Comparison of Nalbuphine and Midazolam on the Cardiovascular Response to Laryngoscopy and Intubation

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Objective: To compare the effects of nalbuphine and midazolam on cardiovascular response to laryngoscopy and intubation during induction of anaesthesia. **Method:** Ninety adult male patients of ASA I or II status were included and divided into three equal groups. Group I was control in which 3 ml of saline was given. Group II received nalbuphine 75µg/kg and Group III received midazolam 30 µg/kg. The cardiovascular response was evaluated at laryngoscopy and every minute after intubation for three minutes.The results were analysed statistically by ANOVA.$p<0.05$ was taken significant. **Results:** A decrease in HR, SBP, DBP, MAP was seen after three minutes in Group II and III but the decrease was more pronounced in Group II.($p<0.05$) **Conclusion**: Premedication with nalbuphine 75µg/kg is more effective than midazolam in blunting the haemodynamic response to laryngoscopy and intubation.
Keywords: Laryngoscopy, endotracheal intubation, nalbuphine, midazolam, anaesthesia/induction.

Laryngoscopy and tracheal intubation produce stress response in the form of tachycardia, hypertension and increased levels of catecholamines[1,2,3]. This may lead to undesirable effects like arrythmias, myocardial infarction, left ventricular failure, cerebral haemorrhage and increase in intraocular pressure[1,3]. These responses have been attenuated by variety of drugs like intravenous opioids, intravenous lignocaine, fentanyl, alfentanil, calcium channel blockers, beta adrenergic blockers, vasodilators and deep anaesthesia with inhalational agents[1].

Nalbuphine, a synthetic agonist-antagonist opioid, reduces cardiac work, but has minimal effect on arterial pressure or heart rate. In higher doses it may cause a fall in blood pressure. It depresses ventilation and has a ceiling effect in this respect[4]. This ceiling effect is accompanied by an equally modest ability to decrease anaesthetic requirement. Midazolam, a short acting water soluble benzodiazepine has minimal cardiovascular depressant effects and it decreases stress response to tracheal intubation[5,6].

Our aim was to compare the effects of nalbuphine and midazolam on haemodynamic responses to endotracheal intubation to help the selection of a better drug in this respect.

Method:

After approval from the Department and hospital committee, 90 adult male patients of ASA I or II status, presenting for elective surgery under general anaesthesia with endotracheal intubation were included. After informed consent, three groups of 30 patients each were made by random allocation. These patients were not taking any medication with significant cardiovascular effects. After preoxygenation for 3 minutes, induction in Group I was done by thiopentone 4mg/kg and suxamethonium 1mg/kg after injecting 3ml of normal saline. The patients in Group II were induced with nalbuphine 75µg/kg prepared in a volume of 3ml, followed by thiopentone 4mg/kg and suxamethonium 1mg/kg while in Group III midazolam 30 µg/kg diluted in volume of 3 ml was given, followed by thiopentone 4mg/kg and suxamethonium 1mg/kg.Following intubation, patients were ventilated with 0.8% halothane and 50% nitrous oxide in oxygen at 10 breaths/min and anaesthesia continued as required. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded non-invasively before induction, at laryngoscopy and intubation and after intubation every minute for three minutes.

Statistical Analysis:

Concluding parameters were analysed statistically by ANOVA. $P<0.05$ was taken as significant.

Results:

Demographic data showed similarity in age and weight between groups (Table 1).

Baseline values did not differ significantly between groups. An increase in heart rate was seen in all three groups at laryngoscopy and intubation. Significant difference was found at intubation and post intubation between each group as the increase in HR persisted for the whole 3 min period after intubation in group I while a decrease in HR from baseline occurred in groups II and III.($p<0.05$) A greater reduction was seen in group II.(Table 2). A significant increase in SBP, DBP and MAP was seen in all three groups at laryngoscopy and intubation but a significant decrease was seen in groups II and III after intubation. The decrease in arterial pressure was greater in Group II than Group III.($p<0.05$)(Table 2)

Table 1:Demographic Data of the three study groups (mean values)[±sd]

	Group I	Group II	Group III
Age in yrs	31±3·3	31·4±3·2	31·2±3·1
Wt in kg	71·4±6	70±7	74·1±5

Table 2: Cardiovascular variables before and after induction (mean ±sd)

	Before induction Mean±sd	At Intubation mean ±sd	After intubation mean ±sd		
			1 min	2 min	3min
Group I					
HR	89±9·8	104±8·9	100±6·4	94±6·9	90±7·6
SBP	125±16	157±12·8	140±10	140±10	122±11
DBP	80±9·3	104±6·7	97±5·3	83±7·1	83±7·1
MAP	95±11·1	122±8·6	111±6·3	97±8·1	96±7·9
Group II					
HR	82±11·7	89±10	83±10·3	81±9·9	79±9·4
SBP	134±17·5	140±10	135±10·2	134±9·8	130±9·5
DBP	87±9·1	90±10·2	90±9·1	85±9·3	85±9·5
MAP	103±11·5	106±11·8	105±10·6	101±9·9	100±10
Group III					
HR	92±16	97±14·5	93±11·3	88±11	87±11
SBP	127±13	135±8·5	135±9·4	130±8	125±5·4
DBP	84±7·1	90±9·2	87±6·2	84±4·8	84±4·3
MAP	98±7·3	105±10·1	103±6·6	99±5·3	97±3·9

Discussion:

This study was designed to compare the effects of an opioid and a benzodiazepine on the pressor response to laryngoscopy and intubation. The haemodynamic observations were noteworthy. Significant attenuation of cardiovascular response to laryngoscopy and tracheal intubation was seen with nalbuphine and midazolam as compared to control group. Analysis of haemodynamic response to laryngoscopy and tracheal intubation showed better suppression with nalbuphine than midazolam. Many techniques and pharmacological agents have been used to suppress these responses. No single technique has been universally accepted. We used nalbuphine and midazolam to suppress these responses.Van Den Berg et al (2004) studied the effects of tramadol, nalbuphine and pethidine on cardiovascular response to laryngoscopy and tracheal intubation[7]. He found reduction in heart rate and systolic arterial pressure with nalbuphine as compared to other drugs that was similar to our study results. The changes in MAP and HR in our study were consistent with a study by O Hare et al who showed that remifentanil 1.0µg/kg when administered as a bolus after induction of anaesthesia prevented the pressor response[8].

Tomoki Nishiyama et al in 2002 found combination of midazolam-thiopental effective in reducing haemodynamic response to tracheal intubation in comparison to induction with thiopental alone. Anaesthesia was induced with 0.1mg/kg midazolam followed by 3mg/kg thiopentone sodium in one group and thiopental 5mg/kg was given in the other group. He found a smaller increase in blood pressure and HR with midazolam-thiopental group[6]. This was different than the results of our study in which a reduction was seen after intubation from baseline. The difference could be due to use of different dosages.

Sampath Shenoy et al in July 2002 showed an increase of 15-18% in HR with midazolam at induction and a decrease in SBP of 10.7%[9]. The change in HR and SBP was different from our study where a 7% increase in HR was seen at induction and a 2% decrease in SBP was seen after intubation. This change could be due to variation in methodology. They had used midazolam 0.25mg/kg as induction agent without any premedication in comparison to our study where we used midazolam as a premedicant.

Foster et al studied the haemodynamic effects of midazolam which produced statistically significant reductions in SBP (5%) and DBP (10%)[10]. These were also slightly different than our results.

I.A. McNeil found significant dose related cardiovascular depression, in their study with the use of a large dose of remifentanil. In their study post- induction heart rate decreased by 14% ($p<0.01$) with remifentanil 2µg/kg, by 19% ($p<0.001$) with remifentanil 4µg/kg, and there was 15% increase with succinylcholine.[11] These results differed in the respect that we found 5% decrease with nalbuphine after 3 minutes of intubation in our study and 2% decrease with midazolam. The difference in HR between the two studies is because of the different opioids and the doses used.

Conclusion

Where control of blood pressure and heart rate is of utmost importance to prevent detrimental effects, there is a need for a safe and effective drug to attenuate the haemodynamic response to laryngoscopy and intubation. In this study where we compared nalbuphine and midazolam, the results suggest that nalbuphine when used as premedicant in dose of 75µg/kg is better in controlling the stress response to laryngoscopy and intubation.

References.

1. Sood D, Narula N, Katyal S, Saini S, Munjal M. Repeat dose of propofol: A prophylaxis against pressor response to laryngoscopy and tracheal intubation. J Anaesth Clin Pharmacol 2002;18:304-8.
2. Farooq M, Chaudhry A.H. Control of heart rate changes with esmolol during tracheal intubation in normotensive and

hypertensive patients. Annals KEMC, Lahore, July-Dec 1996; 2:47-48.
3. Maguire AM, Kumar N, Parker JL, Rowbotham DJ, Thompson JP. Comparison of effects of remifentanil on cardiovascular response to tracheal intubation in hypertensive patients. Br J Anaesth 2001;86(1):90-3.
4. Fee H. Drugs used to supplement anaesthesia. In: Aitkenhead A.R., Graham Smith, eds. Textbook of Anaesthesia. New York: Churchill Livingstone, 1996; 169 - 172.
5. Khan MA, Khan FA. Midazolam and thiopentone co-induction: looking for improvement in quality of anaesthesia. J Pak Med Assoc 2003;53:542-7.
6. Nishiyama T, Misawa K, Yokoyama T, Hanaoka K. Effects of combining midazolam and barbiturate on the response to tracheal intubation: changes in autonomic nervous system. J Clin Anaesth 2002;14:344-8.
7. Van den Berg AA, Halliday EM, Soomro NA, Rasheed A, Baloch M. Reducing cardiovascular response to laryngoscopy and tracheal intubation: a comparison of equipotent doses of tramadol, nalbuphine and pethidine, with placebo. Middle East J Anaesthesiol 2004;17(6):1023-36.
8. O'Hare R, McAtamney D, Mirakhur RK, Hughes D, Carabine U. Bolus dose remifentanil for control of haemodynamic response to tracheal intubation during rapid sequence induction of anaesthesia. BJA 1999;82:283-5.
9. Sampeth Shenoy, Kaul HL, Murlidhar V. Induction characteristics of midazolam and thiopentone – a comparison. J Anaesth Clin Pharmacol 2002;18(3):248-54.
10. Forster A. Utilization of midazolam as an induction agent in anaesthesia. Study on volunteers. Arzneim Forsch Drug Res 1981;31:2243.
11. McNeil I.A, Culbert B, Russell I. Comparison of intubating conditions following propofol and succinylcholine with propofol and remifentanil 2μg/kg 4μg/kg. Br J Anaesth 2000;85:623-5