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ORIGINAL ARTICLE

Effects of Nalbuphine with Morphine on Mean Systolic and Mean Diastolic Blood Pressures after Laryngoscopic Tracheal Intubation in Elective Coronary Artery Bypass Grafting

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ABSTRACT

Background: The raise in mean blood pressure and heart rate associated with intubation and laryngoscopy is harmful for patients of ischemic heart disease, hypertension, raised intracranial and intraocular pressure. To counter this problem nalbuphine began to be used. Nalbuphine is an opioidagonist antagonist which acts on ê receptor as agonist and on µ receptors as antagonist. We chose to study its haemodynamic response to orotracheal intubation.
Aim: To compare the mean systolic and diastolic blood pressure with nalbuphine with morphine after laryngoscopic tracheal intubation in elective coronary artery bypass grafting.
Methods: The study was a randomized controlled trial. 100 patients fulfilling selection criteria were included in the study from Operation theatre of Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Karachi. Patients were randomly divided in two equal groups by using lottery method. In group A, morphine was administered and in group B, Nalbuphine were administered during induction of general anaesthesia. History was taken from patients. Demographic information like age, gender and co-morbid. Patients were followed for results of the study. All information of was noted and entered in the Proforma.
Results: One hundred patients fulfilling selection criteria were included in the study. In group A, morphine was administered and in group B, Nalbuphine were administered during induction of general anaesthesia. Comparison of SBP and DBP has been done between both of the study groups mean and SD of SBP in morphine group was 113.16 and 9.15(p-value=0.007), in nalbuphine group 120.90 and 11.46(p-value=0.03), respectively.
Conclusion: It had been considered that morphine offers better analgesic conditions, but it also cause hemodynamic instability. nalbuphine can help in preventing anaesthesia complications, and cause less hemodynamic instability which results in less requirement of maintenance drugs for attenuation. This study to confirmed that nalbuphine can help in less fluctuation in hemodynamic conditions of the patients as compared to morphine.
Keywords: Coronary artery bypass grafting, systolic blood pressure, diastolic blood pressure, nalbuphine, morphine

INTRODUCTION

To provide symptomatic relief, improve the quality of life, and lengthen life expectancy for CAD patients, CABG was first developed in the 1960s[1]. Laryngoscopy and intubation are harmful for individuals, especially those with hypertension, ischemic heart disease, increased intraocular and intracranial pressure, and elevated heart rate and mean blood pressure[2]. In order to explore its haemodynamic response to orotracheal intubation, this urge led to the introduction of nalbuphine.Nalbuphine is an opioid agonist antagonist which acts on ê receptor as agonist and on µ receptors as antagonist. It is the optimal analgesic to be used in controlled anaesthesia due to its cardiovascular stability, extended duration of analgesia, and probable safety in overdosage[3]. The tachycardia, hypertension, and cardiac workload brought on by laryngoscopy and endotracheal intubation are successfully decreased by nalbuphine[4].

In a study conducted in India, it was reported that with morphine (n=30), the mean SBP was about 114±10mmHg and mean DBP was about 72.5±10mmHg, while with Nalbuphine (n=30), mean SBP was about 119±10mmHg and mean DBP was about 77±10mmHg during intubation in open gynaecological surgery, assuming the same statistics for general anaesthesia in CABG. The difference was found to be insignificant ($p>0.05$)[5]. Rationale of this study is to of this study is to compare the mean systolic and diastolic blood pressure with nalbuphine versus morphine after laryngoscopy and tracheal intubation in elective CABG. The researcher goal is to conduct this study to confirm whether nalbuphine can help in less fluctuation in hemodynamic conditions of the patients as compared to morphine in Pakistan. Whether in future we may be able to implement the results of this study and make nalbuphine a drug of choice in elective surgeries under general anaesthesia. This will update the local guidelines as well as improve our practice.

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METHODOLOGY

This randomized controlled trial was conducted in the Department of Anaesthesia, National Institute of Cardiovascular Diseases, Karachi for a period of six months from April 2016 to October 2016 after approval of study. Sample size of 100 cases; 50 cases in each group are calculated with 95% confidence level, 90% power of test and taking magnitude of SBP i.e., 114±10mmHg with morphine and 119±1.0mmHg with Nalbuphine injection given during laryngoscopy and tracheal intubation in open gynaecological surgery, assuming the same statistics for elective CABG. Sampling technique used was non-probability, consecutive sampling.
Inclusion criteria: Patients of age range 35-75 years of either gender undergoing elective CABG under general anaesthesia with ASA III & IV.
Exclusion criteria:

- Patients not agreed to take part in study
- Patients with known allergy to opioids and anticipated difficult intubation
- Patients with respiratory insufficiency (dyspnoea or asthma or COPD), history of recent head injury and raised intracranial pressure (ICP>15mmHg), renal (creatinine>1.2mg/dl) or hepatic insufficiency (AST>40IU, ALT>40IU), anaemia (Hb<10mg/dl)

- Haemodynamic instability (BP≥140/90mmHg), abnormal thyroid function (TSH>5U/L), administration of opioid in the last 4 hours or chronic use.

Following clearance by the hospital's ethical committee, 100 patients who met the study's eligibility requirements were drawn from the Department of Cardiac Surgery at the National Institute of Cardiovascular Diseases in Karachi. Patient demographics (name, age, gender and BMI) and informed consent were gathered. The lottery approach was used to randomly split the patients into two equal groups. When general anaesthesia was being induced, morphine was given to group A and nalbuphine to group B. Alprazolam 0.25mg was administered orally to the patients the night before and the morning of the procedure. After being moved to the operating room, patients underwent ECG, pulse oximetry, and non-invasive blood pressure monitoring. 90 seconds of bag and mask breathing were followed by endotracheal intubations. After intubation, end tidal carbon dioxide was continuously monitored. Isoflurane in oxygen was used to maintain anaesthesia at a MAC of 1-1.2. Atracurium dosages were administered as needed.

Data analysis: The data were entered and analysed using IBM SPSS 21.0. Age, height, weight, BMI, SBP, and DBP (baseline & after ten min) were quantitative variables that were provided as standard deviation and mean. The mean SBP and DBP in the two groups were compared using independent sample t-tests. P-values under 0.05 were deemed significant. Age, gender, smoking, diabetes mellitus, ASA, and BMI were used to stratify the data. T-tests were used after stratification, with a p-value of 0.05 considered significant.

RESULTS

Patients were randomly divided in two equal groups by using lottery method. In group A, morphine was administered and in group B, Nalbuphine were administered during induction of general anaesthesia. In Table 1, it is showed that patients who included in the study have age range 35-75 mean age of patients on morphine Group was 54.13 with standard deviation 13.76, mean age of patients in nalbuphineGroup was 57.03 with standard deviation 12.86,body mass index of morphine Group were showed mean 29.27 and SD 4.61 body mass index of nalbuphine Group were showed mean 28.20 and SD 5.

Table 1:

Statistics	Age	BMI
Morphine		
n	50	50
Mean	54.13	29.27
Minimum	35	24.6
Maximum	75	30.11
Std. Deviation	13.76	4.61
Nalbuphine		
n	50	50
Mean	57.03	28.20
Minimum	40	26
Maximum	75	31.11
Std. Deviation	12.86	5.95
Overall		
n	50	50
Mean	56.98	24.6
Minimum	35	24.6
Maximum	75	31.11
Std. Deviation	13.20	4.66

In morphine group there were 17(34%) study participants were female and 33(66%) were male. While in nalbuphine group 23(46%) study participants were female and 27(54%) were male. Proportion of male participants were high then female. In morphine group there were 36(72%) study participants were smokers and remaining were non-smokers While in nalbuphine group 40 (80%) study participants were smokers and only 10(20%) were non-smokers this was showed that smoking is the leading factor of heart disease. In morphine group there were 38 (76%) patients were having diabetes mellitus and in nalbuphine group 32(64%) were diabetic rest of them were non-diabetics. In morphine group there were 43(86%) study participants had ASA status III and remaining were having ASA status IV While in nalbuphinegroup 42 (84%) study participants were having ASA status III and only 18(16%) were having ASA status IV. In morphine group there were 35(70%) patients had BMI >27 and in nalbuphine group 32(64%) were overweight and obese.

Table 2:

Groups	Morphine	Nalbuphine
Gender		
Male	17(34%)	23(46%)
Female	33(66%)	27(54%)
Total	50(100%)	50(100%)
Smoking status		
Yes	36(72%)	40(80%)
No	14(28%)	10(20%)
Total	50(100%)	50(100%)
DM		
Yes	38(76%)	32(64%)
No	12(24%)	18(36%)
Total	50(100%)	50(100%)
ASA Status		
Yes	43(86%)	42(84%)
No	7(14%)	8(16%)
Total	50(100%)	50(100%)
BMI		
<27 kg/m^2	*15(30%)*	*18(36%)*
>27 kg/m^2	*35(70%)*	*32(64%)*
Total	*50(100%)*	*50(100%)*

In Table 3 & 4 comparison of SBP and DBP has been done between both of the study groups mean and SD of SBP in morphine group was 113.16 and 9.15(p-value=0.007), in nalbuphine group 120.90 and 11.46 (p-value=0.03), respectively. Result was showed significance difference between both groups in term of hemodynamic responses. Result obtained by using independent t- test as it was mentioned in the data analysis.

Table 3: Comparison of SBP between both groups
Independent t-test applied.

Groups	SBP	
	n	mean±SD
Morphine	50	113.16±9.15
Nalbuphine	50	120.90±11.46

P value 0.07

Table 4. Comparison of DBP between both groups
Independent t-test applied.

Groups	SBP	
	n	mean±SD
Morphine	50	71.76±8.9
Nalbuphine	50	75.09±10.16

P value 0.03

In Table 5 stratification of SBP and DBP between both study groups has been done with regards to age groups, gender, smoking status, diabetes mellitus, ASA status and BMI. Some of the results were showing significant differences which means these factors are affected on hemodynamic responses.

Table 5: Comparison of SBP between both groups with regards to age (35-50)
Independent t-test applied.

Groups	SBP	
	n	mean±SD
Morphine	23	111.21±10.15
Nalbuphine	20	115.39±8.16

P value 0.020

DISCUSSION

Endotracheal intubation and laryngoscopy cause sympathetic activation, which causes tachycardia andhypertension. Instability might result from these hemodynamic changes in cardiac patients during the essential time of anaesthesia induction before the heart condition is treated.[6] Tachycardia in individuals with IHD is a factor that increases the risk of perioperative myocardial ischemia and infarction because heart rate is a significant predictor of myocardial oxygen demand.[7] Therefore, it's crucial for patients with coronary artery disease having coronary revascularization to reduce their sympathetic reaction to laryngoscopy and endotracheal intubation. To correct the angle between the mouth and the glottic aperture during direct laryngoscopy, the oropharyngeal tissues must be stretched, which can be painful and result in a stress reaction.[8] Since major surgical operations like heart surgery need tracheal intubation, efforts to limit sympathetic stimulation are now focused on reducing the straining of tissues in the laryngopharynx and epipharynx. This was accomplished by using blind nasal intubation and eschewing laryngoscopy completely.

The haemodynamic alterations were found to be reduced with the fibreoptic bronchoscope, McCoy laryngoscope, and more recently, the stylescope, as compared to direct laryngoscopy.[9] These categories of patients were non-cardiac patients who were being researched. In 27 patients undergoing CABG, the laryngeal mask airway (LMA) was employed as an additional airway adjunct, and it was discovered to induce less tachycardia than direct laryngoscopy[10]. In order to perform orotracheal intubation on neurosurgical patients requiring general anaesthesia, Koyama et al. developed an airwayscope[11].

Many medications, including α-blockers, vasodilators, opioids, and sedatives, have been tried to obfuscate the pressure response to intubation, but each has drawbacks[12,13]. A good medicine should have a quick beginning of effect, be safe and simple to administer, and have an activity that lasts very briefly. With analgesic effectiveness comparable to morphine and antagonistic potency around one-fourth that of naloxone, nalbuphine is an opioid agonist antagonist which acts on ê receptor as agonist and on µ receptors as antagonist. With a dosage of 0.2-0.4 mg/kg nalbuphine has a start of action that takes place within 2-3 minutes after administration, a duration of action of 3-6 hours, cardiovascular stability, and few adverse effects.[14,15] Patients in the placebo group saw a substantial rise in HR and MAP following tracheal intubation, but nalbuphine at a dosage of 0.2 mg kg-13-5 minutes prior to laryngoscopy reduced the hemodynamic response related to laryngoscopy and tracheal intubation..

Nalbuphine and pethidine both provided excellent control of the hemodynamic response during minor gynaecological surgery, but Chestnutt also observed that the pethidine group experienced greater nausea and vomiting following the procedure.[16] As opposed to Khan[17] and Chestnutt's trial, when a greater dosage was employed, we did not see any nausea or vomiting in our patients. This leads us to the conclusion that nalbuphine (0.2 mg kg 1) given 5 minutes prior to laryngoscopy inhibits an increase in HR and MAP following laryngoscopy and endotracheal intubation.

The goal of the study was to evaluate the analgesic effectiveness of morphine (a mu agonist) vs nalbuphine (a kappa agonist) in female patients. According to several earlier research, opioids may be more effective in girls than in males. The kappa agonists nalbuphine and butorphanol;according to prior research by Gear et al. in 1999, are more significant in terms of this sexual dimorphism feature.[18] Therefore, only women were included in the study, which was conducted with this in mind. On a milligrams basis, nalbuphine's analgesic efficacy is equal to morphine's.

Additionally, the study examined both groups' intraoperative heart rates and systolic and diastolic blood pressure. The insufficient analgesia provided to 5 patients at the beginning of surgery, which may have had an impact on the mean hemodynamic values overall, can be used to explain the statistically significant jump at 10 minutes in the nalbuphine group. The direct depressive impact of morphine on the sinoatrial node and the activation of vagal nuclei in the medulla are thought to be the mechanisms by which it causes bradycardia, particularly when combined with volatile anaesthetic drugs[19]. According to Lake et al. nalbuphine causes less cardiac depression than morphine, even when given at large dosages (3 mg/kg) during cardiac operations[20].

In addition, we evaluated the side effects of both the drugs. While nalbuphine is a kappa agonist and a mild mu antagonist, morphine acts as an agonist on all opioid receptors. Therefore, morphine's analgesic action comprises both supraspinal and spinal components, whereas nalbuphine mostly possesses spinal components. Nalbuphine does not have the side effect of pruritus that morphine does.

Although the difference did not achieve statistical significance, the incidence of pruritus was higher in the morphine group (2 versus 0). Pruritis is a typical side effect of opioid consumption and is brought on by mu receptor agonism. On the other hand, nalbuphine doesn't produce pruritis since it is an antagonist at mu receptors. More PONV has been linked to morphine (48%) than nalbuphine (36%)[21]. Although there was a difference in our study (9 versus 6), no statistically significant difference could be demonstrated. In the postoperative phase, none of the patients displayed respiratory depression.

Endotracheal intubation and laryngoscopy cause sympathetic activation, which causes tachycardiaand hypertension. Before the heart condition is treated, these haemodynamic alterations in cardiac patients might lead to instability during the critical phase of anaesthesia induction. Since major surgical operations like heart surgery need tracheal intubation, efforts to limit sympathetic stimulation are now focused on reducing the stretching of tissues in the laryngo-pharynxand epipharynx.

CONCLUSION

In conclusion, this study was to compare the mean systolic and diastolic blood pressure with nalbuphine versus morphine after laryngoscopy and tracheal intubation in elective CABG. It had been considered that morphine offers better analgesic conditions, but it also cause hemodynamic instability. nalbuphine can help in preventing anaesthesia complications, and cause less hemodynamic instability which results in less requirement of maintenance drugs for attenuation. This study to confirm that nalbuphine can help in less fluctuation in hemodynamic conditions of the patients as compared to morphine. So that in future we may be able to implement the results of this study and make nalbuphine a drug of choice in elective surgeries under general anaesthesia. This will update the local guidelines as well as improve our practice.

Limitations of this study include intraoperative and postoperative haemodynamic variables and sedation were not studied. The decrease in anaesthetic dose requirements was not studied.

Conflict of interest: Nil

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