

# “ANESTHETIC SPARING EFFECT OF INTRAOPERATIVE LIGNOCAINE OR DEXMEDETOMIDINE INFUSION ON SEVOFLURANE DURING GENERAL ANESTHESIA”

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**Background:** Lidocaine and Dexmedetomidine are known to blunt the stress response to surgery, and have anesthetic sparing activity. This study was designed to evaluate and compare the anesthetic sparing effect of intravenous lidocaine with Dexmedetomidine infusion during sevoflurane based general anesthesia and also to assess their effects on hemodynamic parameters.

**Methods:** Forty-eight ASA I–II patients aged between 18–55 yr, scheduled for abdominal surgery lasting less than 2 h, performed under general anesthesia were enrolled and they were randomly allocated to Lidocaine(L), Dexmedetomidine (D) and Saline (S) groups of 16 each. Group L received Inj. Lidocaine at 1.5 mg/kg bolus over 10 min followed by infusion at 1.5 mg/kg/hr, and Group D received Inj. Dexmedetomidine at 1 µg/kg over 10 min, followed by 0.5 µg/kg/hr infusion till the end of surgery. Group S received similar volume of normal saline. Anesthesia was induced with Inj. Propofol and maintained with N<sub>2</sub>O in O<sub>2</sub> and sevoflurane, keeping entropy between 40–60. The hourly sevoflurane requirements and hemodynamic parameters were recorded.

**Results:** Demographic parameters, entropy and duration of surgery were comparable. Mean sevoflurane requirement at 1<sup>st</sup> h in group L and D were 11.6 ± 1.5 ml, and 10.2 ± 1.3 ml respectively, while it was 16.7 ± 4.1 ml in Saline group (P < 0.001). Sevoflurane requirements were significantly lesser in group D compared to group L (P = 0.009). The Mean ET<sub>sevo</sub> concentrations in Group L, D and S were 0.8 ± 0.3, 0.8 ± 0.4 and 1.2 ± 0.5 (P = 0.021), respectively.

**Conclusions:** Both drugs produce significant anesthetic sparing effect during sevoflurane based general anesthesia, but dexmedetomidine has better sparing effect than lignocaine.

**Keywords:** Dexmedetomidine, Intraoperative, Lidocaine, Sevoflurane.

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## Introduction

Intravenous (IV) Lidocaine can be used to provide symptomatic relief from cancer pain<sup>1</sup>, diabetic neuropathies<sup>2,3</sup>, and chronic pain<sup>4,5</sup> without producing any toxic side effects. This analgesic efficacy was attributed to selective depression of pain transmission in the spinal cord<sup>4,5</sup>, and a reduction in tonic neural discharge of active peripheral nerve fibers<sup>6,7</sup>. Because of its NMDA receptor antagonist activity, lidocaine can reduce volatile anesthetic requirements during general anesthesia. Dexmedetomidine, a highly selective  $\alpha$ -2 adrenergic receptor agonist has sedative, analgesic, anesthetic-sparing properties without any respiratory depression<sup>8</sup>. The hypnotic and supraspinal analgesic effects are mediated by the hyperpolarization of noradrenergic neurons, which suppresses neuronal firing in the locus ceruleus due to decreased norepinephrine and histamine release<sup>9</sup>.

There are very few studies that compare intravenous lidocaine and dexmedetomidine with regard to anesthetic sparing effect, specially when objective tools like BIS or entropy were used to guide the depth of anesthesia.

Hence this clinical study was designed to compare the effects of IV lidocaine and dexmedetomidine on sevoflurane requirements during entropy guided general anesthesia.

## Materials and Methods

After obtaining approval from institutional ethical committee, a randomized, prospective, double blind, controlled, clinical study was formulated, and conducted at our hospital from March 2013 to October 2013.

Forty eight patients were randomly allocated into three groups as Group L (Lidocaine group), Group D (Dexmedetomidine) and Group S (Saline group) using computer based random number generation technique.

Informed written consent was obtained from all patients. The patients with American society of Anesthesiologists (ASA) physical status I and II, aged 18-55 yr, scheduled for elective open abdominal surgery expected to last less than 2 hours, under general

anesthesia were included in the study. Hypertensive patients, patients on psychoactive medication, and those allergic to local anesthetics were excluded from the study.

A minimum fasting state of 6-8 hours before anesthesia was ensured in all patients. In the operating theatre IV access was obtained and the standard monitoring consisted of electrocardiography, pulse oximetry, noninvasive blood pressure, entropy sensor, neuromuscular transmission indicator (NMT) and capnography. Midazolam 0.05 mg/kg IV, glycopyrrolate 0.005 mg/kg IV, Fentanyl 2  $\mu$ g/kg IV were used for premedication. The response entropy was measured with Datex Ohmeda entropy S/5 module. All patients were pre-oxygenated with 100% oxygen for 3 minutes.

Group L received a loading dose of lidocaine 1.5 mg/kg IV made to 20 ml with normal saline, over 10 minutes followed by similar volume every hour till the end of surgery. In group D, patients received 1  $\mu$ g/kg of dexmedetomidine, made to 20 ml, in 10 minutes followed by an infusion of dexmedetomidine 0.5  $\mu$ g/kg made up to 20 ml, every hour. Group S received similar volume of normal saline. The drug solutions were prepared by anesthesiologists who were not involved in the management of the case. Anesthesia was induced with Propofol until RE reached 50, and confirmed with loss of response to verbal commands. Atracurium 0.5 mg/kg IV was used to facilitate tracheal intubation. Anesthesia was continued with 60% nitrous oxide in oxygen and sevoflurane, and ventilated to maintain  $ETCO_2$  between 35-40 mmHg. Sevoflurane concentration was adjusted to ensure adequate depth of general anesthesia as guided by entropy (40-60) and also by clinical variables like HR, systolic and diastolic blood pressures (SBP & DBP), and mean arterial pressure (MAP). Adequate muscle relaxation was guided by NMT monitor. The monitored data were recorded continually at baseline, before induction, after induction, 1 minute after intubation and every 5 minutes thereafter, till the end of surgery. Initially fresh gas flow (FGF) of 6 L/min was used until the difference between end inspiratory and end expiratory sevoflurane concentration was nearly equal and later the FGF was reduced to 2 L/min. Infusion of test drug and sevoflurane administration

was cut off on the beginning of skin closure and the fresh gas flow was increased to 6 L/min oxygen. At the end of the skin closure, residual neuromuscular blockade was reversed with neostigmine 0.5 mg/kg and glycopyrrolate 0.01 mg/kg and trachea was extubated after satisfactory recovery. The duration of sevoflurane usage and duration of anesthesia (min) were recorded. The hourly sevoflurane requirements and total consumption of sevoflurane at the end of the procedure were recorded directly from anesthetic agent monitoring module of Datex Ohmeda Avance S5™ anesthesia workstation. The Minimum alveolar anesthetic concentration (MAC) was derived from end tidal concentration of sevoflurane using a nomogram by Nickalls and Mapleson<sup>11</sup>.

Intraoperatively, occurrence of bradycardia and hypotension episodes were noted. Bradycardia was defined as heart rate less than 50 beats/min and hypotension was defined as more than 25% decrease in mean arterial pressure from the baseline. Bradycardia and hypotension if noticed, were treated with atropine 0.5 mg i.v, and fluid boluses and ephedrine 6 mg i.v boluses respectively. Tachycardia was defined as heart rate (HR) more than 110 beats/min and hypertension defined as increase in mean arterial pressure greater than 25% from the baseline and treated with esmolol infusion. If time from discontinuation of anesthetic to spontaneous eye opening exceeded 30 min, it was considered as delayed recovery and recorded.

### Statistical Analysis

Sample size was calculated based on the pilot study done on 10 patients. We hypothesized that dexmedetomidine would have greater anesthetic sparing effect compared to Lidocaine. By keeping the confidence limits at 95% and power at 80%, to detect a 15% reduction in sevoflurane consumption assuming an equal standard deviation and normal distribution of values, the required sample size was 13 patients in each group. However for better validation of results we increased the sample size to 16 in each group. All parametric data were presented as mean + SD, and nominal data were tabulated. One way ANOVA and post hoc analysis with Benferroni's correction and Dunell's correction was applied for all parametric data, chi-square test and Fisher exact test applied for nominal data. Furthermore, independent t-test was applied for intergroup comparison of mean values. P value of less than 0.05 was considered statistically significant. Statistical analysis was conducted with SPSS (Version 17) for windows statistical package.

### Results

Demographic parameters such as age, gender, weight, duration and type of surgery and anesthesia, basal vital parameters and entropy values were similar in all the groups (Table 1). Sevoflurane was used for slightly longer time in group D patients (P = 0.04).

Table 1  
Demographic Characteristics

Parameters	Lidocaine (n = 16)	Dexmedetomidine (n = 16)	Saline (n = 16)	P-value
Age(yrs)	41.2 ± 12.5	48 ± 9.01	46.68 ± 12.48	0.21
Sex (M:F)	7:9	6:10	7:9	
Weight(kg)	55.60 ± 9.08	51.40 ± 5.08	53.87 ± 6.55	0.25
Duration of surgery(min)	76.88 ± 15.15	89.33 ± 30.93	74.38 ± 18.52	0.14
Duration of Anesthesia(min)	92.18 ± 14.94	111.67 ± 38.44	91.88 ± 18.79	0.06
Duration of Sevoflurane Usage(min)	72.8 ± 15.2	93.67 ± 33.57*	77.19 ± 19.15	0.043
Types of surgeries				
Open cholecystectomy	12	9	11	
Open cholecystectomy with common bile duct exploration	2	4	2	0.7
Gastric surgeries	2	3	3	

Table 2  
Sevoflurane Consumption

Parameters	Group L	Group D	Group S	P value
Mean Et <sub>Sevo</sub>	0.78 ± 0.3	0.83 ± 0.42	1.18 ± 0.53*	0.021
Mean Sevoflurane Consumption in 1 <sup>st</sup> hour	11.63 ± 1.58	10.20 ± 1.32 <sup>‡</sup>	16.75 ± 4.07*	< 0.0001

Intraoperatively adequate depth of anesthesia was maintained in all the patients with the help of entropy (Fig. 1) and clinical parameters such as heart rate and blood pressure (Figs. 2 and 3).

Mean Sevoflurane requirement at 1<sup>st</sup> hour in Group S was 16.75 ± 4.07 ml compared to 11.63 ± 1.58 ml in Group L (30.5% reduction), and 10.20 ± 1.32 ml in Group D (39% reduction)(P < 0.01). Post hoc analysis showed significantly lower consumption of sevoflurane in group D compared to group L

(P < 0.01) in the first hour. The end tidal concentration of sevoflurane (Et<sub>Sevo</sub>) was significantly lower in groups L and D compared to group S (P = 0.02). The intergroup comparison indicates that there was no statistically significant difference between Group L and Group D with respect to mean end tidal sevoflurane concentration, although duration of sevoflurane usage was significantly longer in group D (Table 2).

The average MAC was 1.02 ± 0.2, 1.05 ± 0.1, and 1.16 ± 0.2 in Group L, D and group S respectively(P =

Fig. 1  
Response Entropy values mean±SD  
in 3 groups

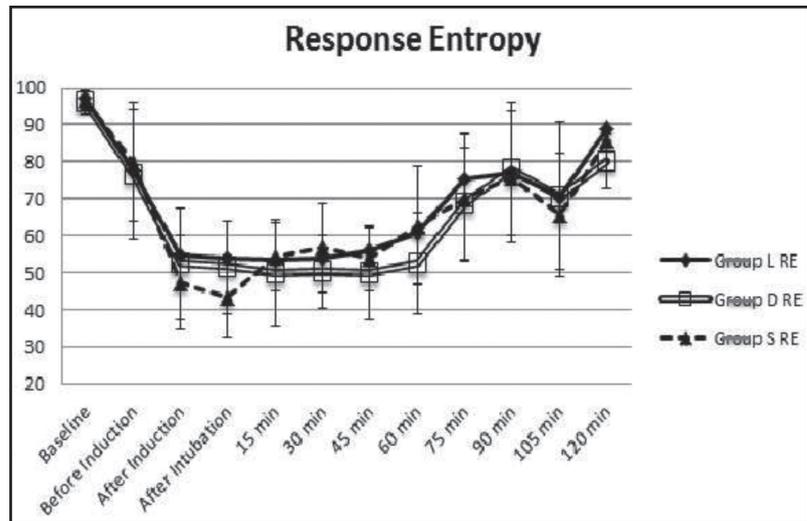


Fig. 2  
The trend in heart rate

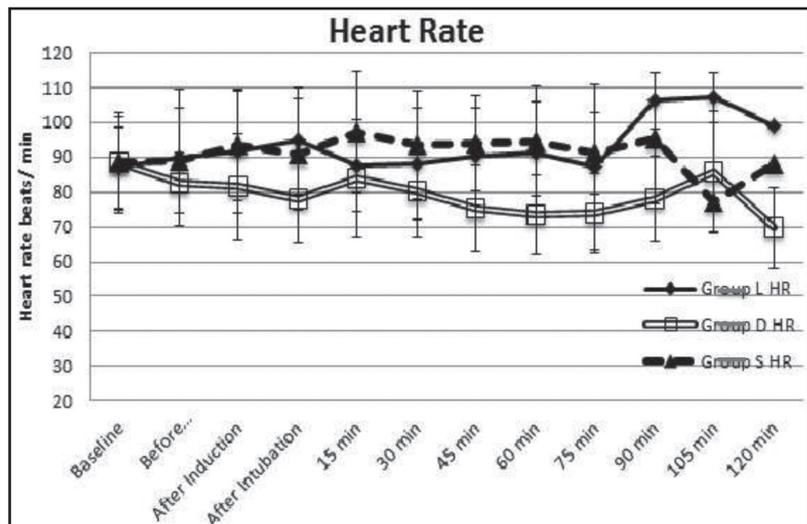
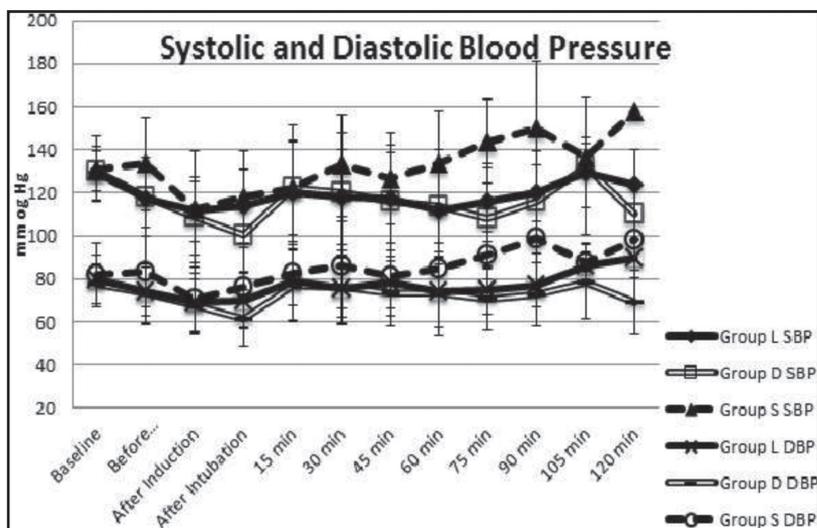


Fig. 3  
Trend in systolic and diastolic blood pressures



0.08). Post hoc analysis did not reveal any statistically significant difference between the groups.

During first hour of anesthesia, the heart rates were significantly lower in Group D compared to other two groups. The mean heart rates in group D were comparable to groups L and S after 1<sup>st</sup> hour. The systolic and diastolic blood pressure was comparable in all the three groups initially, but was significantly higher in group S compared to other two groups after 1<sup>st</sup> hour. None of the patients in any of the three groups had heart rate or blood pressure instability requiring intervention. There was no incidence of delayed recovery in any of the three groups.

## Discussion

The present study shows that intraoperative infusions of lidocaine and dexmedetomidine reduces the sevoflurane consumption during entropy guided general anesthesia. Dexmedetomidine caused greater decreases in sevoflurane consumption compared to lidocaine infusion. Degree of surgical stimulus may influence anesthetic consumption and all attempts were made to maintain uniformity in surgical stimulus in the present study, by recruiting patients undergoing upper abdominal surgeries of duration less than 2 hours.

Following systemic administration, lidocaine, a sodium channel blocker, attenuates skin pain in response to mechanical or chemical stimuli through peripheral and central mechanisms in preclinical

human volunteer tests<sup>12-14</sup>. It was observed that IV lidocaine infusion reduced BIS guided propofol requirement<sup>15,16</sup>. The BIS read zero when lidocaine was inadvertently administered at a dose of 100 mg per minute for 7-8 min<sup>17</sup> indicating that cerebral cortical activity was decreased by systemic lidocaine administration. During the study conducted to explore the effect of lidocaine on MAC, Hodgson and Liru<sup>18</sup> found that during general anesthesia with BIS less than 50, epidural lidocaine reduced sevoflurane requirement by 34%, probably due to rostral migration of lidocaine to the brain cerebrospinal fluid. It was observed that, intraoperative lidocaine infusion reduced sevoflurane requirement by 5% during BIS monitored general anesthesia<sup>19,20</sup>. During 60% nitrous oxide in oxygen anesthesia, in the current study, it was observed that there was 30.5% reduction in sevoflurane requirement during 1<sup>st</sup> hour of anesthesia when lidocaine was infused. The greater reduction in consumption noticed in the present study compared to previous ones may be attributed to the use of nitrous oxide.

Edno Magalhaes and others observed that dexmedetomidine infusion at a rate of 0.5 µg/kg over 10 min before the induction of anesthesia and when later maintained with 0.2-0.7 µg/kg/hr until skin closure attenuated sympatho-adrenal response to tracheal intubation<sup>21</sup>. Uyar et al<sup>22</sup> observed that administration of single IV bolus dose of dexmedetomidine 1 µg/kg over 10 minutes before induction of anesthesia resulted in attenuation of hemodynamic and neuroendocrinal responses to skull pin insertion in patients undergoing

craniotomy. Keniya et al<sup>23</sup> showed that 1 µg/kg bolus followed by 0.2-0.7 µg/kg/hr of dexmedetomidine infusion not only blunted the sympathoadrenal response to tracheal intubation but also reduced the consumption of fentanyl and isoflurane; however, their measurement were based on the inspired concentration of isoflurane. Patel et al<sup>24</sup> reported that dexmedetomidine infusion when given as bolus of 1 µg/kg followed by 0.2-0.8 µg/kg infusion, reduced end-tidal sevoflurane concentration by 21%. In the present study, using bolus IV dexmedetomidine 1 µg/kg combined with infusion of 0.5 µg/kg/hr resulted in 39% reduction in sevoflurane requirements during 1<sup>st</sup> hour of anesthesia. However, end-tidal concentration of sevoflurane in patients receiving dexmedetomidine, in the current study, were lower compared to those reported by Patel et al which may be attributed to the use of fentanyl in the current study. Action of dexmedetomidine at both supraspinal and spinal levels may have attributed to greater reductions in sevoflurane

consumption compared to lidocaine. Though patients receiving dexmedetomidine exhibited significant reduction in heart rate intraoperatively, none of these patients required any treatment.

The main limitations of the study are the fact that the MAC was a derived factor from end-tidal concentration. Also, the serum levels of test drugs were not estimated during this clinical study and hence dose response relationship could not be established.

## Conclusion

IV lidocaine and dexmedetomidine used for preanesthetic and intraoperative infusions produce 30.5% and 39% anesthetic sparing effect respectively during sevoflurane based general anesthesia when compared to normal saline. However dexmedetomidine was found to be significantly more effective than IV lidocaine.

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