# Does Perioperative Lidocaine Infusion Decrease the Mininmum Alveolar Concentration of Isoflurane viz-a-viz Depth of Anaesthesia using Processed Electroencephalogram (Bispectral Index)

**Khairat Mohd[1], Aatif Shah[2], Samiksha Khanooja[3]**

**ABSTRACT**

**Introduction:** Minimal alveolar concentration (MAC) of volatile anaesthetics is that which prevent movement in 50% of subjects in response to a noxious stimulus. MAC is influenced by several drugs like fentanyl, midazolam, propofol, clonidine. Various successful studies have been done to demonstrate the effect of IV anaesthetics and opioids on MAC of various inhaled anaesthetics in balanced anaesthesia settings. To assess the effect of a perioperative lidocaine infusion on the MAC of isoflurane in a balanced anaesthesia technique by correlating it with the depth of anaesthesia as assessed by the Bispectral Index (BIS).

**Material and methods:** It is a prospective randomized study consisting of 100 patients. The patients were categorized into group L and group S, Group L received a bolus of 1.5mg/kg of lidocaine five minutes before the induction of general anaesthesia followed by 1.5mg/kg/hr of lidocaine infusion till the end of the surgical procedure or upto a maximum of three hours (whichever was earlier). Group S received saline similarly. BIS was maintained between 40 to 60 and MAC of isoflurane was measured in both group.

**Result:** Significant difference with regard to MAC of isoflurane used to maintain anaesthesia was noted between the two groups. It was found overall average MAC of isoflurane in Group L was (0.761±0.011) and control group was (0.885±0.020).

**Conclusion:** Our study found that lidocaine loading dose followed by infusion significantly reduces volatile anaesthetic requirement as measured by MAC of isoflurane

**Keywords:** Depth of Anaesthesia, Bispectral Index, Isoflurane, Lidocaine

## INTRODUCTION

The induction of immobility in response to surgical stimulation is an essential feature of general anaesthesia. The capability of volatile anaesthetics to immobilize patients who are exposed to noxious stimulation is measured using the MAC which is defined as "the minimum alveolar concentration of anaesthetic that prevents movement in 50% of subjects in response to a noxious stimulus."[1] The MAC is influenced by several drugs including fentanyl[2], midazolam[3], propofol[4], and clonidine.[5] Several brain-function monitors based on the processed electroencephalogram or evoked potentials have been developed to assess anaesthetic depth. BIS value range from 100 to 0, reflecting the awake state and the absence of brain activity, respectively. BIS values between 40 and 60 indicate adequate general anaesthesia for surgery, and value below 40 indicate a deep hypnotic state.

The effect of intravenous anaesthetics and opioids on the MAC of various inhaled anaesthetics in a balanced anaesthesia setting have been studied.[6,7] In this study we aimed to study the effect of perioperative lidocaine infusion on the MAC of isoflurane in a balanced anaesthesia technique by correlating it with the depth of anaesthesia as assessed by the Bispectral Index (BIS).

## MATERIAL AND METHODS

The study was a prospective, randomized double blinded, placebo controlled trial and included 100 patients. Permission from the Institutional ethical committee was taken and due written informed consent from the participants of the study was taken.

**Inclusion criteria**

1. Patients of both genders above the age of 18 years undergoing general anaesthesia and surgery.
2. ASA physical status I and II.
3. Duration of surgery less than or equal to 3 hours.

**Exclusion criteria**

1. Refusal to participate in the study.
2. Allergic to lidocaine.
3. Pre-existing Respiratory, renal, cardiovascular or hepatic disease.
4. Body weight greater than or equal to 90 kilograms.
5. Pregnant. A thorough menstrual history of every woman in the reproductive age group was taken.
6. History of drug abuse, poor comprehension and a psychiatric disturbance which limited proper patient cooperation.

The patients were categorized into group L (Lidocaine) and

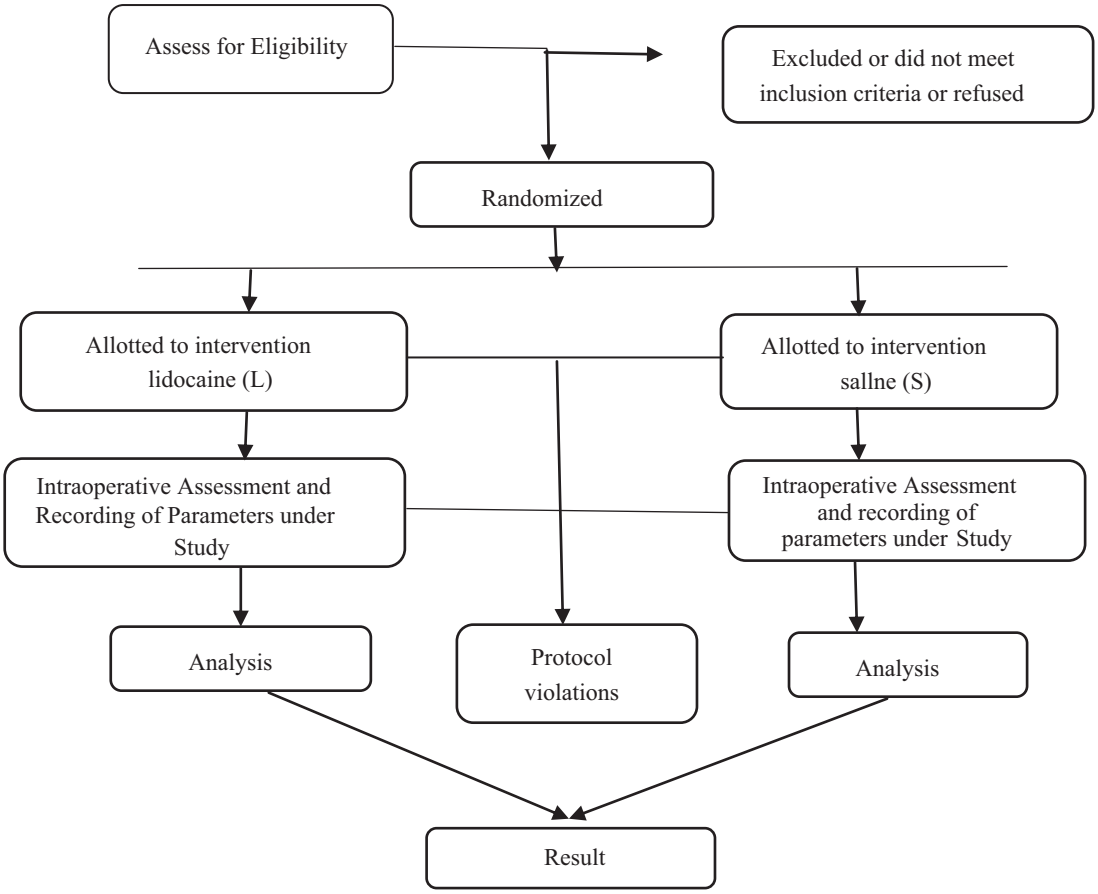
[1]HOD & Professor, Department of Anaesthesiology & Intensive care, HIMSR, Jamia Hamdard, [2]Senior Resident, Department of Anaesthesiology & Intensive Care, SKIMS, Sri Nagar, J&K, [3]Assistant professor, Department of Anaesthesiology & Intensive Care, HIMSR, Jamia Hamdard, India

**Corresponding author:** Dr. Khairat Mohd, HOD & Professor, Department of Anaesthesiology & Intensive Care, HIMSR, Jamia Hamdard, India

**How to cite this article:** Khairat Mohd, Aatif Shah, Samiksha Khanooja. Does perioperative lidocaine infusion decrease the mininmum alveolar concentration of isoflurane viz-a-viz depth of anaesthesia using processed electroencephalogram (bispectral index). International Journal of Contemporary Medical Research 2019;6(8):H10-H14.

**DOI:** http://dx.doi.org/10.21276/ijcmr.2019.6.8.23

Flow study diagram




group S (Saline), each containing fifty patients. A reliable intravenous access was secured on the non-dominant hand. Group L received a bolus of 1.5mg/kg of lidocaine five minutes before the induction of general anaesthesia followed by 1.5mg/kg/hr of lidocaine infusion till the end of the surgical procedure or upto a maximum of three hours (whichever was earlier). Low dose lidocaine well below the maximum recommended dose of 3 mg/kg was used to ensure no toxic effects are seen.[20] Group S was given the same volume of normal saline. Group allotments were done at random and by research personnel not directly involved with patient care. The same research personnel prepared syringes labelled with the study drug to blind subjects enrolled in the study, anaesthesia providers, and investigators collecting the data. All the subjects were premedicated with 0.25 mg Alprazolam tablet and 40mg of pantoprazole tablet.

The patients were shifted to the operating room on a trolley with oxygen facility and $SpO_2$ monitor. BIS electrodes were attached and a baseline reading of BIS was taken. Anaesthesia was induced with 2mg/kg body weight of propofol. Fentanyl 1.5 mcg/kg was used for analgesia on induction and atracurium 0.5mg/kg was used to induce a neuromuscular block. Bag and mask ventilation was done for 3 minutes. Tracheal intubation was performed by a qualified anaesthetist. Anaesthesia maintenance was achieved using oxygen, nitrous, isoflurane and atracurium titrated to maintain a blood pressure within 20% of the baseline and a BIS (bispectral index) between 40 and 60. Gas flows were kept constant between the two groups. During the intraoperative period measurements of MAC of isoflurane used to maintain anaesthesia within the prefixed limits were taken at regular intervals. Intraoperative standard doses of opioid analgesics were given to both Group L and Group S. Neuromuscular blockade was reversed at the end of the surgical procedure using 60 mcg/kg of Neostigmine and 10 mcg/kg of Glycopyrrolate. Ondansteron 0.1 mg/ kg was used as an anti-emetic in both the groups. At the end of the procedure the subjects were given 30mg of IV ketorolac and 1 gm IV paracetamol.

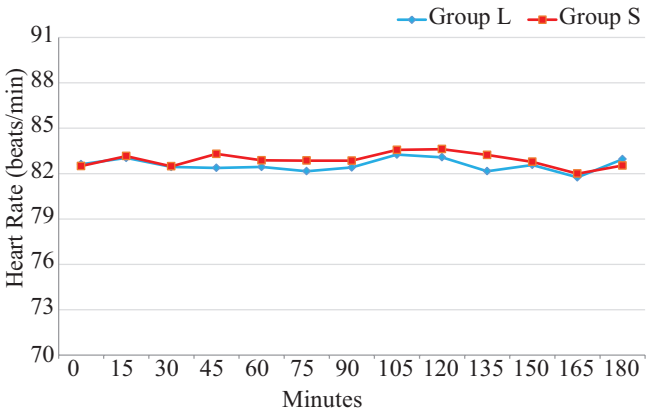
## STATISTICAL ANALYSIS

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were summarized in the form of means and standard deviations and categorical variables were summarized as percentages. Student's independent t-test was employed for parametric data. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

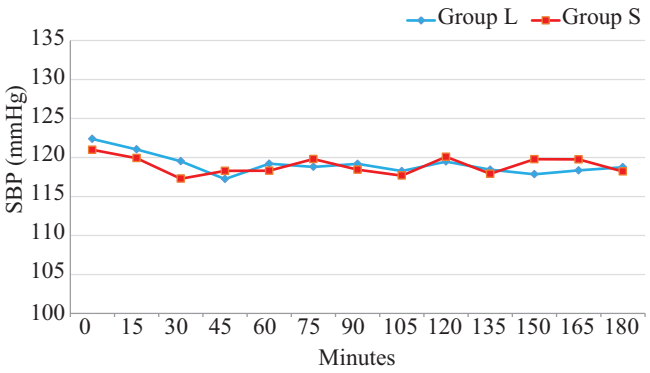
## RESULTS

The two groups were comparable with reference to age (Table-1), sex (Table-2), body weight (Table-3), and duration of surgery (Table-4). They were found to be insignificant.

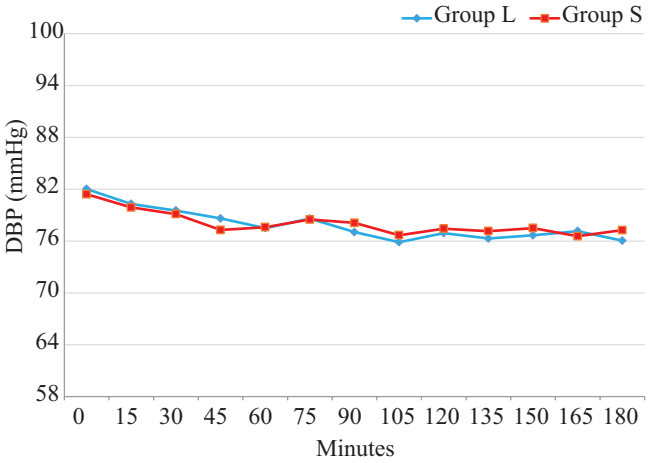
The groups when compared with reference to mean heart rate (graph 1), mean systolic blood pressure (graph 2), and mean diastolic blood pressure (graph 3) at various intervals, the difference was found to be statistically insignificant (p value > 0.05). No patient in either group developed significant change in hemodynamic parameters that demanded intervention.




**Graph-1:** Showing heart rate (beats/min) among two groups at different time intervals




**Graph-2:** Showing SBP (mmHg) among two groups at different time intervals

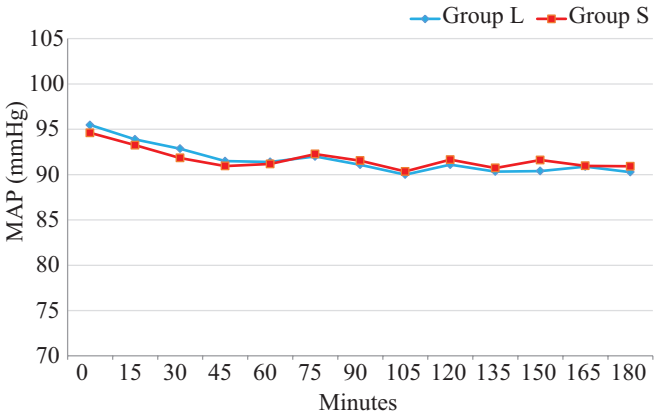



**Graph-3:** Showing DBP (mmHg) among two groups at different time intervals

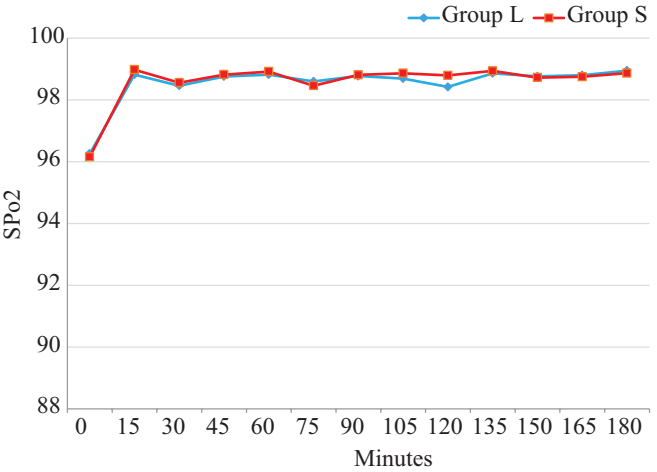
No significant respiratory depression was reported in any patient in this study and none of the patients had a $SpO_2$ value of < 95% on pulse oximetry. (graph 5)

No statistically significant difference was seen with respect to Bispectral Index (BIS) between the two groups (p >0.05). (Graph 6)

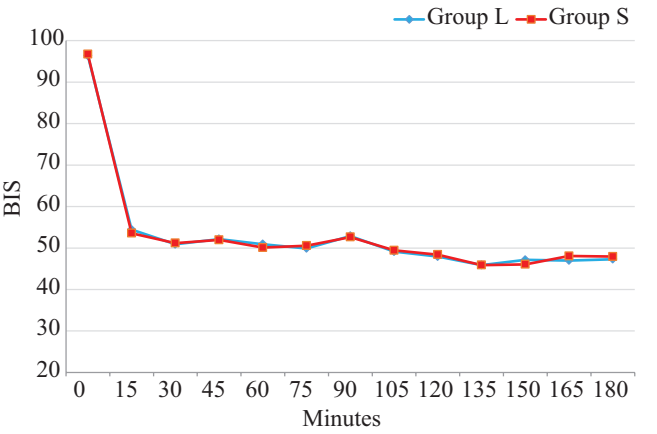
However significant difference with regard to MAC of isoflurane used to maintain anaesthesia was noted between the two groups. It was found overall average MAC of



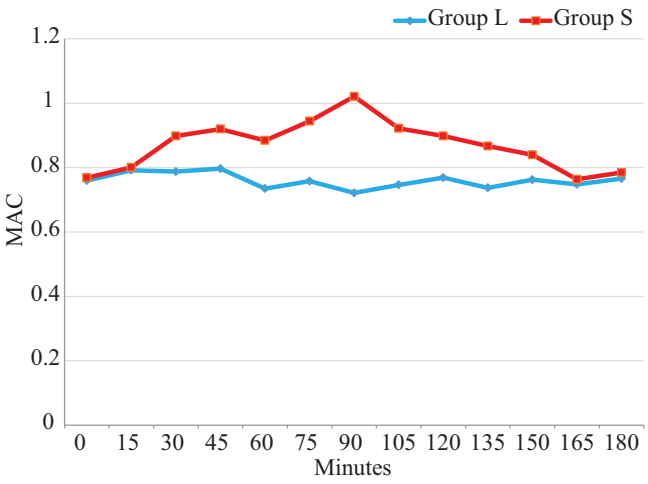

**Graph-4:** Showing MAP(mmHg) among two groups at different time intervals




**Graph-5:** Showing $SpO_2$ among two groups at different time intervals




**Graph-6:** Showing BIS among two groups at different time intervals




**Graph-7:** Showing MAC among two groups at different time intervals

| Age (Years) | Mean | SD | Range | P-value |
|---|---|---|---|---|
| Group L | 37.2 | 10.23 | 17-59 | 0.554 |
| Group S | 38.3 | 9.30 | 19-58 | |

**Table-1:** Age distribution of studied patients

| Gender | Group L | | Group S | | P value |
|---|---|---|---|---|---|
| | No. | %age | No. | %age | |
| Male | 28 | 56.0 | 31 | 62.0 | 0.542 |
| Female | 22 | 44.0 | 19 | 38.0 | |
| Total | 50 | 100 | 50 | 100 | |

**Table-2:** Gender distribution of studied patients

| Weight (kg) | Mean | SD | Range | P-value |
|---|---|---|---|---|
| Group L | 62.2 | 9.16 | 45-81 | 0.677 |
| Group S | 62.9 | 7.49 | 47-82 | |

**Table-3:** Distribution of weight (kg) in studied patients

| Operative time (minutes) | Mean | SD | Range | P value |
|---|---|---|---|---|
| Group L | 144.3 | 34.25 | 85-180 | 0.577 |
| Group S | 140.5 | 33.66 | 82-180 | |

**Table-4:** Showing duration of surgery (minutes) of studied patients

isoflurane in Group L was (0.761±0.011) and control group was (0.885±0.020). The two groups showed statistically significant difference (p=0.001).(graph 7)

## DISCUSSION

Our study found that lidocaine loading dose followed by infusion significantly reduces volatile anaesthetic requirement as measured by MAC of isoflurane required to maintain BIS between 40- 60 without any significant hemodynamic changes

Lidocaine has been used as an intravenous anaesthetic and for pain relief extensively.[8,9,10] Studies showing a MAC reduction effect of intravenous lidocaine in various anaesthetic settings have been done in humans and animals.[11] These studies demonstrate that lidocaine when used as an infusion decreases the MAC of inhaled anaesthetic agents. There is paucity of literature regarding the effect of lidocaine infusion on MAC of isoflurane in humans. We conducted this study with the aim of evaluating the effect of perioperative lidocaine infusion on MAC of isoflurane and its correlation with bispectral index.

Our results are in concondance with the study by Basil P et al who observed an anaesthetic sparing effect of intravenous lidocaine infusion indicated by lower MAC requirements in patients undergoing major abdominal surgery.[12] Weinberg L et al also observed that i.v. lidocaine reduces volatile requirements as measured by end tidal sevoflurane concentration in patients undergoing open prostatectomy.[13] Perioperative lidocaine infusion did not have any effect on remifentanil dosage or on BIS in hypotensive anaesthesia.[14]

The mechanism for MAC reduction with lidocaine is not clear. While lidocaine's analgesic effects may be responsible for the sparing effect on volatile anaesthetic MAC, it may also result from sedative effect of lidocaine as drugs with sedative effect are known to decrease MAC. The analgesic effect of lidocaine has been demonstrated in various studies. Lidocaine decreased the incidence of postoperative pain, hastened the return of intestinal motility and shortened hospital stay in patients undergoing prostatectomy. Postoperative pain decreased by 90% in patients in patients who received i.v. lidocaine intraoperative.

We did not find any significant differences in hemodynamic parameters between the study groups. This contrasts with the study by Weinberg L et al who observed lower values of heart rate and mean arterial pressure in patients receiving lidocaine infusion compared to placebo. This difference can be explained by the fact that end tidal sevoflurane concentrations were measured for calculating volatile agent requirements and MAC was kept constant around 1. Also BIS values were significantly lower in patients receiving lidocaine, reflecting greater depth of anaesthesia which would result in lower heart rate and mean arterial pressure in lidocaine group.

## CONCLUSION

Our study found that lidocaine loading dose followed by infusion significantly reduces volatile anaesthetic requirement as measured by MAC of isoflurane required to maintain BIS between 40- 60 without any significant hemodynamic changes.

## REFERENCES

1. Keith L. Parker, Laurence L. Brunton, John S. Lazo. Mc Graw Hill medical publishing division, Goodman & Gilman's The Pharmacological Basis of Therapeutics, Eleventh Edition page 377.
2. McEwan AI, Smith C, Dyar O, Goodman D, Smith LR, Glass PS. Issoflurane minimum alveolar concentration reduced by fentanyl. Anesthesiology 1993;78:864-9.
3. Inagaki Y, Sumikawa K, Yoshiya I. Anesthetic interaction between midazolam and halothane in humans. Anesth Analg 1993;76:613–7.
4. Luo LL, Zhou LX, Wang J, Wang RR, Huang W,

Zhou J. Effects of propofol on the minimum alveolar concentration of sevoflurane for immobility at skin incision in adult patients. J Clin Anesth 2010;22:527–32.

5. Nishina K, Mikawa K, Uesugi T, Obara H. Oral clonidine premedication reduces minimum alveolar concentration of sevoflurane for laryngeal mask airway insertion in children. Paediatr Anaesth 2006;16:834–9.
6. Keith L. Parker, Laurence L. Brunton, John S. Lazo. Mc Graw Hill. Goodman & Gilman's The Pharmacological Basics of Therapeutics, Eleventh Edition, page 357.
7. Thomas Hamp, Mario Krammel, Ulrike Weber, Rainer Schmid, Alexandra Garf, Walter Plochl. The effect of a bolus dose of intravenous lidocaine on the Minimum Alveolar Concentration of Sevoflurane: A prospective,Randomized, Double Blinded, Placebo-Controlled Trial. Anesth Analg 2013;117:323-8.
8. Richard C, Gilbert A, Hanson R, Albert B, and Robert A. Intravenous Use of Xylocaine. Current Researches in Anaesthesia and Analgesia 1951;30:301-313.
9. Cassuto Jean, Wallin Gunnar, Hogstrom Seth, Faxen Anders, Rimback Gunnar. Inhibition of Postoperative Pain by continuous Low-Dose Intravenous Infusion of Lidocaine. Nesth Analg 1985;64:971-4.
10. Gildasio S. De Oliveria, Paul Fitzgerald, Lauren F. Streicher, R-Jay Marcus and McCarthy J. Robert. Anesth Anal 2012;115:261-67.
11. Richard S. Himes, Cosmo A. DiFazio, Robert G. Burney. Effects of Lidocaine on the Anesthetic Requirements for Nitrous Oxide and Halothane. Anesthesiology 1977;47:437-440.
12. Bazin P, Padley J, Ho M, Stevens J, Ben-Menachem E. The effect of intravenous lidocaine infusion on bispectral index during major abdominal surgery. J Clin Monit Comput. 2018;32:533-539.
13. Weinberg L, Jang J, Rachbuch C, Tan C,Hu R, McNicol L. The effects of intravenous lignocaine on depth of anaesthesia and intraoperative haemodynamics during open radical prostatectomy. BMC Res Notes. 2017; 10: 248.
14. Uzun S, Yuce Y, Erden A, Aypar U. Impact of perioperative lidocaine infusion and bis monitorization on remifentanil dosage in hypotensive anesthesia. Eur Rev Med Pharmacol Sci. 2014;18:559-65.

**Source of Support:** Nil; **Conflict of Interest:** None

**Submitted:** 03-04-2019; **Accepted:** 19-07-2019; **Published:** 14-08-2019