Original Article

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Nalbuphine versus Dexmeditomedine Effect on Hemodynamic Stress Response During Intubation

Mary Mammen[1], Sreekumar MR[2]

Author's Affiliation:

[1]Assistance Professor, Department of Anesthesiology, PIMS, Thiruvalla 689101, Kerala, [2]Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala 689105, India.

Abstract

Aims: Sympathetic system gets stimulated ondirect laryngoscopy and intubationand catecholamines are released. This response though of short duration, is hazardous to compromised subjects with brain and cardiac dysfunction. Vagus nerve also can be stimulated during laryngoscopy and intubation.

Ourstudy is to find out the effects of Nalbuphine Hcl 5mgm and Dexmedetomidine 25mgm on hemodynamic variables SBP, DBP, MAP and HR at the time of laryngoscopy and intubation. Study was carried out in Pushpagiri Institute of Medical Sciences. Consecutive sampling technique was used to select study population.

Methodology: We selected 100 subjects, ASA1 and 2, were randomly grouped into 2 groups of 50 each. All our subjects received 500ml crystalloid solution. Allsubjects were induced on Propofol and intubated on succinylcholine. The stress response was assessed by observing hemodynamic variables SBP, DBP, MAP and HR.

Statistical Analysis: Data was digitized and analyzed using SPSS22.0. Independent sample test was used to assess the difference in parameters. Data was stratified on the basis of age and weight of 2 groups. P-value of less than 0.05 was considered statistically significant.

Conclusions: Dexmedetomidine influences HR and the effect is more as age advances. In subjects heavier than 80kg, mean HR was higher. The effect of Dexmedetomidine on heart rate was statistically significant at a P value less than 0.05. Nalbuphine, according to studies, increases BP and HR. In our study, this rise in MAP was observed in subjects heavier than 70kg. But this finding was not statistically significant.

Keywords: Nalbuphine Hcl; Dexmedetomidine; Laryngoscopy; Intubation stress.

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Corresponding Author: Mary Mammen, Assistance Professor, Department of Anesthesiology, PIMS, Thiruvalla 689101, Kerala, India.

Email: marymammen121@gmail.com

Introduction

General anesthesia involves direct laryngoscopy, intubation and mechanical ventilation. Direct laryngoscopy stimulates proprioceptors at the base of the tongue and the hypothalamic pituitary axis is stimulated. Sympathetic system in turn release catecholamines and blood pressure and heart rate increases. The sympathetic response though brief can adversely affect subjects with compromised brain functions and cardiac functions.Vagus nerve stimulation can cause bradycardia and even cardiac arrest.Various pharmacological methods are being formulated to alleviate this stress response.

Nalbuphine hydrochloride is a phenanthrene opioid derivative N-Cyclobutyl methyl 4 5. a-c poxy[3,6] a1[4] Morphine.[8] Analgesic potency of Nalbuphine is 0.8 to 0.9 times that of morphine. Nalbuphine 10mgm=10mgm Morphine=75mgm Pethidine. It is a partial agonist at both mu and kappa receptors and possess agonist–antagonist property. Unlike Morphine,Nalbuphine is cardiac stable and does not produce respiratory depression and bronchospasm. It has antipruritic property too. Routes of administration can be IM,IV or S/C. Onset of action after iv route isin 2 to 3 mts and is metabolized in the liver. The dose given is 0.5 to 3mgm/kg.[8] We have used 0.1 mgm for our study in Group 1 and given a fixed dose of inj.5 mgm Nalbuphine iv as the first drug of iv induction for all our subjects in group 1.

Dexmedetomidine an alpha2 agonist dexorotatoryS. enantiomore of medetomidine an imidazolederivative.[8] It is a sedative hypnotic with sympatholytic and analgesic properties. It suppresses shivering and preserves hypercapnic response.Premedication dose is 0.33-0.67ugm iv. Different doses of the drug have been tried to find the ideal dose of drug to alleviate the pressor response during laryngoscopy and intubation.We have used 25 mic.gm iv as the first drug of iv induction for all our subjects in Group2. inj. Dexmedetomidine. Both drugs were diluted and given by second person and observer monitor hemodynamic variabilities from the time of induction every 3 minutes for next 15 mts.

Our observational study considered 100 subjects all belonging to ASA1 and 2. We have followed standard protocol for preanesthetic checkup, premedication and period of fasting. Our subjects were randomly grouped into 2 groups of 50 each Group 1 received 5mgm Nalbuphine diluted to 5ml as the first drug during induction and Group 2 received 25ugm Dexmedetomidine. Technique of anesthesia followed standard protocol. All our subjects received 500 ml ringer lactate. All our subjects were induced with inj. Propofol 2mgm/kg and intubated on 100mgm succinyl scholine. Anesthesia was maintained with nitrousoxide, O_2, vecuronium and sevoflurane. Standard monitors were used to observe the hemodynamic variants.

Objectives

- To observe MAPandHR of Subjects from the time of induction and then, every 3 minutes for 15 minutes after inj. Nalbuphine Hcl 5mgm IV was given as first drug of induction.
- To observe whether age of the subjects affect the hemodynamic variability in Group1. (Nalbuphine Hcl 5 mg).
- To observe whether weight of the subjects affect hemodynamic variability in Group1 (Nalbuphine Hcl).
- To observe MAP and HR of Subjects from the time of induction, andthen every 3 minutes for 15 minutes after inj. Dexmedetomidine 25mcg IV was given as first drug of induction (Group 2).
- To observe whether age of the subjects affect the hemodynamic variability in Group2 (inj. Dexmedetomidine 25mcg IV).
- To observe whether weight of the subjects affect hemodynamic variability in Group2 (inj. Dexmedetomidine 25mcg iv).

Methods

Study Design

A consecutive sampling technique was used to select study population.

Sample Size

Minimal sample size per each group using the formula $\frac{2(sd)^2(za+zb)^2}{\Delta^2}$

Sample size is 50 per group

Sampling Method

By block randomization and allocation concealed by sealed envelope.

Ethical Clearance

An ethical clearance was obtained from institution and an individual written and informed consent was obtained from each subject before enrolling them

Procedure

Exclusion Criteria

- Subjects with known allergy.
- Subjects with difficult airway(Mallampatti 3and 4).
- Age below 18 years and above 70 years.
- Emergency surgeries.
- Pregnancy with surgical problems.
- Subjects with cardiac problems.

We have observed 100 subjects coming for various surgical procedures under general anesthesia age between 18 to 70 years with Mallampatti score 1 and 2. All of them belonged to ASA1 and 2 considering the exclusion criteria given above. Preanesthetic checkup was done the day before. All of them were given Tab. Ranitidine 150mgm, Tab. Metaclopramide 10mg and Alprazolam 0.5 mg orally 2hrs. before surgery. All our subjects followed standard protocol for fasting. After getting informed risk consent our subjects were taken to the operation theatre. All our subjects were given 500 ml crystalloid through 20g iv cannula on nondominant hand. Standard monitors were used to monitor the hemodynamic variables.

All our subjects were monitored with ECG, NIBP, SPO_2. Preoxygenation was given for 3 minutes. Group1 received 5mg of Nalbuphine Hcl diluted to 5 ml as the first drug of iv induction and group 2 received 25 mcgm of Dexmed diluted to 5ml as first drug of induction. Hemodynamic variabilities were noted.Baseline value was taken as SBP, DBP, and HR at the onset of induction andthen every 3 mts for 15 mt. Values were collected, recorded and statistically analysed.

A rise in MAP more than 20% from baseline was considered hypertension and a fall in MAP less than 20% from baseline was treated with 3mgm ephedrine iv. A fall in HR less than 40/ mt was treated with rescue drug (inj. Atropine 0.6 mg iv) None of our subjects needed rescue drugs.

Results

Data was digitized using Microsoft excel and analyzed using SPSS 22.0. The mean and standard deviation of HR, SBP, DBP and MAP of the 2 groups at various time points were found out. The differences in these parameters between the 2 groups were assessed using Independent Sample t–test. The data was stratified on the basis of age and weight to compare the 2 groups. Pvalue of less than0.05 was taken as statistically significant.

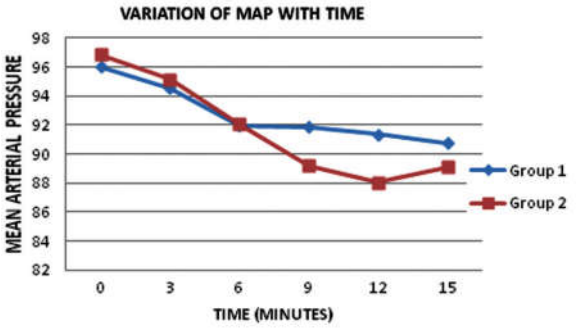

Fig. 1: Comparison of Mean Arterial pressure between the 2 groups in relation to time.

Mean Arterial Pressure of two groups were comparable. There is a significant fall in MAP from baseline between 3 and 6 minutes in both groups. No significant statistical difference was noted between the 2 groups.

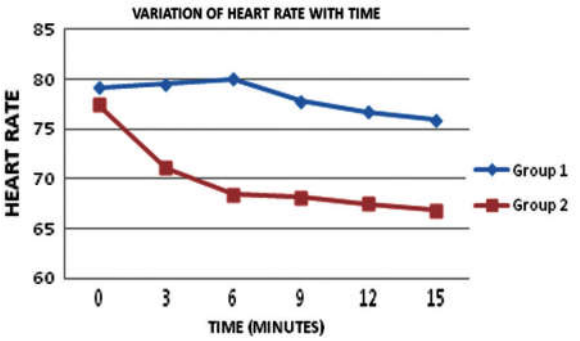

Fig. 2: Comparison of mean heart rate between group1 and group2 in relation with time.

Mean Heart rate of two groups are comparable. There is a statistically significant fall in HR from baseline in group 2 from 3 to 15 minutes. Significant p value (<0.05) noted between 2 groups at 3 to 15 minutes. Dominant action of Dexmed on the heart is decreasing tachycardia through blocking cardioaccelerator nerves and vagomimetic action through alpha 2A-AR receptor.

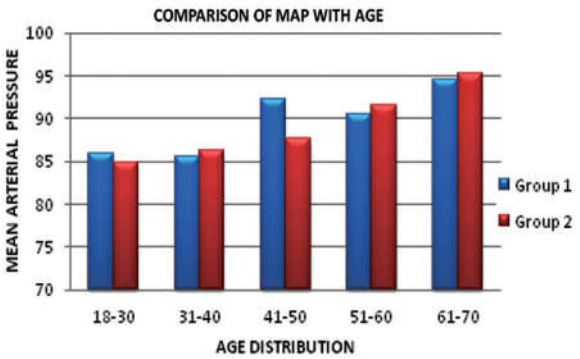

Fig. 3: Comparison of Mean Arterial Pressure in group 1 and group2 in relation to age.

MAP of Group 1 was found to be higher than Group 2 for the age group of 40-50 years but on statistical analysis there was no significant difference. The subjects were divided into 2 groups inrelation to age in both groups.[1] Group 18 to 40 years and the other 40 to70 years for statistical analysis. Dexmed evokes a biphasic response on BP. A short hypertensive response and subsequent hypotensive response mediated by 2 alpha-AR subtypes. Alpha 2 AB-AR for hypertensive response and hypotension by 2 alpha A-AR receptor.[11]

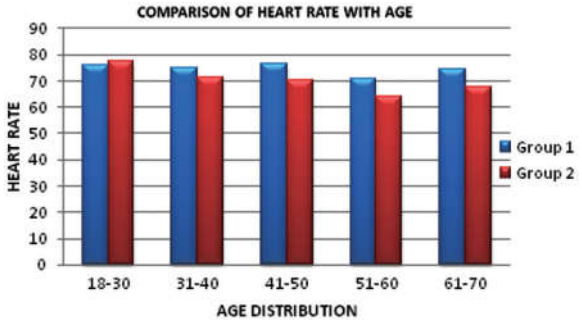

Fig. 4: Comparison of Mean Heart Rate in Group 1 and 2 in relation to age of the subjects.

Mean Heart rate in both groups were comparable with age up to 40 years. There is a significant (p value <0.05) fall in Heart rate in age between 40-70 years in Group2.In our study we had kept a HR of 40/mt as lower limit.None of our subjects needed rescue drug Atropine.[11]

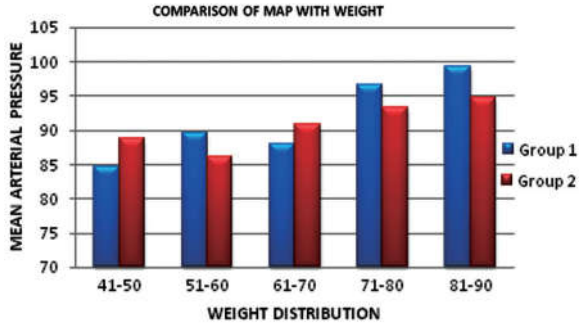

Fig. 5: Comparison of Mean Arterial Pressure in Group 1 and 2 in relation to weight of the subjects.

Mean Arterial Pressure in both Groups were comparable with weight. MAP was found to be higher in Group 1 between 70-90kg. On statistical analysis there was no significant difference with weight. These group of subjects may need higher dose of Inj Nalbuphine Hcl.The stimulation of alpha 2 b receptors on vascular smooth muscles is postulated to be the cause of increase in BP with Dexmed when given as single IV dose.

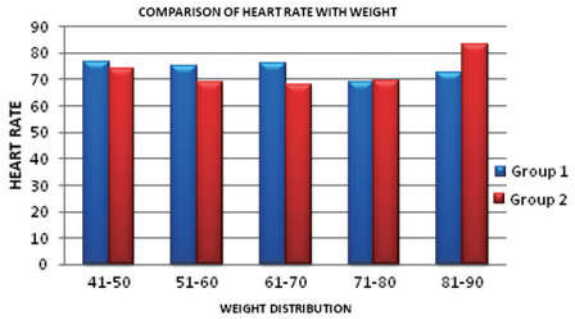

Fig. 6: Comparison of Mean Heart in Group 1 and Group 2 in relation to weight of the subjects.

Mean Heart Rate of both groups were comparable with relation to weight of the subjects. On statistical analysis there was no significant difference between the 2 groups. The Mean Heart rate was higher in subjects with Weight more than 80kg Group 2. Dexmed is a very short acting drug which gets distributed in 6mts. May be an iv infusion would have been more effective than single dose.[4]

Discussion

Group 1 subjects who received Nalbuphine were hemodynamically stable from the time of induction to next 15 minutes on observation.The MAP was higher in subjects with weight more than 80 kg. The dose of Nalbuphine was not enoughto nullify sympathetic response in these subjects. Dexmedetomidine lowered HR in Group 2. The fall in HR was more obvious in subjects above 50 years. But in subjects weighing more than 80kg, the MAP was higher indicating the need for continuous level of drug concentration through an IV infusion. Dexmed being a very short acting drug the hypotensive response is short.[6] The statistical significance was noted with HR on comparison between 2 groups and is related to its alpha 2 agonist property.

Nalbuphine a drug with agonist antagonist property is mainly used for perop and post-operative analgesia.[11] NNSudafule[12] in their comparative study on efficacy of Nalbuphine with pentazocine noted a rise in heartrate and blood pressure after intubation with Nalbuphine.Their iv dose was 0.3 mg / kg. Our drug dose is 0.1mg/kg.But we have given a fixed dose of inj. Nalbuphine Hcl(5mgm) to all our subjects and did not find any significant change in HR and.None of our subjects showed a significant rise or fall in MAP in Group1. Our induction agent Inj. Propofol 2 mgm/kg might have influenced the results.

Hariprasad et al[6] in their study on Nalbuphine

did not find any statistically significant risein heart rate. His study was on 4o patients. We also agree with his findings. Our Group 1 included 50 subjects and our drug dose was 0.1 mgm/kg. Their dose was 0.2mgm/kg. Hariprasad used isoflurane where as we used sevoflurane. Chowda et al.[5] agree to the above finding. Sohaib Basheer et al.[9] noted a significant rise in HBP, DBP and MAP with Nalbuphine. Tariq Mohammed[14] had used 0.02mg/kg Nalbuphine and found it to have stable hemodynamics in his subjects.

Dexmedetomidine is an alpha 2 agonist with sympatholytic properties.[7] It is a sedative, amnestic, analgesic with antishivering property. Dexmed is used as a safe anaesthetic adjuvant in both general and regional anesthesia.[7] It is the active dextroen antiomore of medetomidine a methylated derivative of etomidate. Sandeep Kundra[13] has used Dexmed in his study and states that it provides goodhemodynamic stability. We had given single bolus dose of Dexmed diluted to 5ml iv over 5 minutes as the first drug of iv induction. We have noted a fall in HR from baseline in our study,but not below 40/ mt.[8] A brief biphasic dose dependent cardiovascular response has been reported after initial administration of Dexmed resulting in an initial increase in BP and Fall in HR.[1] This response is more in young and healthy. Our study agrees with this finding. Manpreet Kaur et al[8] describes Dexmed can be used safely in controlled hypotension and the dose advised is 1micgm/kg to suppress laryngeal reflex during intubation.

Bajwa and Kulashethra[3] state that dexmedetomidine blunts hyperdynamic response to laryngoscopy and surgery. In the heart, dominant action is to decrease tachycardia by blocking cardio accelerator and bradycardia via vagomimeticaction. Due to its central sympatholytic effect it can be used to alleviate pressor response.Anilo Nova[2] suggests 1mcgm/kg Dexmedbolus dose to suppress hemodynamic response to laryngoscopy and intubation.

We have noted a rise in HR in group 2 in subjects aged above 60 years. This group may need a higher dose. Misra[10] in his study, found Dexmed better than Nalbuphine to suppress laryngotracheal reflex during intubation. We also noted a fall in HR from baseline. Our lower limit was 40/ mt. Lowest HR we observed in this study was 42/mt.

Conclusion

Nalbuphine maintains hemodynamic stability during laryngoscopy and intubation. It can be safely given intra venously. Dexmedetomidine gives stable MAP at our doseof 25 micgm iv. The effect of Dexmedetomidine on heart rate was statistically significant with a P value less than 0.05. Vagolytic effect was more than that on blood pressure. The fall in HR was more in older age group. Weight of the subjects modified the results in both groups.

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