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COMPARATIVE EVALUATION OF EFFECTS OF DEXMEDETOMIDINE AND CLONIDINE PREMEDICATION ON PERIOPERATIVE HEMODYNAMIC STABILITY AND POSTOPERATIVE ANALGESIA IN UPPER ABDOMINAL SURGERIES.

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ABSTRACT **Background and Aim:** Maintenance of perioperative hemodynamic stability and providing postoperative analgesia is of utmost importance in the all types of surgeries to prevent morbidity and mortality. Present study aims to compare the effects of dexmedetomidine and clonidine premedication on perioperative hemodynamic stability and postoperative analgesia in upper abdominal surgeries. **Method:** One hundred patients of both sexes aged 20-50 years belonging to ASA Grade I and II scheduled for elective upper abdominal surgeries under general anaesthesia were randomly divided into two groups of 50 each (n=50). Group I patients were given 2 ug/kg of clonidine and group II patients were given 1 ug/kg of dexmedetomidine, each diluted in 20 ml with normal saline and given over 10 min intravenously before induction of anaesthesia. Hemodynamic parameters (heart rate, systolic, diastolic and mean blood pressures), SpO2, Respiratory rate, duration of analgesia and sedation scores were recorded at predecided time intervals and analysed for statistical significance. **Results:** The mean trend of HR was slightly higher in Group-II at 1-5 minutes and specially after 45 min till extubation. RR, SpO2, SBP, DBP and MAP did not differ significantly between the two groups (p>005). The time to rescue analgesic requirement was significantly shorter in group I as compared to Group II (p<0.001). Mean sedation score of group-II at the time of extubation was significantly higher as compared to Group I (p<0.001).

KEYWORDS : dexmedetomidine, clonidine, perioperative hemodynamic stability, post operative analgesia, upper abdominal surgeries.

INTRODUCTION

Upper abdominal surgery is defined as a surgery involving an incision above or extending above the umbilicus, therefore including surgeries involving stomach, intestines, gallbladder, liver, spleen, pancreas and kidneys. General anaesthesia is the preferred technique for conducting such surgeries. During preoperative period, attempts are made to optimize the patient for surgery and limit anxiety. Benzodiazepines are the drugs of choice to reduce anxiety but they also have the side effects of respiratory depression and excessive sedation. At the time of laryngoscopy and tracheal intubation, the pressor response leads to increase in catecholamines release which results in elevation of blood pressure and heart rate[1]. This increases the chances of bleeding during surgery. The excessive bleeding hampers visibility and may also necessitate blood transfusion and the duration of surgery may also increase. The increased duration of surgery may be associated with infection. Hence, it is very important to maintain hemodynamic stability during perioperative period. For this, the patients are given inhalational agents, analgesics, sedatives, hypotensive agents and also beta blockers[2,3]. Inadequate pain relief during perioperative period has negative clinical outcomes such as decrease in vital capacity and alveolar ventilation, tachycardia, hypertension, myocardial ischemia, myocardial infarction etc. Hence, it is very important to provide effective analgesia during this period. Alpha-2 agonists are being used in modern anaesthesia practice due to their beneficial effects like sedation, analgesia, attenuation of stress response and reduction in anaesthetic drug requirement. They also maintain perioperative hemodynamic parameters[1,3,8]. Clonidine and dexmedetomidine are two currently used drugs with dexmedetomidine having higher selectivity for α-2 receptors.[4,5] Premedication with alpha-2 agonists blunts the stress response to surgical stimuli and reduces the requirement of narcotic and anaesthetic drugs. The sedative, anxiolytic and sympatholytic properties of this class of drugs have made them drugs of particular interest for premedication.[6] To the best of our knowledge, no clinical study has compared the effects of dexmedetomidine and clonidine premedication for perioperative hemodynamic stability and postoperative analgesia in cases of upper abdominal surgeries. We, therefore, proposed to conduct a prospective, randomized double blind, controlled study to compare the hemodynamic and analgesic efficacy of these two α-2 agonists in upper abdominal surgeries.

MATERIAL AND METHODS

This randomised prospective study was conducted at Gandhi Medical College Bhopal after obtaining Institutional ethics committee approval and informed written consent from each patient for participation in the study. One hundred patients of both sexes aged 20-50 years belonging to ASA Grade I and II scheduled for elective upper abdominal surgeries under general anaesthesia were randomly divided into two groups of 50 each (n=50). Patients with history of hypertension, ischemic heart disease, aortic stenosis, left ventricular failure, asthma, chronic obstructive pulmonary disease, liver or renal disease, patients taking antipsychotics, analgesics, sedatives, β blockers or MAO inhibitors, pregnant or breast-feeding females and patients allergic to the study drug were excluded from the study. Preanaesthetic checkup of all the patients was done. All routine investigations like hemogram, urine analysis, blood urea, blood sugar, ECG & relevant specific investigations were done. The patients were given nil per oral orders according to ASA fasting guidelines. Inside the operation theatre, after intravenous cannulation, all patients were given injections glycopyrolate 0.2 mg, ondansetron 4mg, ranitidine 50 mg and fentanyl 2mcg/kg as premedication. Before induction of anaesthesia, group-I patients were given 2 mcg/kg of clonidine while group II patients were given 1 mcg/kg of dexmedetomidine. Each drug was diluted in 20 ml of normal saline and given over 10 min intravenously before induction. After that, the patients were induced with inj propofol 2.5 mg/kg and inj. succinylcholine 1 mg/kg and were intubated. Anaesthesia was maintained with 50% O_2 + 50% N_2O and 1% isoflurane and inj atracurium 0.5 mg/kg followed by 0.1 mg/kg intermittently. IPPV was done to maintain EtCO2 between 35-45 mm of Hg.

Each patient was observed for Heart Rate, Systolic blood pressure, Diastolic blood pressure, Mean Arterial Pressure, Respiratory rate and SPO_2 at 0 minute, 1 min, 5 min, 15 min, 30 min, 45 min, 60 min, 75 min, 90 min, 105 min and 120 min. At the end of surgery, the residual neuromuscular blockade was reversed with inj. glycopyrrolate 0.01 mg/kg and inj. neostigmine 0.05 mg/kg i.v. and patients were extubated after complete reversal of neuromuscular blockade. Patients were also observed for any side effects and complications viz., hypotension, bradycardia, hypoxia, sedation, desaturation etc. and managed accordingly upto a period of 16 hrs.

Postoperative pain was assessed on 10 points visual analogue scale (VAS) at the end of surgery and every 30 minutes in the postoperative period till VAS score was >3. Rescue analgesia was given as injection diclofenac intravenously.

Statistical Analysis

Statistical analysis was done using computer software (SPSS version 20). Data was summarized as Mean ± SD. The difference in mean was analyzed by

Student's t test. Groups were also compared by two factor repeated one way measure analysis of variance (ANOVA). The difference in

proportion was compared by chi-squire test. A p-value less than 0.05 ($p<0.05$) was considered statistically significant.

OBSERVATIONS AND RESULTS

The mean trend of HR in both groups was almost similar over the periods with slightly being higher in Group II at 1 & 5 min and specially after 45 min till extubation.

SBP between the two groups at all periods was not significantly different. ($p>0.05$) The mean trend of DBP was higher in Group I after 75 min till extubation as compared to Group II. The mean MAP trend in both groups was higher in Group I after 60 min till extubation as compared to Group II. MAP between the two groups at most periods did not differ statistically. ($p>005$).

The mean trend of RR and SPO2 was similar over the periods. ($p>0.05$).

The time to rescue analgesia requirement was significantly longer in group I as compared to group II ($p<0.001$).

The mean sedation score of group II at the time of extubation ($p<0.001$) was significantly higher as compared to group I.

The difference in incidence of complications in both groups was insignificant ($p>0.05$) .

DISCUSSION

We studied the two most commonly used α-2 agonists in the anaesthesia practice and compared their efficacy in reducing stress response and hemodynamic changes associated with upper abdominal surgeries and postoperative pain relief.

Hemodynamic effects of dexmedetomidine are due to central sympatholytic and peripheral vasoconstrictive effects.[7,8,9] 0.25-1 mcg/kg iv dexmedetomidine is used for blunting intubation response.[10,11,12] Numerous studies have shown that dexmedetomidine attenuates the cardiovascular response to intubation.[14,15,16] Our findings were consistent with previous studies. It was found that SBP was lower with dexmedetomidine at intubation, during surgical procedure, at extubation and during postoperative period as compared to clonidine, however, the difference between the two drugs was statistically insignificant. We can safely conclude that dexmedetomidine and clonidine stabilize SBP and reduce the rise in SBP during various phases of anaesthesia and surgery. It was observed that the SBP stabilising effect of dexmedetomidine lasted till extubation while clonidine was less effective in preventing the hemodynamic response to extubation. Similarly, clonidine and dexmedetomidine reduce DBP and prevent its rise during intubation and surgery but do not suppress the increase of DBP during extubation completely.

In initial stage of surgery, both the drugs were equally efficacious in preventing the rise in MAP but towards the end of surgery, patients who received clonidine experienced an increase in MAP.

The mean heart rate was lower in dexmedetomidine group as compared to clonidine group throughout the procedure but it was statistically insignificant. However, the heart rate was lower in each groups as compared to baseline and it was statistically significant. The heart rate lowering effect of both the study drugs reduces the myocardial oxygen demand which is very useful in patients suffering from coronary artery disease. Dexmedetomidine is more effective in this regard and our finding was consistent with previous study.[17] This effect of dexmedetomidine is due to significant attenuation of sympathoadrenal response to tracheal intubation compared to clonidine and it was also seen in earlier studies.[18]

In an earlier study, inj. clonidine 1 μg/kg attenuated hemodynamic stress response to pneumoperitoneum but not due to intubation and extubation.[19] But clonidine 2μg/kg prevented hemodynamic stress response to pneumoperitoneum and also to intubation and extubation. .[19]. In our study, we used 2 μg/kg of clonidine and response to laryngoscopy and intubation were prevented but the response to extubation was not suppressed completely although this difference was not statistically significant as compared to 1μg/kg dexmedetomidine. So 1μg/kg dose of dexmedetomidine is more effective than 1 μg/kg of clonidine and its effect is comparable to 2 μg/kg of clonidine.[20]

The time to rescue analgesic was longer in patients who received dexmedetomidine as compared to those who received clonidine, thus proving that dexmedetomidine has longer duration of analgesia as compared to clonidine.

Patients were more sedated in dexmedetomidine group as compared to clonidine group. But none of the patients required any type of airway or ventilator support. No significant complications were noted in any of the groups. Thus, both the drugs were found to be safe.

Limitation :The present study was performed with a small sample size, so there is need to replicate this study in a larger sample size.

CONCLUSION

Dexmedetomidine provides better hemodynamic stability as compared to clonidine during perioperative period about 5 minutes after induction till end of surgery. After surgery dexmedetomidine provides prolonged analgesic effect as compared to clonidine. Neither of the drugs caused any significant complication.

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