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Original Research Paper

Anesthesiology

A PROSPECTIVE RANDOMISED STUDY TO ASSESS WHETHER PROPHYLACTIC ATROPINE ADMINISTRATION ATTENUATES THE NEGATIVE HAEMODYNAMIC EFFECTS OF INDUCTION OF ANAESTHESIA WITH PROPOFOL AND FENTANYL

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ABSTRACT

INTRODUCTION: To provide optimal surgical conditions safely and to avoid particular complications, balanced general anaesthesia by administering a combination of propofol and fentanyl as analgesics. This type of balanced anaesthesia often induces unwanted bradycardia and hypotension, raising concerns regarding haemodynamic stability and tissue oxygenation. It is possible that atropine could replace the common clinical practice of administering vasoactive medication such as phenylephrine or norepinephrine to maintain mean arterial pressure (MAP) levels. **AIM OF THE STUDY:** To study the effect of atropine in suppressing the negative haemodynamic effects of induction agents- propofol and fentanyl in patients receiving general anaesthesia. **MATERIALS AND METHODS:** This is a prospective randomised interventional study carried out in Department of Anaesthesiology in Kanyakumari Government Medical College from January 2018 to June 2019. Patients were allocated into two groups (25 patients each) by randomization. After preoxygenation **Group A:** Patient receives Atropine. Patient in **Group S:** Receives Saline. BMI, Height, weight, Heart rate, Non-invasive blood pressure, Mean arterial pressure were recorded for every minute for 15 minutes. **RESULTS:** The demographic parameters like age, height, weight and BMI were similar in both groups. Comparing the SBP of both group, at base and 1 minute the difference of SBP was small. After that, the SBP was increasing trend in Atropine subjects and SBP was decreasing trend in saline subjects ($P<0.001$). Comparing the DBP between the two groups, Base and 1 minutes, the DBP of both groups were not differed significantly ($P>0.05$),after that the DBP of Atropine group DBP was increasing trend and the DBP of saline group was decreasing trend ($P<0.001$). The HR of the both groups were increasing and decreasing accordingly ($P<0.001$). Comparing the MAP of both groups at base through 15 minutes,MAP of both group at 1minute was not differed significantly ($P>0.05$),after that the MAP of Atropine subjects were increasing and Saline subjects were decreasing trend $P<0.001$). Percentage of fall of parameters (SBP, DBP, HR, and MAP) was more significant at 5 and 15 mins compared to 10 mins in both group. This may be due to the intubation response after the 5th minute of induction. All values were significant with $P<0.001$. **CONCLUSION:** Administration of atropine before Propofol and Fentanyl induction during general anaesthesia can significantly attenuate the fall in Systolic Blood Pressure, Diastolic Blood Pressure, Heart Rate and Mean Arterial Pressure.

KEYWORDS : Atropine, Propofol, hypotension, Systolic and Diastolic blood pressure.

INTRODUCTION:

Anaesthetising the patients for various surgical procedures often involves combination of specific challenges , such as no patient movement, deep analgesia, fast and reliable induction and reversal of anaesthesia, swift postoperative recovery and avoidance of postoperative nausea and vomiting (PONV).To provide optimal surgical conditions safely and to avoid complications, balanced general anaesthesia with a relatively high-analgesic contribution is often desired. This state that can be readily achieved by administering a combination of propofol and fentanyl. Although very effective in achieving this combination of desired effects, induction of this type of balanced anaesthesia often induces unwanted bradycardia and hypotension, raising concerns regarding haemodynamic stability and tissue oxygenation. Fentanyl and Propofol are known to have suppressive effect on the heart rate (HR), which can be reversed by atropine, and such reversal may not only mitigate bradycardia and promote a desired increase in arterial BP, but also increases cardiac index (CI) and tissue oxygenation. It is possible that atropine could replace the common clinical practice of administering vasoactive medication such as phenylephrine or norepinephrine to maintain mean arterial pressure (MAP) levels, particularly as such vasoactive medication is often considered to induce negative effects on CI and tissue oxygenation.

AIM OF THE STUDY:

To study the effect of atropine in suppressing the negative haemodynamic effects of induction agents-propofol and fentanyl in patients receiving general anaesthesia.

MATERIALS AND METHODS:

This is a prospective randomised interventional study carried out in Department of Anaesthesiology in Kanyakumari Government Medical College after obtaining institutional ethical committee approval and written informed consent from the patients.

Randomization: Sample was randomized by closed envelope method.

Sample size is calculated using this formula

$$N = \frac{2 \times \{Z\alpha + z(1-\beta)\}^2 6^2}{\Delta^2}$$

where Zα -alpha error-1.96 (for 2 tailed study)

Z_1-β-beta error for 80% power.

6-standard deviation-10 mmHg

Δ-expected improvement-10 mmHg

The effect sample size calculated was 25.68.For convenience the sample size was calculated to be 25 in each group.

Group allocation:

Patients were allocated into two groups by randomization. **Group A** (n= 25): Patients receives Atropine. **Group S** (n= 25): Patients receives Saline.

Blinding: Double Blinded

INCLUSION CRITERIA: Age 18-60 Years, Patients Posted For Elective Surgery, ASA I and II

EXCLUSION CRITERIA:

ASA III and IV, Patients with contraindications of atropine, Patients with IHD/CAD, Patients with ECG showing tachyarrhythmia, Emergency surgeries, BMI>35, Anticipated difficult airway

INTERVENTION:

All patients were kept at fasting status for 8hrs before surgery. After written informed consent patients were randomized by closed envelope technique. In operation theatre monitors-ECG, NIBP, SPO2 were connected to the patient and baseline monitors recorded. Premedication were not administered and preoxygenated with of 100% for 3 minutes. Atropine (0.6mg/ml-1cc) or saline (1cc) was administered just before induction according to the group assigned Patients were induced with Propofol-2 mg/kg, Fentanyl-2 mcg/kg and Atracurium 0.5mg/kg and intubated with appropriate size cuffed ET tube, cuff was inflated and tube secured.

PARAMETERS MONITORED:

1.Heart rate 2.Non Invasive Blood Pressure 3.Mean Arterial Pressure (All the above three parameters were monitored before administration of atropine (T0) and every minute after induction thereafter until 15 (T1 -T15)). 4. Complications like severe hypotension, severe bradycardia and allergies if any were monitored.

STATISTICAL ANALYSIS AND INTERPRETATIONS:

The study subjects of Atropine group and Saline groups were described and compared. The continuous variables were compared between the two groups by Student independent "t" test. The categorical variables were interpreted by χ^2 test. The trends of physiological variables were illustrated by the curves of repeated measures of ANOVA (Analysis of Variance). The above statistical procedures were under taken with the help of the statistical package namely IBM SPSS version*20. The P-values less than or equal to 0.05 ($P \leq 0.05$) were treated as statistically significant.

RESULTS:

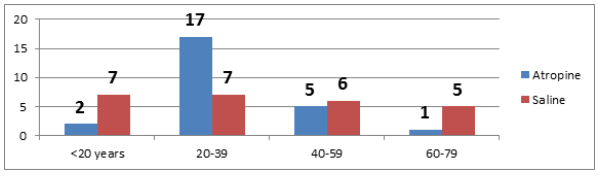


Fig-1: Comparison of age between the two groups:

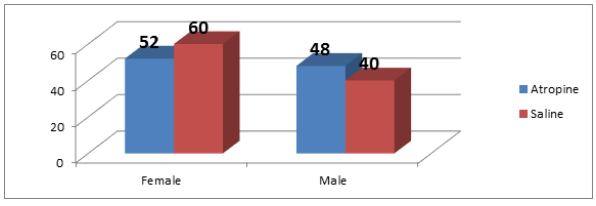


Fig-2. Comparison of gender between the two groups:

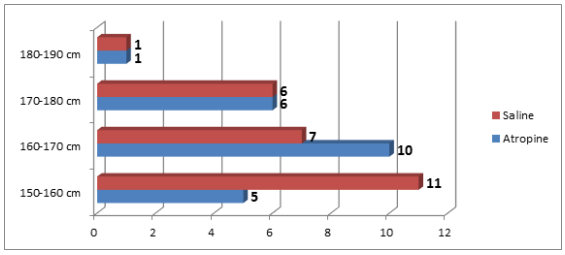


Fig-3: Comparison of heights between the two groups:

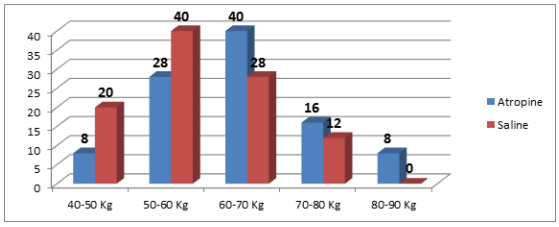


Fig-4: Comparison of weights between the two groups.

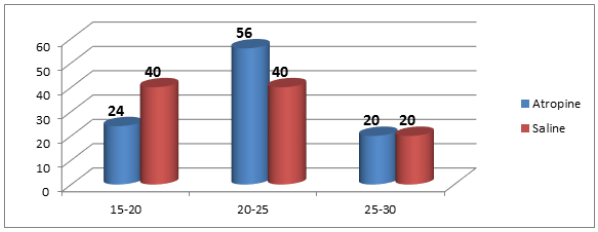
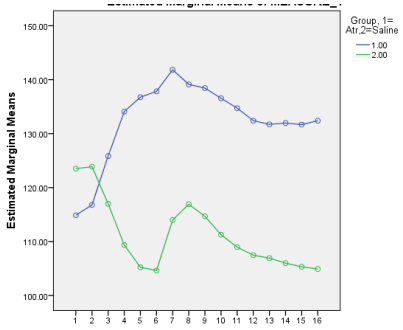


Fig-5: Comparison of BMI between the two groups:

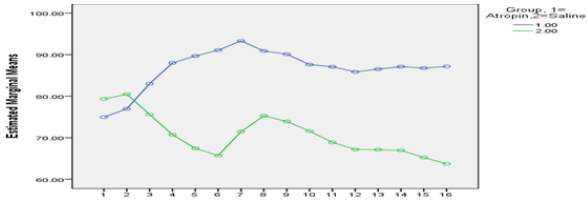
Trends of SBP from Base through 15 minutes.



Time Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Fig-6: Comparison and trends of SBP of Atropine and saline groups

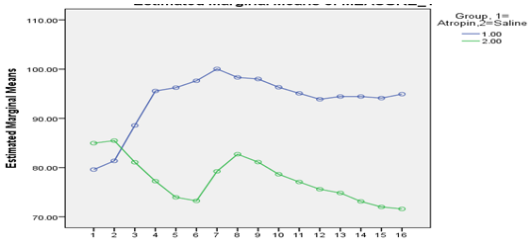
Trends of DBP from base through 15 minutes.



Time Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Fig-7: Trends of DBP between the Atropine and Saline groups.

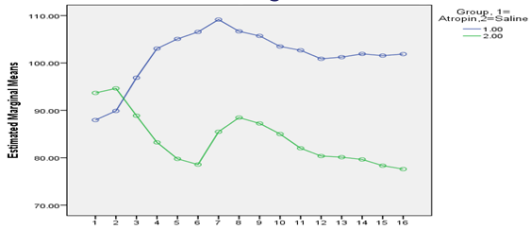
Trends of HR from base through 15 minutes.



Time Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

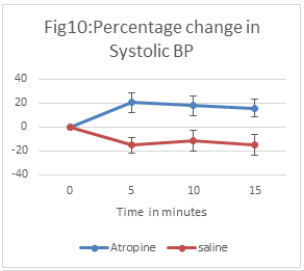
Fig-8: Comparison of trends of HR between the Atropine and saline groups

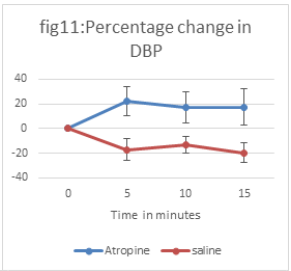
Trends of MAP from base through 15 minutes.

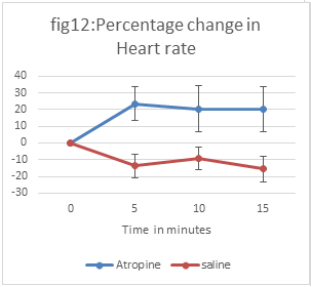


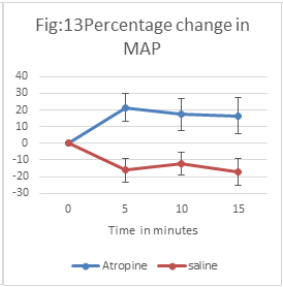
Time Base 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Fig-9: MAP trends between the two groups at base through 15 minutes:









DISCUSSION:

Induction of anaesthesia with propofol and fentanyl in a dose sufficient manner to tolerate laryngoscopy is known to induce significant bradycardia and hypotension in a majority of patients. The high level of antinociception, in synergism with a low concentration of propofol provides excellent analgesic and hypnotic conditions and complete akinesia during surgery. Simultaneously, the combination also prevents intraoperative or postoperative events that predispose to increases in intraocular pressure or pharyngeal reflexes and allows timely extubation and fast cognitive recovery. However, this combination of Fentanyl and propofol may significantly jeopardise haemodynamic homeostasis. Fentanyl provokes dose dependent depressor effects on both sinus and atrioventricular (AV) node function, manifested by a significant prolongation of sinus node recovery time, sinoatrial conduction time and Wenckebach cycle length, and inhibits both intra-atrial conduction and sinus node automaticity. These effects can be mitigated by administration of fluid or giving various vasopressor agents like atropine, ephedrine, phenylephrine, norepinephrine, epinephrine. Phenylephrine showed variable individual responses and ethnic variations. Alpha$_1$ receptor-mediated vasoconstriction caused by phenylephrine typically reduces CO due to decreased stroke volume and arterial compliance. Atropine by inhibiting presynaptic muscarinic receptors facilitates norepinephrine release. Though norepinephrine also cause arterial vasoconstriction, it increases CO compared with phenylephrine, due to positive inotropic effects. So cardiac output is better preserved with atropine compared with others. In our study, atropine completely prevented the occurrence of bradycardia, with a fully preserved HR after the induction of anaesthesia, compared with a significantly decreased HR in the saline group at this time.

Although there was a short period of increased HR with atropine, this was within acceptable limits and lasted only few minutes. The increase in HR is not entirely attributable to atropine as it coincided with endotracheal intubation. Most importantly MAP was preserved significantly better in the atropine group compared with the control group. Although direct inhibition of myocardium or atrio-ventricular conduction by propofol has also been suggested as a cause of the Brady arrhythmia, relative activation of the parasympathetic nerve system including varoreflex resetting or attenuation of varoreflex regulation is generally considered responsible. Administration of vagolytics would thus be reasonable for preventing propofol-induced bradycardia and some investigators have recommended this strategy. The demographic parameters like age, height, weight and BMI were similar in both groups. Comparing the SBP of both group, at base and 1 minute the difference of SBP was small. After that, the SBP was increasing trend in Atropine subjects and SBP was decreasing trend in saline subjects ($P<0.001$). Compares the DBP between the two groups, Base and 1 minutes, the DBP of both groups were not differed significantly ($P>0.05$). After that the DBP of Atropine group DBP was increasing trend and the DBP of saline group was decreasing trend ($P<0.001$). The HR of the both groups were increasing and decreasing accordingly ($P<0.001$). Compares the MAP of both groups at base through 15 minutes. The MAP of both groups were at 1minute was not differed significantly ($P>0.05$). After that the MAP of Atropine subjects were increasing and Saline subjects were decreasing trend $P<0.001$).

The percentage change in Systolic BP in saline group vs atropine group was - 15.2±6.5% vs 20.3±8.2%,-11.6±8.9% vs 17.8±8.3% ,-14.8±8.8 vs 8.8% at 5 ,10,15 mins respectively. Percentage change in diastolic BP was -17.3±9.0% vs 22.0±11.7,-13.1±7.00% vs 17.0±13.2%,-20.0±8.0% vs 17.3±15.0% at 5,10,15 mins respectively. Percentage change in heart rate was -13.6±7.2% vs 23.3±10.3%,-9.1±7.0% vs 20.4±14.0%,-15.6±7.7% vs 20.1±13.9% at 5,10,15 mins respectively. Percentage of change in mean arterial pressure was -16.2±7.3% vs 21.5±8.6% ,-12.3±6.9% vs 17.3±9.6%,-17.1±8.1% vs -16.4±11.0% at 5 ,10,15 mins respectively.

CONCLUSION:

Administration of atropine before Propofol and Fentanyl induction during general anaesthesia can significantly attenuate the fall in Systolic Blood Pressure, Diastolic Blood Pressure, Heart Rate, Mean Arterial Pressure.

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