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A Study of Dexmedetomidine as a General Anesthetic Adjuvant in Patients Undergoing Abdominal Surgeries

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Abstract: Adjuvants are commonly used during general anesthesia in order to reduce the requirements of the general anesthetics. Dexmedetomidine is one of an important general anesthetic adjuvant used because of its useful properties like sedative, analgesic and anxiolytic. It has other important useful properties like cardioprotection, neuroprotection and minimal respiratory depression. We in the present study tried to evaluate the efficacy of dexmedetomidine in different concentration when used as an infusion during general anesthesia in patients undergoing routine abdominal surgeries. Methods: the study was conducted in Rajiv Gandhi Institute of Medical Sciences and Hospital [RIMS], Adilabad. The patients were selected from those undergoing abdominal surgeries. They were randomly divided into three groups. Group A (n=20) patients acting as controls received IV saline 10ml. Group B received Dexmedetomidine 0.5 µg/Kg/hr IV and Group C received Dexmedetomidine 1 µg/Kg/hr IV. Anesthesia was maintained with N_2O to O_2 mixture of 60:40. MAP values were maintained within 25% of the baseline values. Recovery times from tracheal extubation, modified Alderete score, VAS scores, tolerating liquids, and passage of flatus was noted. Results: The mean duration of surgery in Group A was 145.45 ± 20.06 minutes, mean duration of anesthesia was 180 ± 25 minutes. The mean duration of infusion of dexmedetomidine was 160 ± 20. For group B the values were 130.12 ± 24.75, 160.0 ± 22.0, and 140 ± 90 minutes respectively. The values for group C were 121.59 ± 18.16, 145 ± 26 and 125 ± 15minutes. The P values between group A and C were significant in Mean duration of anesthesia and mean duration of infusion. The time to suction catheter response was significantly higher in Group C. The modified Aldrete scores in Group B and Group C were found to be significant when compared to Group A similarly postoperative nausea and vomiting was significantly lesser in group C and VAS scores of pain were also significantly lesser in the Group C as compared to Group A and B. conclusion: Dexmedetomidine is low concentrations may be useful to provide sedation and mild analgesia at the same time preserving the cardiovascular and respiratory functions. Therefore dexmedetomidine when used as a general anesthetic adjuvant during routine abdominal surgeries reduces the sevoflurane and opioid requirements and results in better recovery of the patients.

Keywords: Dexmedetomidine, Abdominal surgeries, Anesthetic adjuvant.

INTRODUCTION

Dexmedetomidine is a highly selective α_2A receptor antagonist possessing sedative, hypnotic, anxiolytic, sympatholytic and analgesic properties without producing significant respiratory depression [1-4] In the CNS the activation of the α_2 receptors leads to sedation and reduction of tonic sympathetic outflow and augmentation of cardiac vagal activity [5, 6]. This can result in a decrease in heart rate (HR) and cardiac output (CO) [7, 8]. It has the ability to reduce both anesthetic and opioid analgesic required during the perioperative periods [9-11]. The analgesic activity of α_2 agonists seems to be mediated by both supraspinal and spinal mechanisms. It is thought that central α_2 adrenoreceptors in the locus ceruleus and in the dorsal horn of the spinal cord are involved in this activity [12, 13] Dexmedetomidine has been used during anesthetic practices like sedation during mechanical ventilation, postoperative anxiolysis, prevention of emergence agitation and treatments of substance withdrawal [14 - 16]. Several studies have reported the benefits of dexmedetomidine including neuroprotection, cardioprotection, and renoprotection [17]. Because of its central sympatholytic actions dexmedetomidine decreases the mean arterial blood pressure [MAP] and heart rate [HR] by reducing nor-epinephrine release [18, 19]. Due to the useful blunting hemodynamic responses in the perioperative period it is used along with the general anesthetics. The IV doses varying from 0.25 µg/kg to 1 µg/kg for attenuating intubation response

[20-23] the optimum dose for attenuating the pressor response seems to be 1 µg/kg [1] Dexmedetomidine does not delay recovery or prolonged sedation when boluses are administered before induction or before extubation. Bradycardia and hypotension are considered major side effects of dexmedetomidine infusion rapidly. Bradycardia is due to reflex response for hypertension during an initial part of infusion. The subsequent decrease in heart rate is due to decrease in sympathetic outflow [24]. Hypertensive responses have been observed with higher doses (1–4 µg/kg). This is due to initial stimulation of α-2B receptors present in vascular smooth muscles. This hypertensive episode settles once there is a decrease in the central sympathetic outflow. Dexmedetomidine infusions continued during postoperative periods have been associated with lesser hemodynamic fluctuations and decrease in plasma catecholamines [25] A Gurbet *et al;* have shown that continuous IV dexmedetomidine administration during abdominal surgeries significantly reduces the amount of PCA morphine that patients require to remain comfortable postoperatively, without affecting time to extubation. Intraoperative, systemically administered dexmedetomidine was also associated with fewer morphine-related side effects compared with placebo. [9] With this background we aimed to evaluate the effects of dexmedetomidine when used as an adjuvant in two concentrations 0.5 mcg/Kg and 1.0mcg/kg in randomly selected patients undergoing elective abdominal surgeries.

MATERIALS AND METHODS

This study was performed in Rajiv Gandhi Institute of Medical Sciences [RIMS], Adilabad. Institutional Ethical committee permission was obtained prior to the study. Informed consent was obtained from all the patients regarding the procedure. Fifty (n=50) patients age ranging from (23-50 years) were included in the study. All were undergoing elective abdominal surgeries. They belonged to ASA classification I/II free from medical conditions like hypertension, diabetes mellitus, cardiovascular disease, respiratory diseases. The (n=50) patients were randomly divided into three groups, Group A (n=20) received normal saline 10ml IV, Group B (n=15) received Dexmedetomidine 0.5 µg/Kg/hr IV and group C (n=15) Dexmedetomidine 1.0 µg/Kg/hr IV. Glycopyrrolate 4µg/Kg, IM, midazolam 0.03 mg/kg, Ondansetron 4mg IV was given prior to anesthesia. Intraoperative monitoring devices included noninvasive arterial blood pressure, electrocardiography and pulse oximetry were used. Patients were randomly selected and received Normal saline 10ml in group A and a loading dose of dexmedetomidine infusion was 1µg/Kg was started and continued for 15 minutes. After 15 minutes dexmedetomidine infusion was maintained to 0.5 µg/Kg in group B and 1.0 µg/Kg in group C. Anesthesia was induced with propofol 5 mg IV incremental doses to reach entropy value of 40-60, Eyelash reflex was checked. Succinylcholine 1.5mg/kg was administered IV to facilitate intubation. The patients were intubated with appropriate sized endotracheal tube orally and placement was confirmed with auscultation and End-tidal CO_2 concentration.

Anesthesia was maintained with sevoflurane with O_2 (1.5 L/min) and N_2O (1.5 L/min) and with N_2O to O_2 mixture of 60:40. Anesthetic depth was maintained to reach the target value of around 40 by manipulating sevoflurane vaporizer setting. The intraoperative anesthetic requirement was gauged by hemodynamics (HR and BP, the endpoint for the requirement for both was considered a 20% increase from baseline value). Ventilation was controlled to maintain End Tidal CO_2 concentration of 30-35 mmHg. Hemodynamic values were recorded at the time of induction of anesthesia, at the 5 min of tracheal intubation, at skin incision and MAP values were maintained within 25% of the baseline values. Upon the completion of wound closure, sevoflurane was discontinued and the inspired oxygen flow rate was maintained to 5 L/min. The time from discontinuation of sevoflurane to eye-opening, obeying commands were recorded. After emergence from anesthesia, patients were administered Fentanyl 25-20 g IV boluses to control post-operative acute pain. Finally, recovery times from tracheal extubation to ambulation without assistance, tolerating liquids, and passage of flatus was also noted.

RESULTS

The total number of patients involved in the present study was (n=50) they were divided randomly into three groups. Group A having (n=20) patients they were taken as controls they received they received IV saline 10ml. Group B having (n=15) taken as received Dexmedetomidine 0.5 µg/Kg/hr IV. Group C having (n=15) patients received Dexmedetomidine 1.0 µg/Kg/hr IV. The most common surgical procedure patients were undergoing was appendectomy followed by 9 cases each of cholecystectomies and hysterectomies. The mean duration of surgery in Group A was 145.45 ± 20.06 minutes, mean duration of anesthesia was 180 ± 25 minutes. The mean duration of infusion of Dexmedetomidine was 160 ± 20. For group B the values were 130.12 ± 24.75, 160.0 ± 22.0, and 140 ± 90 minutes respectively. The values for group C were 121.59 ± 18.16, 145 ± 26 and 125 ± 15minutes. The P values between group A and C were significant in Mean duration of anesthesia and mean duration of infusion (table 1) The end-tidal concentration of sevoflurane was significantly lower in Group C during the surgery. After tracheal intubation MAP and HR were significantly increased in control group but remained unchanged in Group A and Group C.

Table-1: Profile of patients included in the study

Groups	Age in years	Sex M/F	ASA I/II	Type of surgery			Mean Duration of surgery (min)	Mean Duration of Anesthesia (min)	Mean duration of infusion
				Append-ectomy	**Cholecys tectomy**	**Hystere ctomy**			
Group A (n=20)	*37.5 ± 12.92*	*13/7*	*9/11*	*15*	*3*	*2*	*145.45 ± 20.06*	*180 ± 25*	*160 ± 20*
Group B (n=15)	*41.6 ± 12.06*	*7/8*	*8/7*	*9*	*3*	*3*	*130.12 ± 24.75*	*160 ± 22*	*140 ± 19*
Group C (n=15)	*41 ± 8.94*	*6/9*	*5/10*	*8*	*3*	*4*	*121.59 ± 18.16*	*145 ± 26*	*125 ± 15*
P values	*>0.5*	--	*>0.5*	*>0.5*	*>0.5*	*>0.5*	*0.1*	*0.04**	*0.05**

***** Significant

The recovery profiles of the patients after the surgical procedures were recorded that included time to obey verbal commands, time to respond to suction catheter, time to complete tracheal extubation after turning off the vaporizer. The observations were made according to modified Aldrete scores [26] and occurrence of postoperative nausea and vomiting [PNOV] and postoperative pain by visual analog scales (0= no pain 10= worst possible pain). The parameters were recorded by independent observers unaware to which group the patient belongs. The time to suction catheter response was significantly higher in Group C. The modified Aldrete scores in Group B and Group C were found to be significant when compared to Group A similarly postoperative nausea and vomiting were significantly lesser in group C and VAS scores of pain were also significantly lesser in the Group C as compared to Group A and B given in table 2.

Table-2: Recovery profiles of the patients with Aldrete Scores, VAS, and PNOV

Recovery Variables	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)
Time to obey verbal commands (min)	*5.5 ± 3.5*	*6.5 ± 2.5*	*5.5 ± 3.0*
Time to suction catheter response (min)	*8.81 ± 2.5*	*9.10 ± 1.5*	*9.59 ± 2.97**
Time to tracheal extubation	*13.8 ± 4.0*	*11.5 ± 3.5*	*10.5 ± 4.0*
Modified Aldrete Score at recovery room > 8 (min)	*18.5 ± 9.5*	*8.5 ± 5.5**	*6.75 ± 4.5**
PNOV	*3.8*	*3.27*	*1.94**
Visual Analogue Scale [VAS] (0-10)	*5.6 ± 1.5*	*4.9 ± 1.16**	*4.2 ± 1.5**
Time for ambulation (hrs)	*10.00 ± 1.5*	*9.5 ± 1.5*	*9.0 ± 1.0*
Time for oral intake (hrs)	*20.0 ± 6.0*	*18.10 ± 4.5*	*17.5 ± 5.5*
Time for passing flatus (hrs)	*30.0 ± 4.5*	*28.80 ± 6.5*	*30.5 ± 9.5*

* Significant p-value

DISCUSSION

Dexmedetomidine is an imidazole compound with specific α_2 adrenergic receptor antagonism [27]. It binds with transmembrane G protein binding receptors in the brain and spinal cord with dose-dependent α_2 selectivity [28]. Stimulation of the α_2 adrenoreceptor subtypes mediates sedative and antinociceptive actions α_{2A}, vasoconstrictive cardiovascular effect α_{2B}, and modulating dopaminergic neurotransmission, hypothermia, and variety of behavior response α_{2C} [29]. Compared with other sedative Dexmedetomidine has favorable properties as it provides good sedation without respiratory depression. In the present study we investigated the effect of Dexmedetomidine in two concentrations 0.5 µgm/Kg and 1.0 µgm/Kg compared with control Group A that did not received Dexmedetomidine. The sedation produced by Dexmedetomidine in Group B and Group C was found to be better in our study. In a similar study by Aantaa *et al.,* [11] using Dexmedetomidine in dose of 0.5 µgm/Kg and 1.0 µgm/Kg found the Dexmedetomidine induced sedation within 5 minutes and reached its maximum effects in 15 minutes. We in the present study had similar observations probably because of the same concentrations of Dexmedetomidine being used in our study. Dexmedetomidine has been shown to produce biphasic hemodynamic responses during its use, vasodilation due to its pre-synaptic effect on sympathetic nervous system at high concentration and vasoconstriction by postsynaptic effect on vascular system at low concentration the net effect is initial rise in MAP followed by reduction in MAP and HR [30] This study did not found any such effect because of the low doses used and also because of slow rate of infusion of Dexmedetomidine causing slow rise in the plasma concentration. In the present study the

concentrations of 0.5µgm/Kg and 1.0 µgm/Kg were effective in blunting hemodynamic response to intubation as compared to controls produced during intubation. Gaurishanker RM *et al.,* [31] found that low doses of Dexmedetomidine 0.4 µgm/Kg in patients undergoing laparoscopic Cholecystectomies found that Dex was effective in attenuating the responses to intubation agreeing with our findings. In this study we found that the there was 45.5% reduction in the induction dose of propofol in group B and 59.5% reduction of dose of propofol in Group C. Poonam *et al;* [32] in a similar study found 62.5% reduction in propofol with Dexmedetomidine infusion of 1.0 µgm/Kg and the Isoflurane requirements were reduced by 30% to maintain the same depth of anesthesia. In our study end tidal Sevoflurane concentration and Sevoflurane consumption was 40.5 ml in group A, 31.5 ml in Group B and 25.5ml in group C to produce similar DOA. Similar observations were also made by HW Shin *et al.,* [28] Among the recovery variables in the present study the time to suction catheter response was significantly lesser in the Group C as compared to group A and modified Aldrete scores > 8 at the recovery room was reached earlier in group C followed by group B and group A similar observations has been made by Chirag RP *et al.,* using dex in concentration of 0.2 – 0.8 µgm/Kg with Sevoflurane anesthesia [33]. The VAS scores were lower in Group B and Group C indicating better analgesic effects when Dexmedetomidine was used. No significant differences were found when other variables were compared such as time for ambulation, oral intake of fluids and passing of flatus. Therefore it may be concluded that Dexmedetomidine at lower doses when used as adjuvant to general anesthesia reduced the amount of anesthetics and opioid requirements and produces more rapid recovery from anesthesia. Patients were able to return to baseline level of consciousness early in dexmedetomidine infusion groups.

CONCLUSION

Within the limitations of the present study, it can be concluded that Dexmedetomidine is low concentrations may be useful to provide sedation and mild analgesia at the same time preserving the cardiovascular and respiratory functions. Therefore Dexmedetomidine when used as a general anesthetic adjuvant during routine abdominal surgeries reduces the sevoflurane and opioid requirements and results in better recovery of the patients.

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