Original Article

Effect Of Intraoperative Dexmedetomidine Infusion On Sevoflurane Requirement And Awareness In Major Abdominal Surgical Procedures

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Abstract

Background: Dexmedetomidine is alpha agonist drug with multiple uses in perioperative anaesthesia care. The drug deceases the requirement of inhalational agents. This study is a randomized, double-blinded trial that aimed to investigate the use of the sedative and analgesic medication dexmedetomidine in patients undergoing elective major abdominal surgeries under general anaesthesia.

Methods: Sixty patients scheduled to undergo General anesthesia were included in the study and were randomly assigned to either the Dexmedetomidine group or the Placebo group. The study was approved by the hospital's ethical committee and had specific inclusion and exclusion criteria for patients. The interventions included pre-medication and standard monitoring, as well as the administration of a range of drugs, including dexmedetomidine and a placebo, during the induction and maintenance of anaesthesia. The study aimed to maintain a specific level of sedation and monitor various vital signs throughout the surgery. The BIS index was maintained and the sevoflurane requirements were analysed.

Results: The total sevoflurane volume required by the Dexmedetomidine was less when compared to placebo group. Sevoflurane volume consumed by Dexmedetomidine group was 30% less in the 1st hour, 23% less in the 2nd hour and 22% less in the 3rd hour when compared to the placebo group. The study found that the mean duration of surgery in the Dexmedetomidine group (162.97±19.32) was not significantly different from that in the Placebo group (159.50±18.88) with a P value of 0.442. However, the hourly average sevoflurane consumption was significantly less in the Dexmedetomidine group (8.34±1.94 ml) compared to the Placebo group (13.55±2.36 ml) at the end of the first hour of surgery, and the difference remained statistically significant at the end of the 2nd and 3rd hour of surgery.

Conclusion: Intraoperative use of Dexmedetomidine infusion has decreased the amount of sevoflurane required when compared to placebo group under BIS guided anaesthesia without any major adverse events like bradycardia and hypotension. It also provided additional postoperative analgesia as indicated by the VAS score.

Key words: anaesthesia, dexmedetomidine, sevoflurane, requirements

INTRODUCTION

The α2 agonist has been introduced to clinical anaesthesia for its sympatholytic, sedative, anaesthetic sparing effects and haemodynamic stabilising properties. Dexmedetomidine, the pharmacologically active d-isomer of medetomidine (4,[5]-[1-(2,3-dimethylphenyl)-ethyl] imidazole is a highly specific and selective α2 adrenoreceptor agonist[(1).] The alpha-2 receptor activation results in reduction in norepinephrine release, which can be used therapeutically to induce sympatholysis[(2)]. Dexmedetomidine was first marketed for Intensive Care Unit (ICU) sedation, to make use of highly selective adrenergic alpha-2 receptor agonist activity. Unlike commonly used sedatives such as propofol or Midazolam, Dexmedetomidine produces an "interactive'' form of sedation, in which patients can be aroused easily with stimulation, and are cooperative once aroused[(3)]. In healthy normotensive patients, the use of dexmedetomidine during anaesthetic induction suppressed a decrease in blood pressure due to anaesthetic induction and blunted the hemodynamic responses to endotracheal intubation[(4)].

In addition to sedative effects, Dexmedetomidine has been labelled as "analgesia sparing" by the Food and Drug Administration (FDA)[(5)]. Dexmedetomidine when co-administered with opioids has no depressant effects on respiration,

but its analgesic effects offer a significant advantage of patients at risk for respiratory decompensation. The sevoflurane requirements can come down by other methods also. [6,7].
Intraoperative awareness is a disturbing experience for all patients undergoing general anaesthesia. This may lead to post traumatic stress which may last for years. To reduce the incidence of awareness during general anaesthesia, devices have been developed in the recent years that process two-channel EEG signals and create a dimensionless variable to indicate level of wakefulness. The Bispectral index (BIS) is most commonly used in this regard. In our study, we hypothesized that Dexmedetomidine may be effective to reduce the awareness during the surgery[8][9].

MATERIALS AND METHODS:

Study Primer: This is a randomized, double blinded study conducted between November 2018 to October 2020. 60 patients undergoing elective major abdominal surgeries under general anaesthesia in SCB medical college & hospital were included during the study. The study was approved by Hospital Ethical Committee (IEC-SCBMCH-372-2020). Patients were allocated into one of the two groups, Dexmedetomidine group (GROUP D) & Placebo group (GROUP) 30 each, based on computer-generated random numbers that were enclosed in a sealed envelope opened only at the time of induction.

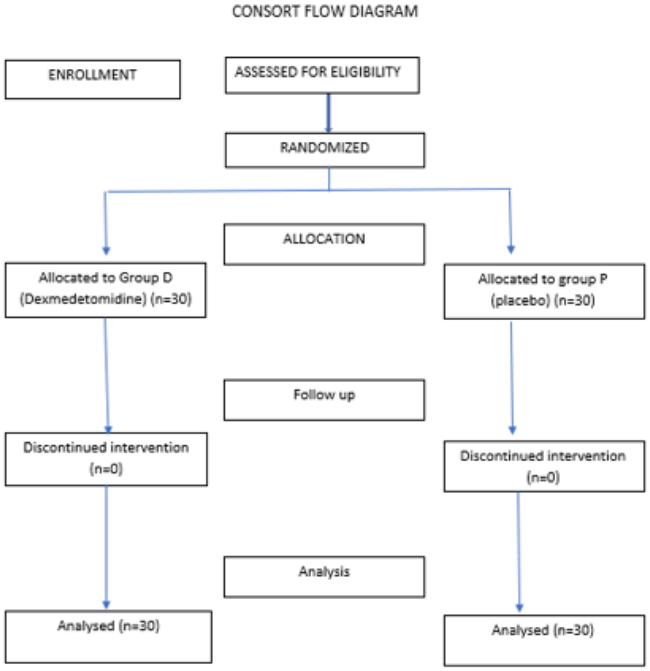
Inclusion And Exclusion Criteria:-Patients belonging to ASA grade I and grade II, Age 20-60 years of both genders posted for major abdominal surgeries who are willing to be part the study were included. Diabetic and Hypertensive patients, Patients on psychoactive medication, patients with history of alcohol or drug abuse, patients with coronary artery disease and obese patients were excluded from the study.

Interventions:-All patients will be pre-medicated with tab. Alprazolam 0.5 mg oral, the night before surgery and a minimum fasting state of 8 h before anaesthesia will be ensured in all patients. The standard monitoring consisted of electrocardiography, pulse oximetry (SpO2), non-invasive blood pressure, neuromuscular transmission monitor and capnography. Before induction of general anaesthesia, an epidural catheter will be placed in all patients for the purpose of providing postoperative analgesia. The skin will be cleaned with alcohol and dried, the BIS sensor will be placed on the forehead and temple using a frontal-temporal montage.
Premedication prior to the induction of GA: Inj. Ondansetron 4mg IV will be given 15 minutes before induction in all patients to prevent postoperative nausea and vomiting. inj. Midazolam 0.05 mg/kg IV, inj. Glycopyrrolate 0.01mg/kg IV, inj. Fentanyl 2µg/kg IV will be administered. And all patients will be preoxygenated with 100% oxygen for 3 min. Group D patients will be given an initial dose of inj. Dexmedetomidine 1µg/kg IV made to 20 mL with normal saline, over 10 min. Group P patients will be receiving similar volume of normal saline over 10 min. The study drug and placebo infusions will be prepared by an anaesthesiologist who was not involved in the study and the anaesthesiologist recording the details will be unaware of the type of infusion patients are receiving.
Baseline vitals will be obtained prior to induction (Blood Pressure, oxygen saturation, heart rate). Blood pressure will be measured every one minute during induction and intubation. During induction with Inj. Propofol 2mg/kg IV and for neuromuscular blockade Inj. Atracurium 0.5mg/kg was given. Following which mask ventilation will be done for 3-4 minutes and intubation will be done with appropriate size ETT.

Maintenance of anaesthesia: For Group D Patients Immediately after induction, Dexmedetomidine will be given as continuous infusion at a rate of 0.5 µ g/kg/hr made to 20ml with normal saline throughout the surgery and sevoflurane will be adjusted to achieve the same BIS score obtained in Group P at I MAC of sevoflurane. For Placebo group similar volume of normal saline will be administered in group P, till the end of the surgery Anaesthesia was maintained by sevoflurane at 1 MAC (2%). In both groups continuous infusion of atracurium at rate of 10µ/kg/min will be given.
Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and peripheral oxygen saturation (SpO2) will be monitored throughout anaesthesia and recorded every 5 minutes. Bispectral index numbers will be recorded 2min before incision, 2min after incision, every 15 minutes during the operation and at the end of surgery. Our target during surgery was to keep BIS values maintain between 45-55. Top up doses of Atracurium will be guided by NMT monitor. Infusion of Dexmedetomidine will be stopped at the end of surgery. Sevoflurane administration will be turned off at the beginning of skin suturing. At the end of the surgery, residual neuromuscular blockade will be reversed with inj. Neostigmine 0.5 mg/kg and inj. Glycopyrrolate 0.005 mg/kg and trachea extubated after satisfactory recovery and presence of response to oral commands. The total and hourly Sevoflurane requirements will be measured at the end of every hour. The usage of Sevoflurane during anaesthesia can be calculated using Dion's Formula: Usage of volatile anaesthetic(mL) = [Dialed concentration × Total fresh gas flow × Duration at that concentration × Molecular weight]/ [2412 × Density]. The recovery from anaesthesia will be measured from the time when all anaesthetics were turned off. The time required for extubation and later Ramsay sedation score (RSS) after extubation was also observed. Excessive sedation was defined as score greater than 4-6. The post-operative pain at 1st hour will be assessed using visual analogue scale (VAS). Patients with a VAS score of 3 or more were received diclofenac 75mg intramuscularly. Hypotension (defined by a decrease in MAP below 20% of baseline or systolic pressure- 90 mmHg) was treated with adjustment of sevoflurane and additional Ringer's solution (200ml over a 5 min period). Bradycardia (HR-50 beats/min) was treated with intravenous atropine 0.5mg. The occurrence of any complication in the preoperative and postoperative period will be noted, particularly in relation to respiratory or cardiovascular problems.

STASISTICAL ANALYSIS:

Statistical analysis will be conducted with statistical package for social sciences (SPSS) Version 21 for windows statistical package. All the parametric data are presented as mean ± SD and non-parametric data in tables. Parametric data will be assessed with independent sample t-test. Bonferroni's correction will applied as appropriate. Those values with normal distribution were tested with independent t test and others were tested with Mann Whitney U test. P value of less than 0.05 was considered as statistically significant.



RESULTS:

The demographic parameters such as age, sex, height, weight, and the ASA status of the patients were comparable in both the study groups [table 1]. In our study we included both the laparoscopic and open abdominal surgeries, of which majority of the case are of laparoscopic procedures. Yet the type of surgeries is almost comparable in both groups [table 2].

Table 1: Demographic parameters

PARAMETERS	GROUP 'D'	GROUP 'P'
MEAN AGE	40.57±9.67	42.00±7.56
GENDER (MALE: FEMALE)	16:14	13:17
WEIGHT	73.17±6.61	72.33±8.55
HEIGHT	162.37±6.94	161.67±7.40
ASA (1:2)	24:6	22:8

Table 2: Type of surgeries

Type of surgery	GROUP D (n=30)	GROUP P (n=30)
Laparoscopic cholecystectomy	19	17
Laparoscopic appendectomy	4	5
Open cholecystectomy	3	4
Gastrectomy	2	2
Laparoscopic hernia repair	2	2

The mean and standard deviation of baseline heart rate, baseline mean arterial pressure, baseline spo2 among two groups were compared. MANN WHITNEY U test was done to determine whether there is a significant difference in the baseline heart rate, baseline spo2 and Independent t test was done to determine the significance between the two groups. The results obtained from the analysis shows that there is no statistically difference with respect to baseline heart rate, baseline mean arterial pressure and baseline spo2 and the two groups are comparable [Table 3].

Table 3 – hemodynamics

GROUP	MEAN	SD	P VALUE
BHR			
DEXMEDETOMIDINE GROUP	90.33	7.27	0.267**
PLACEBO GROUP	92.90	10.88	
BMAP			
DEXMEDETOMIDINE GROUP	82.53	7.13	0.351*
PLACEBO GROUP	84.73	10.63	
BSPO2			
DEXMEDETOMIDINE GROUP	99.13	0.93	0.786**
PLACEBO GROUP	99.07	0.94	

**-MANN WHITNEY U TEST, *- INDEPENDENT T TEST

On comparing the baseline heart rate and pre-induction heart rate there is no statistical difference between the two groups. There was a clinically and statistically significant reduction in heart rate (HR) in the Dexmedetomidine group starting from induction throughout the surgery and also there is statistically significant difference at 15 minutes after the postoperative period. The mean arterial pressure between the two groups after intubation at 15, 30, 60, 75, 90, 105 minutes were compared and yields P value <0.05 which were significant. The mean arterial pressure during pre-induction, during induction, at 45, 120 and postop 15 minutes yields a P value >0.05 which were insignificant [Table 4&5].

Table 4- hemodynamics

Group	Dexmedetomidine group	Placebo group	P Value
BASELINE HR	90.33±7.27	92.90±10.88	0.267**
PRE-INDUCTION HR	91.57±5.71	89.70±2.83	0.114*
HR DURING INDUCTION	94.43±4.35	99.17±4.17	0.001**
HR AFTER INDUCTION	76.80±5.39	100.83±5.53	0.001**
HR AFTER INTUBATION	80.67±6.74	99.37±6.44	0.001*
HR 15"	82.80±6.05	95.67±5.01	0.001*
HR 30"	79.53±5.65	92.90±6.70	0.001**
HR 45"	83.67±5.71	95.40±6.49	0.001**
HR 60"	77.30±6.89	92.90±5.80	0.001**
HR 75"	80.40±6.48	91.13±5.57	0.001**
HR 90"	82.03±6.38	87.87±5.20	0.001**
HR 105"	83.17±5.86	86.37±4.67	0.001**
HR 120"	87.67±4.02	91.53±5.73	0.001**
HR POST OP 15"	90.17±8.22	96.60±5.39	0.001**

Table 5

Group	Dexmedetomidine group **(Mean± SD)**	Placebo group **(Mean± SD)**	P Value
BASELINE MAP	82.53±7.13	84.73±10.63	0.351*
PRE-INDUCTION MAP	86.37±6.48	87.17±8.63	0.620**
MAP DURING INDUCTION	83.90±4.40	86.33±10.70	0.110**
MAP AFTER INDUCTION	81.93±4.87	82.50±8.68	0.150*
MAP AFTER INTUBATION	75.93±4.29	82.07±6.37	0.001*
MAP 15"	74.27±3.82	84.77±6.29	0.001*
MAP 30"	76.73±4.50	86.0±11.93	0.001*
MAP 45"	77.87±3.53	82.67±8.55	0.005**
MAP 60"	79.73±3.81	84.97±5.90	0.001**
MAP 75"	77.53±3.40	87.20±8.38	0.001*
MAP 90"	76.20±2.94	85.43±8.11	0.001*
MAP 105"	76.10±2.70	82.97±9.93	0.005**
MAP 120"	79.0±4.75	82.03±6.36	0.370**
MAP POST OP 15"	83.97±3.28	81.5±6.61	0.271**

Duration of surgery is similar in both study groups. The mean duration of surgery in Group D is 162.97±19.32 and in Group P is 159.50±18.88. On analysis the P value is 0.442 which statistically insignificant between the groups. Hourly average sevoflurane consumption was calculated based on the DION's formula. At the end of 1st hour of surgery, the sevoflurane consumed was 8.34±1.94 ml in Group D when compared to 13.55±2.36 ml in Group P. similarly the sevoflurane consumed at the end of 2nd and 3rd hour of surgery were given in the table 6. The sevoflurane consumed in Group D is much less than the Group P. There is statistically significant difference between the two groups as suggested by the P values (0.001).

Table 6- sevoflurane consumption

SEVOFLURANE CONSUMPTION	**GROUP D**	**GROUP P**	**P VALUE**
AT THE END OF 1HR (Mean± SD)	8.34±1.94	13.55±2.36	0.001
AT THE END OF 2HR (Mean± SD)	8.67±1.73	10.97±1.69	0.001
AT THE END OF 3HR (Mean± SD)	7.90±1.54	10.15±1.94	0.001

Post operative Ramsay sedation score in dexmedetomidine group was 2.5± 0.40 and 1±1.54 in placebo group. The analysis shows statistically significant difference between both groups (P value 0.001). Similarly, there is statistically significance in VAS score measured 1 hour after the postoperative period between the both groups. The VAS score in Group D was 2±0.94 and 4±0.29 (P value 0.001).

DISCUSSION

Dexmedetomidine, a highly selective α2-adrenergic receptor agonist has generated lot of interest for its sedative, analgesic, perioperative sympatholytic, anaesthetic-sparing, and hemodynamic stabilizing properties with a relatively high ratio of α2/α1 activity.

The sevoflurane volume consumed by the study and the control group were calculated. There was statistically significant reduction in the sevoflurane requirement throughout the surgery. There was about 38% reduction in the sevoflurane requirement in the 1st hour of anaesthesia, as suggested by 8.34±1.94ml in group D compared to 13.55±2.36ml in group P (P<0.001). Also, there is significant reduction in the sevoflurane requirement in the 2nd and the 3rd hour of surgery, as suggested by 8.67±1.73ml in group D compared to 10.97±1.69ml in placebo group in 2nd hour (P<0.05), which is 23% less than the placebo group and 7.90±1.54 ml in consumed in group D compared to 10.15±1.94 ml in group P in the third hour of surgery (P<0.05), which is 22% less than the placebo group. So, there is statistically significant amount of decrease in sevoflurane consumption is seen in 1st, 2nd & 3rd hour surgeries. But there is higher amount of decrease in sevoflurane consumption is seen during 1st hour when compared to 2nd and 3rd hour. Other studies also found significant reduction in sevoflurane consumption while using dexmedetomidine infusion[10,11].

Ramsay sedation score was used to assess the postoperative sedation in patients of both study and control group. The median value of Ramsay sedation score in the study group was 2.5± 0.40 and the median value in the placebo group is 1±1.54. There is statistically significant difference between the median value of study and the control group (P<0.001).

The postoperative pain between the two groups were assessed using visual analogue scale (VAS). In VAS the score ranges from 1 to 10 indicating less to worst possible pain in increasing order. In our study, Group D where Dexmedetomidine infusion was given had less postoperative pain than the placebo group. The pain assessed by VAS at first hour of postoperative period was 2±0.94 in Dexmedetomidine group, which was significantly lower against 4±0.29 in placebo group (P<0.001). In group P, 19 patients and 3 patients in group D required epidural analgesia at the end of 1 hour postoperatively. Remaining 11 patients in group P and 27 patients in group D received epidural analgesia by the end of 2 hours.

During maintenance of anaesthesia, group D showed a statistical decrease in heart rate and the mean arterial pressure. There is significance decrease in heart rate in group D starting from induction and throughout the surgery (P<0.001) when compared to the placebo group. On average there is 8% decrease in heart rate from baseline in group D as compared to 3% rise in group B. on comparing the MAP between the two groups, there is statistical difference in decrease in MAP starting from induction till 105th minute of the surgery. On an average when comparing with the baseline there is 6% decrease in MAP in group D when compared to 1.5% decrease in blood pressure in group P. Significant reduction in MAP in Group D helped in decreasing the blood loss in few major open surgeries like gastrectomy.

In our study, no major side effects were observed. 3 patients in group D developed bradycardia which was treated with 0.6mg IV. There was no incidence of bradycardia in group P. although there was significant difference in MAP between 2 groups, there was no incidence of hypotension observed in both groups. Incidence of side effects like bradycardia, hypotension and hypoxia were very less in both the groups.

Dexmedetomidine can be used in a variety of settings, including the intensive care unit, the operating room, and the emergency department. It has been shown to be effective at reducing the use of opioids, which can help to decrease the risk of opioid-related side effects such as respiratory depression and delirium. One of the main benefits of dexmedetomidine is that it allows patients to remain more alert and responsive to verbal commands during sedation, which can make it easier for healthcare providers to monitor and communicate with the patient.[12,13,14] But in our study, we used the same as an adjunct to General anaesthesia to decrease the requirements of inhalational agents.

CONCLUSION

The total sevoflurane volume required by the Dexmedetomidine was less when compared to placebo group. Sevoflurane volume consumed by Dexmedetomidine group was 30% less in the 1st hour, 23% less in the 2nd hour and 22% less in the 3rd hour when compared to the placebo group. Intraoperative use of Dexmedetomidine infusion has decreased the amount of sevoflurane required when compared to placebo group under BIS guided anaesthesia without any major adverse events like bradycardia and hypotension. It also provided additional postoperative analgesia as indicated by the VAS score.

Conflict of interest- NIL

Financial aid -NIL

Concept, data collection- PN, design and data- BG, manuscript and communication- SPS

Ethical issues – Yes- (IEC-SCBMCH-372-2020)

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