{1} was administered to two children of 4.1 and 5.5 year old. Acetoaminophen was also administered four times a day in this study. In our study, we administered two different therapeutic doses 0.1 mg kg^{1} and 0.25 mg kg^{1} of nalbuphine at induction of general anaesthesia in children of age range 5–12 years. The result of our study showed a reduced requirement of analgesia in immediate recovery room in group A, as CHEOPS score was 4± 0.18 till 50–90 minutes.

A study by Diana Moyao_Garcia, Juan C. Hernandez. Palacious et al[27] on nalbuphine versus tramadol administered through continuous intravenous infusion for postoperative pain control in children. The bolus/infusion regimen of Tramadol evaluated in this study appears to have better postoperative analgesic efficacy than the bolus/infusion regimen of nalbuphine. Incidence of PONV was high in Tramadol regimen as compared to nalbuphine regimen. In posttonsillectomy analgesia, PONV is undesirable.

A study by G.B. Bikhazi[28], to compare the parentral analgesic properties and side effects liability of 0.1-0.12 mg kg^{-1} intramuscular nalbuphine hydrochloride to the same dose of morphine hydrochloride in postoperative paediatric patients concluded that nalbuphine and morphine were equipotent on milligram to milligram basis for the relief of moderate to serve post-operative pain. In this study, the postsurgical patients were for circumcision under general anaesthesia on outpatient basis. In this study, they administered analgesic (morphine or nalbuphine) in postoperative period as on demand basis. The safety of Nalbuphine is similar to our study but the dose of Nalbuphine, they used 0.1 - 0.12 mg I.m. While we compare this dose with the 0.25 mg kg^{-1} I.V dose and we administered at the time of induction of general anaesthesia of tonsillectomy patients.

Michelle c. White and Judith a. Molan[29], they used guidelines, a combination of paracetamol, nonsteroidal antiinflammatory drugs and fentanyl, provide excellent analgesia with minimal postoperative nausea and vomiting after elective tonsillectomy and adenotonsillectomy. As a result the routine use of morphine and antiemetics can be avoided. In our set up, fentanyl is not available. Nonsteroidal anti inflammatory drugs also avoided as the risk of reoperation. In our study, we used nalbuphine in two different doses to achieve the maximum analgesic effect without significant postoperative nausea and vomiting and respiratory depression like Morphine.

Inadequate analgesia in the recovery room affects the efficiency of recovery room. The age group of children of 5–12 year are usually anxious to wake up pain free. A more child centered approach to the postoperative analgesia is desirable, without the risk of respiratory depression, PONV, bleeding.

The outcome of our study, that children were relatively healthy and undergoing routine elective tonsillectomy without comorbidities as OSAS (Obstructive Sleep Apnea Syndrome), Down's syndrome, airways anomalies, cardirespiratory, neuromuscular disease. But the challenge stressed when risk factors are present. Incidence of nausea, vomiting were less in our study as shown in table 4, it can be explained as we used propofol as induction agent. The use of propofol in balanced or total intravenous anaesthesia (TIVA) significantly reduces the incidence of post op nausea vomiting[24]. We administered dexamethasone 0.1mg kg^{-1}

intraoperatively. Reported consensus opinion is that dexamethasone promotes earlier return to oral intake after adenotonsillectomy[30]. Its anti inflammatory and with heightened analgesic sensitivity to opioids may have facilitated a reduction of opioid dosages [31]. Analyzing the risk to benefit ratio of analgesic drug therapy, we used 0.1 mg kg^{-1} of Nalbuphine and 0.25 mg kg^{-1} of Nalbuphine at the induction time in two groups of similar age, weight and duration of surgery as show in Table 2 .We organized recovery room facility as it was near to operating room and was under supervision of consultant anaesthetist. In recovery room, dedicated trained staff nurse, routine monitoring and airway management equipment was available. The risk of respiratory depression and PONV was readily accessible to manage. Pain score was assessed and recorded to keep pain free recovery room stay. All patients were fully awake within one hour after operation in recovery room. No patient in this study suffered from any serious complications and none of the patients required re-operation for bleeding.

CONCLUSION

We conclude that Nalbuphine in therapeutic doses of 0.25 mg kg^{-1} at the time of induction of general anaesthesia is effective dose to keep the pain free wake up and recovery room stay for children of 5 to 12 year for tonsillectomy without the comorbidities as OSAS (Obstructive Sleep Apnea Syndrome), airways anomalies. It provides child centered approach to post op analgesia for tonsillectomy without significant side effects.

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