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Perioperative Hemodynamics and Post-Operative Analgesia Among Patients Administered with Lidocaine and Dexmedetomidine as Analgesic Adjuvants

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ABSTRACT
Introduction: *Laparoscopic gynecologic surgery enables patients to achieve early ambulation and prompt discharge from hospital by reducing postoperative morbidity and analgesic needs. Application of anesthetic adjuvants intraoperatively further accelerates these recovery phases, which are beneficial from one than other from several critical aspects.*
Objectives: *In the present study the perioperative hemodynamic and analgesic effect of dexmedetomidine and lidocaine have been compared when they are infused as anesthetic adjuvants.*
Methodology: *A prospective observational study have been designed and conducted at Dhaka Medical College Hospital. After evaluating for the selection criteria, 50 purposively selected female patients with ASA grade I & II who have been scheduled for intended gynecologic surgery with laparoscopy. Prior data collection, the ethical approval from the concerning ethical review committee has been obtained and informed written consent from the patients have been collected. Patients were randomly assigned in two groups, Group A and Group B; with proper anesthetic protocol, Group A initially received IV 0.5µg/kg dexmedetomidine hydrochloride gradually over 10 min, and then, IV infusion of 0.5µg/kg/h through a syringe pump. Group B received a loading dose of intravenous 1.5mg/kg lidocaine hydrochloride gradually over 10 min, and then IV infusion of 1.5 mg/ kg/h through a syringe pump. The perioperative cardiovascular parameters, such as, heart rate, blood pressure, mean arterial pressure at different time points have been evaluated along with time of 1st analgesic demand and total number of post-operative analgesic requirements also have been recorded and compared between the study groups.*
Results: *The hemodynamic parameters among the dexmedetomidine and lidocaine group was insignificantly different ($p>0.05$). The time for first post-operative analgesic requirement also was comparable between the group ($p>0.05$).. However, patients in lidocaine group required significantly reduced number of analgesic in 24 hour in PACU compared to dexmedetomidine group of patients in ($p<0.05$).*
Conclusions: *Dexmedetomidine and lidocaine are equivalently effective in maintaining intraoperative hemodynamic response in patients undergoing gynecologic laparoscopic surgery. Moreover, post-operative total analgesic consumption was significantly low among patients who received IV lidocaine infusion. Thus, lidocaine can be used as an anesthetic adjunct as effectively as dexmedetomidine which can be beneficial in terms of cost-effectiveness and ease of availability.*
Keywords: *Gynecologic laparoscopic surgery, Anesthetic adjuvants, Lidocaine, Dexmedetomidine, Hemodynamic stability, Post-operative analgesia*

I. INTRODUCTION

Laparoscopic surgeries are accompanied with challenges to its anesthetic achievement, broadly due to haemodynamic alteration. [1] During the procedure, the general anesthesia causes marked elevation of stress responses at various time points such as during laryngoscopy, tracheal intubation, pneumoperitoneum and extubation. [2] Creating pneumoperitoneum in laparoscopic surgeries, causes rise of intra-abdominal pressure raising the diaphragm, which adversely impacts the cardiovascular system which can lead to diminished cardiac output, increased arterial pressure and elevated systemic and pulmonary vascular resistance leading to hypertension, tachycardia, even amplifies the risk of myocardial ischemia that can pose a life threatening condition of the patients who are vulnerable.[3,4] Moreover, the trendelenburg position which is preferred for sufficient disclosure of pelvic structures during gynecologic surgical procedures causes difficulty for anesthetic managements due to physiologic alterations such as autotransfusion, increase intraocular pressure and intracranial pressure. [5] Effective postoperative pain control is another challenge where pain relief is required not only for patients' comfort and satisfaction but also to expedite their early mobilization with enhanced quality of life; with less postoperative cognitive impairment and reduced risk for persistent postoperative pain. This results in better overall outcome and reduced clinical expenses. Postoperative pain management with opioids are accompanied with significant adverse effects, such as, nausea, vomiting, respiratory distress, and paralytic ileus during postoperative period, which further delay early ambulation and hospital discharge. [6,7] To reverse these consequences various adjuvants are used to general anesthesia in expectation to stabilizing the hemodynamic responses to laryngoscopy, tracheal intubation, pneumoperitonium and extubation in addition to minimizing the postoperative analgesic requirements. Along with cost effectiveness, patients with poor tolerance to opioids are taken into consideration to be benefited with these anesthetic adjuncts.

In this regard, intravenous dexmedetomidine has gained immense popularity owing to its perioperative intravenous use which effectively blunts the haemodynamic response to stress responses, provide sedation without respiratory depression, and enables reduced requirements of post-operative analgesic consumption. [2,8,9] Dexmedetomidine is an extremely selective and definitive agonist of alpha-two adrenoceptor with its expedient properties of analgesia, sedation, anxiolytic effect, and sympatholytic action. [10] These actions are led by attenuation of sympathoadrenal responses caused by α-2 adrenoceptor agonist induced decreased systemic noradrenaline release resulting in decreased hemodynamic alteration. [11,12] However, dexmedetomidine requires monitored administration in patients with bradycardia or hypotension as it can cause deterioration of these conditions specifically in heart failure patients. [13]

Lidocaine on the other hand is gaining acceptance for its analgesic, anti-inflammatory, anti-hyperalgesia properties which is easily obtainable, inexpensive, safe, and its analgesic action offers reduced postoperative pain intensity and thus lessens the opioid consumption. [6,14] Short half-life, made this a preferable choice for uninterrupted intravenous administration. [15] It has been used as an anti-arrhythmic drug, and contrary to the dexmedetomidine it has cardio-protective effects against myocardial ischaemia. [16] The perioperative intravenous administration observed to offer control on haemodynamic alteration and is an effective technique for the management of pain during postoperative period facilitating prompt post-surgical recovery without any distinctive adverse effects. [17] Along with the benefit of this, lidocaine can be infused intravenously before the anesthesia induction to prevent haemodynamic changes that develops due to intubation. [18]

This research work was aimed to evaluate the effectiveness of dexmedetomidine and lidocaine infusion on intraoperative haemodynamic response and post-operative analgesic demand in gynecologic laparoscopic surgery.

II. METHODOLOGY

Subjects and methods: A prospective observational study have been designed and conducted at the Department of Anesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital. After evaluating for the selection criteria, 50 purposively selected female patients with ASA grade I & II who have been admitted for gynecologic laparoscopic surgery. Prior data collection, the ethical approval from the concerning ethical review committee and informed written consent from the patients have been obtained. Patients were randomly allocated in two groups, where Group A administered with dexmedetomidine hydrochloride and Group B administered with lidocaine hydrochloride.

Anesthetic procedures: Before the scheduled time of operation the patients kept fasting for at least 6 hours according to their individualized schedule of operation as per hospital protocol. After shifting the patients into the waiting area of the operation theatre 2 intravenous line was secured by 18G cannula and all the patients received a uniform premedication by Inj Ondansetron, Inj Ranitidine one-hour prior induction. After that, anesthetic adjuvants were administered according to study groups. Then IV fluids are given through one cannula, and another line was taken up for the infusion pump. After starting the infusion pump, Anaesthesia was induced with 2 mg/kg propofol IV, followed by 2 mg/kg succinylcholine, 2 mcg/kg fentanyl IV and patient was intubated. Then intraoperative muscle relaxant was maintained by vecuronium. Anaesthesia was maintained with 33% oxygen, 66% nitrous oxide and halothane in the range of 0.6%-0.8%. IPPV was given using circle absorbing system. Ventilation was maintained with tidal volume 10-12ml/kg, respiratory rate 14 breaths/min, PEEP 5cm H_2O to maintain to maintain the patient near eucapnic. Infusion of study drugs was stopped after at the time of exsufflation.

Administration of study drugs: Group A administered with a loading dose of IV 0.5μg/kg dexmedetomidine hydrochloride slowly over 10 min, subsequently IV infusion of 0.5μg/kg/h through a syringe pump. Group B administered with a loading dose of IV 1.5mg/kg lidocaine hydrochloride slowly over 10 min, subsequently IV infusion of 1.5 mg/ kg/h through a syringe pump.

Data collection: The data were collected and filled in the prefixed data sheet by principal researcher. In operation theatre, one anesthesiologist recorded patient's base line haemodynamics (systolic and diastolic blood pressure, heart rate). Then the principal researcher prepared the drugs and administered to the patient. Intraoperative haemodynamic parameters were measured and data were collected at different time points (base line, after drug preload, after intubation skin incision, after insufflation, 15 min, 30 min interval, after exsufflation, after extubation). The time was recorded in minute when patients required/request 1st dose of analgesic. First rescue analgesic (I/V Pethidine, 0.5 mg/kg) was given when VAS ≥4. The total number of intravenous pethidine hydrochloride infusion was recorded within 24 hours.

Statistical analysis: Following data collection, data was entered and secured and analyzed with SPSS version 22 (IBM Corp., Armonk, NY). A level of p value less than 0.05 was considered statistically significant.

III. RESULT

In this study, the study groups were comparable according to their background variables (p>0.05) (Table I). The record of heart rate of the patients showed that, except for the after drug preload time and after extubation, the mean heart rate (HR) was higher at all-time interval in Group A compared to Group B, however, this difference in mean was not statistically different (p>0.05). In both groups, just after drug preloading a reduction in pulse rate from the baseline have been observed followed by a surge just after intubation. Then again pulse rate continued to fall until skin incision in both groups followed by a slight increase after insufflation. Yet again HR started to decrease up to exsufflation followed by an escalation till extubation. Each reading at every time point was significantly different from the adjacent reading in both groups, however the difference in mean HR was not statistically different in between the group (p>0.05) (Figure I).

Table-I: Background characteristics of the patients (N=50)

Variables			Group A (n_1=25)	Group B (n_2=25)	P value
Age (in years)	**Mean ± SD**		26.6±4.84	27.04±4.44	0.739[a]
BMI (kg/m²)	**Mean ± SD**		25.35±2.24	25.32±1.89	0.959[a]
ASA	**I**	**N (%)**	19 (76%)	21 (84%)	0.725[b]
	II	**N (%)**	6 (24%)	4 (16%)	
Duration surgery (in minute)	**Mean ± SD**		41.68±7.36	40.88±7.32	0.702[a]

[a] denotes, p value reached from Student t-test, [b] denotes, p value reached from Pearson chi-squared Test (χ^2).

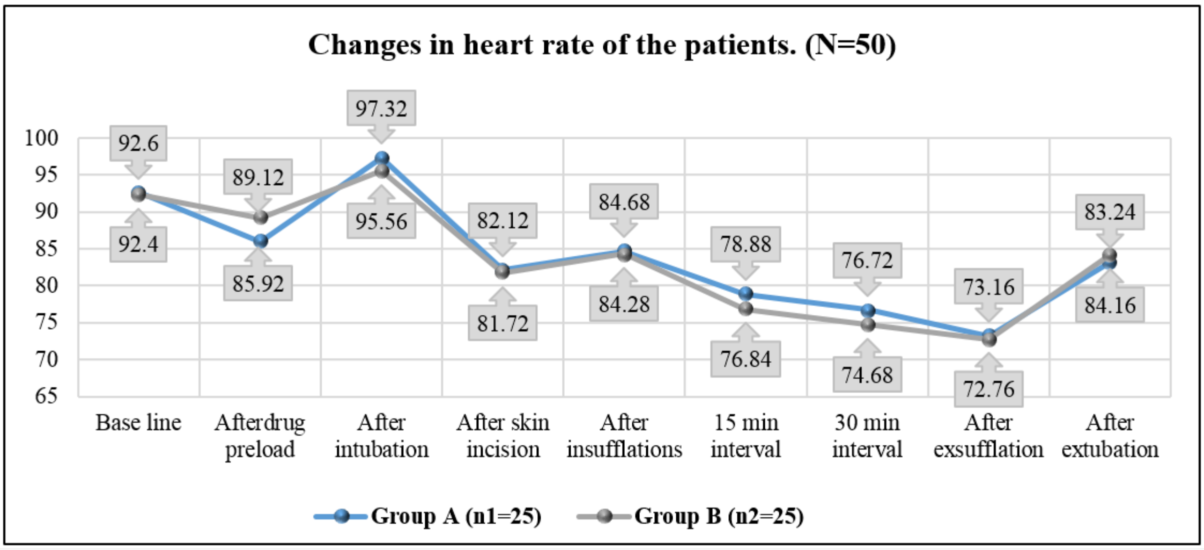

Figure I: Changes in heart rate of the patients. (N=50)

There was a significant reduction in SBP from baseline just after drug preloading followed by a rise after intubation in both the groups. Then again systolic BP started to fall significantly until skin incision in both groups followed by a slight increase after insufflation. Yet again SBP started to decrease up to exsufflation followed by an escalation till extubation. In cases of both the groups, the changes in mean SBP at every point compared to adjacent point was statistically significant (p<0.05). The readings od diastolic BP demonstrated a significant decline in DBP at just after drug preloading followed by a surge at just after intubation in both groups from baseline. Then again diastolic BP started to fall significantly until skin incision in both groups followed by a slight increase after insufflation. Yet again DBP started to decrease up to exsufflation followed by an escalation till extubation. Paired sample T test found significant change at every follow up point (except after insufflation, 30 min interval and after exsufflation) compared to previous adjacent point (p value <0.05) (Figure II).

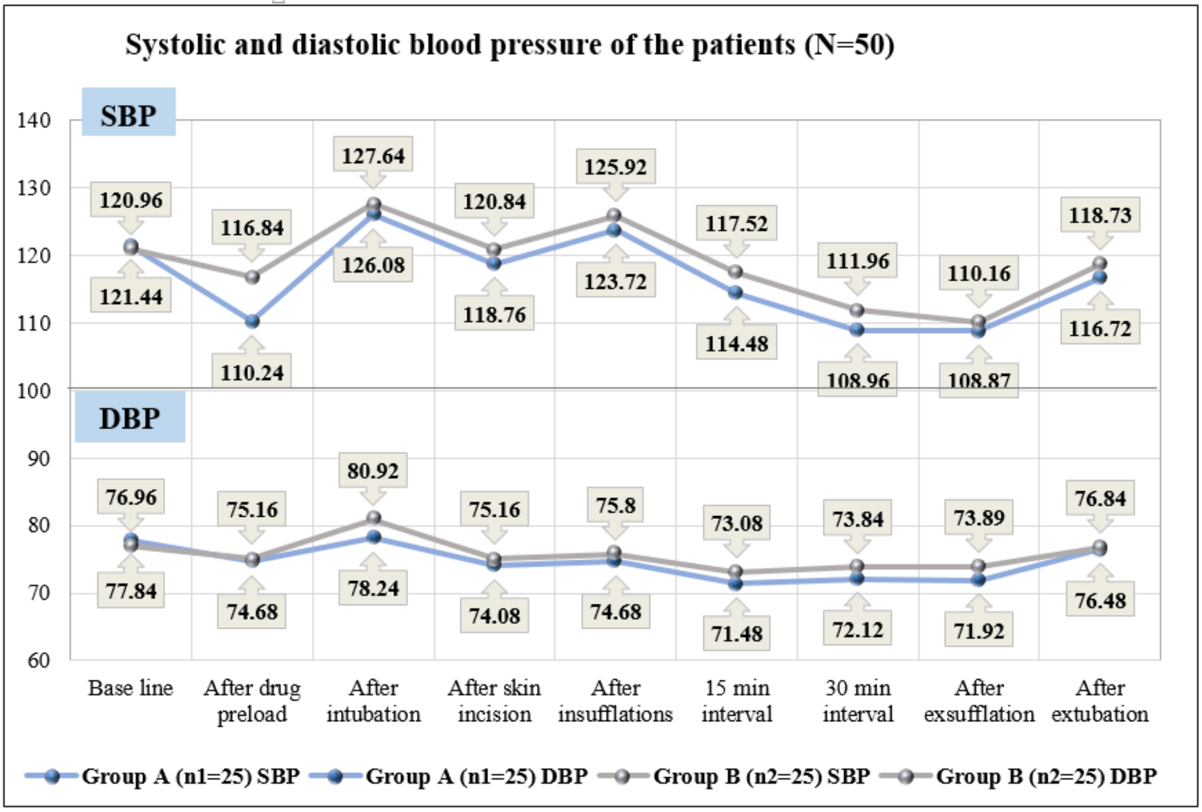

Figure II: Systolic and diastolic blood pressure of the patients (N=50)

The MAP was lower in Group A than Group B at every point reading. In both groups, there was a significant reduction in MAP just after drug preloading followed by a surge just after intubation from baseline. Then again mean arterial pressure started to fall significantly until skin incision in both groups followed by a slight increase after insufflation. Yet again MAP started to decrease up to exsufflation followed by an escalation till extubation. Paired sample t test found significant change at every follow up point compared to previous adjacent point (p value <0.05), however the intergroup changes in MAP was not significant at any point (p>0.05) (Figure III).

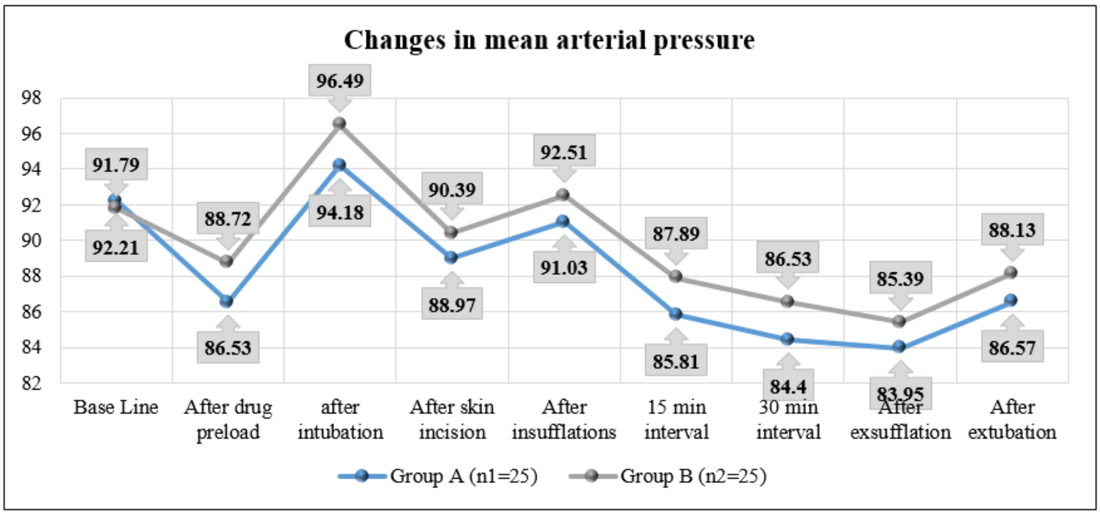

Figure III: Changes in mean arterial pressure

Time of first analgesic demand in PACU was 208.68±18.98 min in Group A and 210.72±19.18 min in Group B, the difference in mean time of first analgesic demand was not significant (p>0.05). Patients in Group B required significantly reduced number of analgesics in 24 hours in PACU compared to Group A (p<0.05) (Table II).

Table-II: Distribution of patient according to their 1st analgesic (pethidine) demand and total **number of analgesic consumptions**

Analgesic parameters	Group A (n1=25) Mean ± SD	Group B (n2=25) Mean ± SD	P value
Time of 1st analgesic demand (min)	208.68±18.98	210.72±19.18	0.707
Total number of analgesic consumptions	1.92±0.70	1.32±.63	<0.003

p value reached from Student t-test

IV. DISCUSSION

In laparoscopic surgery, intubation, pneumoperitoneum, extubation all leads to significant increase of systemic vascular resistance and increase blood pressure due to activation of sympathetic nervous system. Dexmedetomidine effectively blunts the hemodynamic consequences by postsynaptic stimulation of alpha2-adrenoceptors in the CNS, consequents in decrease in sympathetic action which causes sympatholysis-mediated vasodilatation in peripheral vasculature. [19] Lidocaine effectively blunts perioperative hemodynamic consequences resulting from peripheral vasodilating effect of vascular smooth muscle by moderating the discharge of adrenaline and provoking vascular endothelium to release vasodilators. [20] This study compared the effect of intraoperative intravenous infusion of dexmedetomidine and lidocaine on the perioperative heart rate, blood pressure, mean arterial pressure at various time intervals. Additionally, the time of postoperative 1st analgesic demand and total number of post-operative analgesic requirements also have been documented and compared between the study groups. The study groups in this study was comparable in terms of age, sex, BMI, ASA status, surgical indication and surgical time (p>0.05).

In this study the mean heart rate were slightly elevated among dexmedetomidine group patients than the lidocaine group of patients at most of the readings (at base line, after intubation, after skin incision, after insufflation, 15 min interval, 30 min interval, after exsufflation and after extubation) except for the time point of after drug preload. However, this finding was not statistically significantly different among the groups (p>0.05). In previous study findings, it has been observed that, administration of bolus dose of dexmedetomidine with 0.5µg/kg over 10 min and intra-operative infusion with 0.5µg/kg/h significantly attenuates the heart rate compared to the saline infused group of patients (p<0.05). [4] Analogously, another study showed that, bolus dose of lidocaine with 1.5mg/kg was followed by infusion with 1.5mg/kg significantly attenuates the heart rate compared to the saline infused group of patients (p<0.05). [21] Study which compared the effect of dexmedetomidine and lidocaine with the same dose as the present study found that the mean heart rate was not significantly different among the groups. [22]

The average SBP, DBP and MAP among the sample were higher in lidocaine group of patients compared to dexmedetomidine group of patients at all-time points without any significant difference (p>0.05). Manne et al. in their research work observed that, compared to saline infused group, dexmedetomidine administered group attenuates the SBP, DBP and MAP significantly (p<0.05). [2] Again, in one study it has been observed that, compared to the saline infused group, lidocaine infused group showed steady MAP which found to be statistically significant (p<0.05).[21] Current study result is consistent with the study of Anis et al. who showed that both lidocaine and dexmedetomidine infusions reduced the elevations of haemodynamic response during laparoscopic gynecologic surgery. They concluded that lidocaine infusion can be considered an effective modality similar to dexmedetomidine infusion to control the hemodynamic response in diagnostic laparoscopic gynecologic surgery. [23] In another study, Cho et al. reported with their study findings that, the difference in mean SBP, DBP and MAP among the groups infused with lidocaine and dexmedetomidine at all-time points in laparoscopic cholecystectomy surgery was not statistically different. [8] In laparoscopic surgery patients, Singh et al. found that, the HR and MAP was insignificantly different among the groups received dexmedetomidine compared to lidocaine (p>0.05). [24]

In this work, the time for 1st analgesic demand in Group A received dexmedetomidine was 210.72±19.18 min and Group B received lidocaine was 208.68±18.98 min without any significant difference (p >0.05). In the study by Murthy et al. the time of first analgesic requirement in patients received lidocaine compared to the saline infused group was significantly higher. [21] Similarly, in the study by Bielka et al. the time of first analgesic demand requirement in patients received dexmedetomidine compared to the saline infused group was significantly delayed. [25]

In this study the lidocaine group of patients had significantly lower total number of post-operative analgesic requirements compared to the dexmedetomidine group of patients. Substantial to these findings, Andjelković et al. also reported that perioperative intravenous infusion of lidocaine reduce postoperative analgesic requirement significantly on the first and second postoperative day after laparoscopic cholecystectomy then dexmedetomidine infusion. [26] In another study, Cho et al. found that difference in analgesic sparing effect between dexmedetomidine and lidocaine groups were insignificant.[8] The present work revealed that, intraoperative intravenous infusion of lidocaine and dexmedetomidine infusion both effectively maintain intraoperative hemodynamic response in patients undergoing laparoscopic gynecologic surgery. Moreover, lidocaine reduced post-operative analgesics requirement more efficiently than dexmedetomidine.

V. CONCLUSION

Though dexmedetomidine and lidocaine use different pharmacokinetic mechanism but their effectiveness are similar in maintaining intraoperative hemodynamic response in patients undergoing gynecologic laparoscopic surgery regarding their heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure. Moreover, post-operative total analgesic consumption was significantly low among patients who received IV Lidocaine infusion.

VI. LIMITATIONS

Neuromuscular blockade and depth of anesthesia were perceived only by clinical observation. Use of bispectral index and neuromascular evaluation could have been a better guide. Minute ventilation increased to eucapnic the patients during laparoscopic surgery. Use of capnograpy could have been better guide.

VII. RECOMMENDATION

Lidocaine can be used as an anesthetic adjunct as effectively as dexmedetomidine with comparable hemodynamic obtunding effect in patients undergoing gynecologic laparoscopic surgery. Poor candidates of dexmedetomidine can be administered with lidocaine in such procedures.

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Conflicts of interest

None

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