

Impact of perioperative lidocaine infusion and bis monitorization on remifentanyl dosage in hypotensive anesthesia

S. UZUN, Y. YUCE¹, A. ERDEN, U. AYPAR

Anaesthesiology and Reanimation Department, Hacettepe University Faculty of Medicine, Ankara, Turkey

¹Anaesthesiology and Reanimation Department, Kelkit State Hospital, Gumushane, Turkey

Abstract. – BACKGROUND: Combination of local and regional anesthetic agents are widely used in emergency and surgical setting and the interaction between the medications used in general anesthesia and these local and/or regional anesthetic becomes a growing concern in current patient management system. The interaction between general anesthetic agents and the local anesthetic agents given epidurally, spinally, intravenously or intramuscularly and the effects of BIS monitorisation on combined propofol-remifentanyl anesthesia are examined in several studies. In literature, there is no research investigating the effect of lidocaine infusion on remifentanyl and anesthetic dosage used in hypotensive anesthesia. The aim of this study is to examine this effect.

PATIENTS AND METHODS: We studied 39, ASA I-II patients undergoing elective transsphenoidal endoscopic hypophyseal adenoma excision procedure. After preoperative examination and informed consent of the patient, monitorisation with non invasive blood pressure measurement, electrocardiography, pulse oxymeter and Bispectral Index (BIS) was performed. 0.9% NaCl infusion was started via a 20 G route. Lidocaine (1%) was given as 1.5 mg.kg⁻¹ hour⁻¹ infusion after 1.5 mg.kg⁻¹ bolus dosage given in 10 minutes. Lidocaine infusion was started at the same time with anesthesia induction and was stopped after surgery. 0.9% NaCl was given as bolus dosage and as infusion in control group. Induction was maintained via propofol (1%) with 10 mg (1 ml) doses given in 5 seconds and it was applied in every 15 seconds until BIS < 45¹. During maintenance of anesthesia desflurane-remifentanyl-oxygen (50%)-air (50%) mixture was used. Desflurane was titrated by BIS measurement between 40 and 50¹². Remifentanyl infusion was started after propofol induction with 0.1 µg.kg⁻¹.min⁻¹ dosage and it was titrated between 0.1-0.5 µg.kg⁻¹.min⁻¹ levels. For intubation, rocuronium with 0.8 mg kg⁻¹ dosage was given during induction. After the surgical procedure, it was antagonised with neostigmine and atropine. For postoperative analgesia 1 g paracetamol was given

IV after the surgery within 15 minutes and it was reapplied with 1 gr doses in every 6 hours. After extubation, the pain of the patients was examined at 15. minute at the recovery room with VRS (VRS; 0-no pain, 1-slight pain, 2-moderate pain, 3-severe pain). If VRS was greater than 2, 50 mg dolantine was given IM. For prevention of nausea and vomiting, 8 mg ondansetron was given IV. Perioperative total doses of remifentanyl, desflurane (ml) (anesthesia machine records) and lidocaine (mg) were recorded after the surgery. Perioperative hemodynamic parameters (systolic, diastolic, mean blood pressures, heart rates) were recorded after monitorisation (basal), after intubation, after the start of the surgery and after extubation.

RESULTS: There were no statistically significant difference between two groups with respect to patient characteristics (age, gender, weight, length, Basal Mass Index = BMI) ($p > 0.05$). The duration of anesthesia and surgery were also not different statistically ($p > 0.05$). There were no statistically significant difference between two groups with respect to remifentanyl dose ($p > 0.05$). There were no statistically significant difference between two groups with respect to eye opening and extubation times ($p > 0.05$). When usage rates and amounts of dolantine, paracetamol and novalgine were compared, we found no statistically significant difference between two groups ($p > 0.05$). Basal mean arterial blood pressure measurements of the patients and mean arterial blood pressure measurements of the patients after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery and after extubation showed no statistically significant difference ($p > 0.05$). Basal heart rate measurements and the heart rates after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery and after extubation showed no statistically significant difference ($p > 0.05$). Basal BIS measurements and BIS measurements after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery

and after extubation showed no statistically significant difference ($p > 0.05$).

CONCLUSIONS: We found no statistically significant difference between two groups about different parameters. But new investigations with different local anesthetic agents may show significant difference and usage of these local anesthetic agents may be advised.

Key Words:

Local anesthetics, Hypotensive anesthesia, BIS monitorisation, Remifentanyl.

Introduction

Combination of local and regional anesthetic agents are widely used in emergency and surgical setting and the interaction between the medications used in general anesthesia and these local and/or regional anesthetic becomes a growing concern in current patient management system. The interaction between general anesthetic agents and the local anesthetic agents given epidurally, spinally, intravenously or intramuscularly and the effects of BIS monitorization on combined propofol-remifentanyl anesthesia are examined in several studies¹⁻⁸.

Senturk et al⁹ showed the preoperative intramuscular bupivacaine can decrease dosage of propofol in induction and maintenance. Similarly some investigators declared that the demand of general anesthetic agents had decreased when epidural and general anesthesia were performed together^{10,11}.

Nowadays Na channel blockers are commonly used in neuropathic pain treatment. The analgesic and antihyperalgesic effect of perioperative lidocaine was observed in several researches and the decrease in postoperative analgesic demand was reported^{14,15}. Koppert et al¹⁶ declared that lidocaine ensures analgesia during surgery and decreases central hyperalgesia by its effect on mechanosensitive receptors. In another study it was found that it does not increase postoperative analgesia after total hip arthroplasty and it has no effect on nociceptive pain threshold by von Frey filaments¹⁷. The decrease in propofol doses used during intubation and morphine usage after the surgical procedure was reported in thoracic surgery by the usage of lidocaine¹⁵.

In literature, there is no research investigating the effect of lidocaine infusion on remifentanyl and anesthetic dosage used in hypotensive anesthesia. The aim of this work is to examine this effect.

Patients and Methods

We studied 39, ASA I-II patients undergoing elective transsphenoidal endoscopic hypophyseal adenoma excision procedure. After preoperative examination and informed consent of the patient, monitorization with non invasive blood pressure measurement, electrocardiography, pulse oxymeter and Bispectral Index (BIS) was performed. 0.9% NaCl infusion was started via a 20 G route. Lidocaine (1%) was given as 1.5 mg.kg⁻¹ hour⁻¹ infusion after 1.5 mg.kg⁻¹ bolus dosage given in 10 minutes. Lidocaine infusion was started at the same time with anesthesia induction and was stopped after surgery. 0.9% NaCl was given as bolus dosage and as infusion in control group.

Induction was maintained via propofol (1%) with 10 mg (1 ml) doses given in 5 seconds and it was applied in every 15 seconds until BIS < 45'. During maintenance of anesthesia desflurane-remifentanyl-oxygen (50%)-air (50%) mixture was used. Desflurane was titrated by BIS measurement between 40 and 50¹². Remifentanyl infusion was started after propofol induction with 0.1 µg.kg⁻¹.min⁻¹ dosage and it was titrated between 0.1-0.5 µg.kg⁻¹.min⁻¹ levels.

During hypotensive anesthesia the target mean blood pressure level was 60-70 mmHg and the remifentanyl dose was increased 0.05 µg.kg⁻¹.min⁻¹ in every 1 minute until this target level was achieved. If there was failure to achieve this level despite the application of remifentanyl in 0.5 µg.kg⁻¹.min⁻¹ dosage, esmolol infusion was started.

For intubation, rocuronium with 0.8 mg kg⁻¹ dosage was given during induction. After the surgical procedure, it was antagonized with neostigmine and atropine.

For postoperative analgesia 1 g paracetamol was given IV after the surgery within 15 minutes and it was reapplied with 1 g doses in every 6 hours. After extubation, the pain of the patients was examined at 15 minute at the recovery room with verbal rating scale (VRS) (VRS; 0-no pain, 1-slight pain, 2-moderate pain, 3-severe pain). If VRS was greater than 2, 50 mg dolantine was given IM. For prevention of nausea and vomiting, 8 mg ondansetron was given IV. Perioperative total doses of remifentanyl, desflurane (ml) (anesthesia machine records) and lidocaine (mg) were recorded after the surgery. Perioperative hemodynamic parameters (systolic, diastolic, mean blood pressures, heart rates) were recorded after monitorization (basal), after intubation, after the start of the surgery and after extubation.

Table I. Distribution and evaluation of descriptive characteristics in two groups.

Min-Max	Mean $\pm$ SD		Lidocaine group (n=16)	Control group (n=23)	p^a
			Mean $\pm$ SD	Mean $\pm$ SD	
Age (year)	18.0-73.0	43.44 $\pm$ 12.42	41.81 $\pm$ 11.70	44.57 $\pm$ 13.04	0.503
Weight (kg)	55.0-125.0	81.64 $\pm$ 16.99	78.63 $\pm$ 16.12	83.74 $\pm$ 17.63	0.362
Length (m)	1.55-1.92	1.69 $\pm$ 0.09	1.69 $\pm$ 0.10	1.70 $\pm$ 0.09	0.822
BMI (kg/m ²)	19.59-42.25	28.50 $\pm$ 5.23	27.43 $\pm$ 4.12	29.16 $\pm$ 5.87	0.315
	n	%	n (%)	n (%)	p^b
Gender	Female	18	8 (50.0%)	10 (43.5%)	0.940
	Male	21	8 (50.0%)	13 (56.5%)	

^aStudent *t* test; ^bYates continuity correction test.

Statistical Analysis

For statistical analysis NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Kansville, UT, USA) program was used. During evaluation of descriptive data (mean, standard deviation, median, Frequency, Rate, Minimum, Maximum) as well as quantitative data, Student's *t* test was used in comparison of normal distribution parameters. The Mann-Whitney U test was used if there is no normal distribution of parameters. Yates Continuity Correction test (Yates chi-square) was used for the comparison of qualitative data. For intragroup comparison of normal distribution of parameters, paired sample *t* test was used. Significance was evaluated at $p < 0.01$ and $p < 0.05$ levels.

Results

This study was performed in Anesthesiology and Reanimation Department of Hacettepe Uni-

versity Faculty of Medicine with 39 patients 46.2% ($n = 18$) of which were female and 53.8% ($n = 21$) of which were male. There were no statistically significant difference between two groups with respect to patient characteristics (age, gender, weight, length, Basal Mass Index = BMI) ($p > 0.05$) (Table I).

The duration of anesthesia and surgery were also not different statistically ($p > 0.05$) (Table II).

Mean dose of lidocaine was 35.10 $\pm$ 6.86 in lidocaine group. The desflurane dose was 105.31 $\pm$ 21.25 in lidocaine group whereas it was 99.22 $\pm$ 25.79 in control group. There were no statistically significant difference between two groups with respect to desflurane dose ($p > 0.05$) (Table II).

The remifentanyl dose was 25.48 $\pm$ 11.47 (median = 21.7) in lidocaine group whereas it was 26.77 $\pm$ 14.53 (median = 30.0) in control group. There were no statistically significant difference between two groups with respect to remifentanyl dose ($p > 0.05$) (Table II).

Table II. Evaluation of anesthesia and surgery durations, eye opening and extubation times and drug doses in two groups.

	Lidocaine group (n=16)	Control group (n=23)	p^a
	Mean $\pm$ SD	Mean $\pm$ SD	
Duration of anesthesia	125.06 $\pm$ 23.01	112.57 $\pm$ 25.26	0.124 ^a
Duration of surgery	91.19 $\pm$ 19.69	78.74 $\pm$ 22.86	0.085 ^a
Lidocaine dosage	35.10 $\pm$ 6.86	0.00 $\pm$ 0.00 (0)	-
Desflurane dosage	105.31 $\pm$ 21.25	99.22 $\pm$ 25.79	0.441 ^a
Remifentanyl dosage; (median)	25.48 $\pm$ 11.47 (21.7)	26.77 $\pm$ 14.53 (30)	0.797 ^b
Eye opening time; (median)	7.71 $\pm$ 2.41 (7.3)	7.03 $\pm$ 2.83 (6.6)	0.271 ^b
Extubation time; (median)	7.82 $\pm$ 3.27 (7.2)	7.13 $\pm$ 2.86 (7.1)	0.530 ^b

^aStudent *t* test; ^bMann-Whitney U test.

Table III. Evaluation of Dolantine, Paracetamol, Novalgine usage and dose amounts in two groups.

		Lidocaine group (n=16)	Control group (n=23)	p
Dolantine Usage	(-); n (%)	6 (37.5%)	17 (73.9%)	0.052 ^a
	(+); n (%)	10 (62.5%)	6 (26.1%)	
	Dosage; Mean $\pm$ SD	72.50 $\pm$ 21.89	62.50 $\pm$ 13.69	0.380 ^b
	(Median)	(75.0)	(62.5)	
Paracetamol Usage	(-); n (%)	6 (37.5%)	9 (40.9%)	1.000 ^a
	(+); n (%)	10 (62.5%)	13 (59.1%)	
	Dosage; Mean $\pm$ SD	1750.00 $\pm$ 424.92	1964.29 $\pm$ 887.18	0.683 ^b
	(Median)	(2000.0)	(2000.0)	
Novalgine Usage	(-); n (%)	5 (31.3%)	12 (52.2%)	0.333 ^a
	(+); n (%)	11 (68.8%)	11 (47.8%)	
	Dosage; Mean $\pm$ SD	2363.64 $\pm$ 1026.91	2000.00 $\pm$ 894.43	0.376 ^b
	(Median)	(2000.0)	(2000.0)	

^aYates continuity correction test; ^bMann-Whitney U test.

There were no statistically significant difference between two groups with respect to eye opening and extubation times ($p > 0.05$) (Table II).

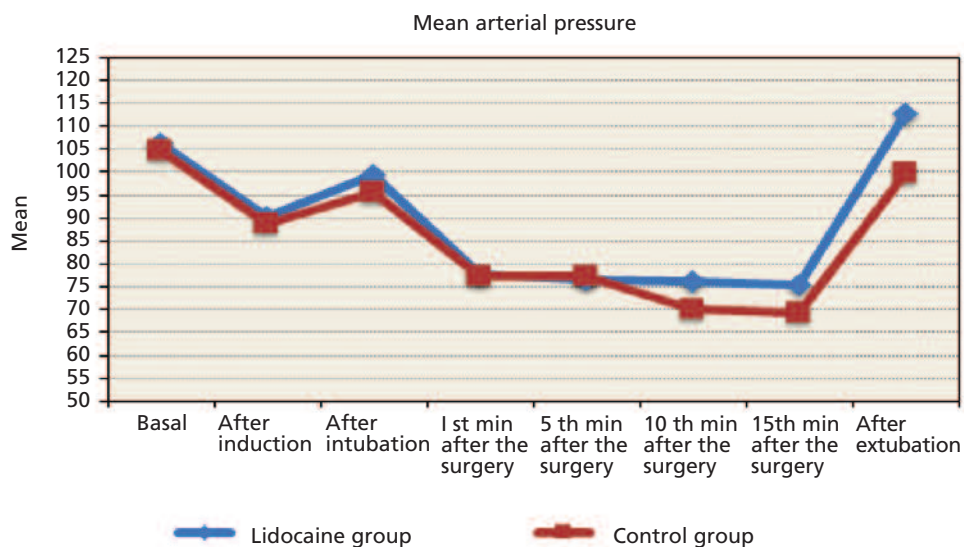
When usage rates and amounts of dolantine, paracetamol and novalgine were compared, we found no statistically significant difference between two groups ($p > 0.05$) (Table III).

Basal mean arterial blood pressure measurements of the patients and mean arterial blood pressure measurements of the patients after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery

and after extubation showed no statistically significant difference ($p > 0.05$) (Figure 1).

Basal heart rate measurements and the heart rates after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery and after extubation showed no statistically significant difference ($p > 0.05$) (Figure 2).

Basal BIS measurements and BIS measurements after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery and after extubation showed no statistically significant difference ($p > 0.05$) (Figure 3).

**Figure 1.** Changes in mean arterial pressures in two groups during follow up.

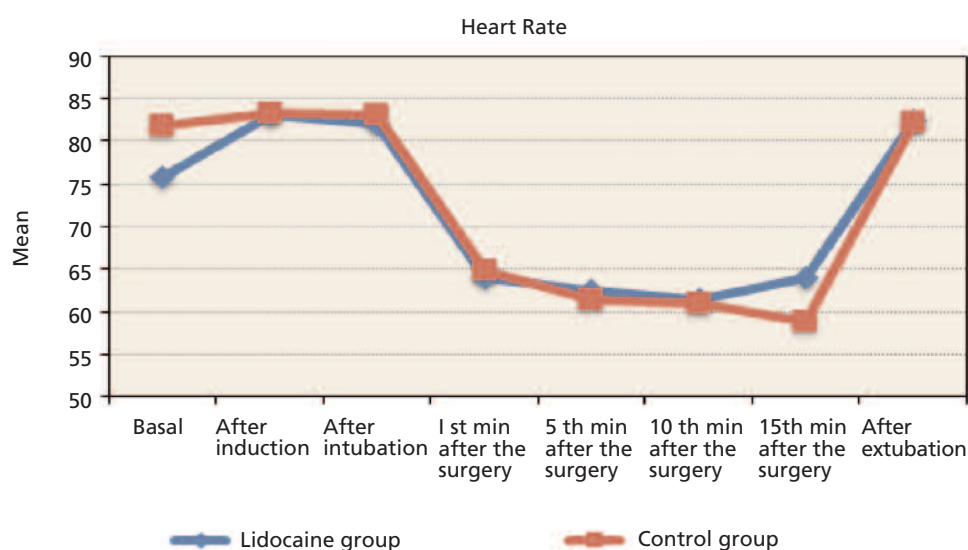


Figure 2. Changes in heart rate measurements in two groups during follow up.

Discussion

As local and regional anesthesia are commonly used, the interaction between drugs used in general anesthesia and these local and/or regional anesthetic procedures becomes a popular subject in recent years. The interaction between general anesthetic agents and local anesthetic agents given epidurally, spinally, intravenously or intramuscularly and the effects of BIS monitorization on combined propofol-remifentanyl

anesthesia are examined in several studies^{1,2,7,8}. Tverskoy et al¹ showed in their report that IM lidocaine or bupivacaine increased the hypnotic effect of IV thiopentone in a dose dependent manner, thus the same hypnotic effect could be seen with less doses of thiopentone in patients who have been applied local anesthetics compared with ones without any local anesthesia. Ben-Shlomo et al² in a similar study declared the same effect for propofol with same local anesthetics.

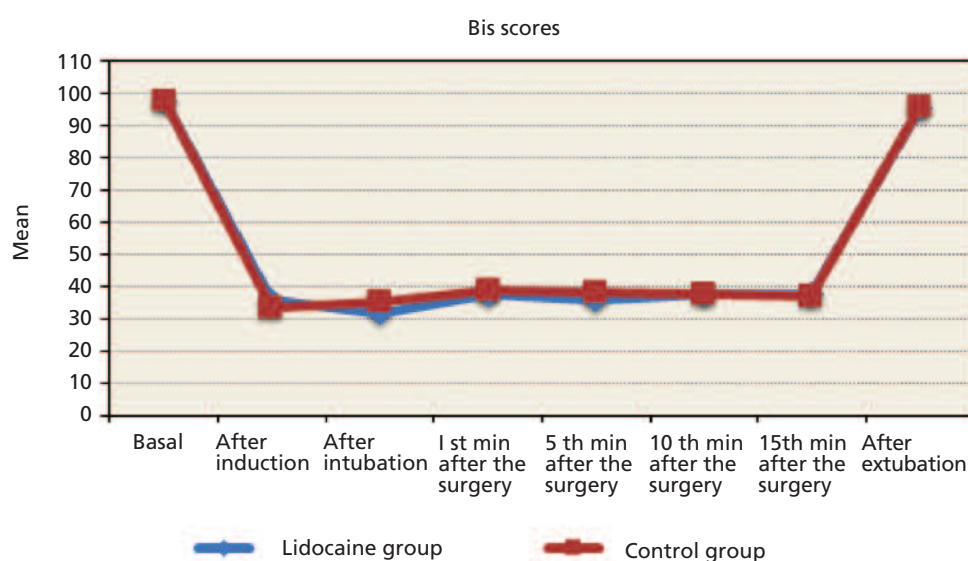


Figure 3. Changes in BIS measurements in two groups during follow up.

The effect of BIS monitorization in patients with propofol-remifentanyl anesthesia is the subject of many researches in literature³⁻⁶. Bresil et al³ reported that BIS monitorization did not decrease the anesthetic agent usage and it did not decrease the time for extubation in propofol-remifentanyl anesthesia. On the other hand, Koitabashi et al⁴ demonstrated that remifentanyl increased the hypnotic effect of propofol by basal BIS measurements. Bouillon et al⁵ showed the great decrease of propofol dosage with remifentanyl by BIS monitorization. Similarly Lysakowski et al⁶ reported the loss of consciousness with lower doses of propofol and higher BIS 50 levels in presence of opioids. In our work there is no statistically significant difference between two groups when patients' basal BIS measurements and BIS measurements after induction, after intubation, 1 minute, 5 minutes, 10 minutes, 15 minutes after discharge of surgery and after extubation were compared ($p > 0.05$). This result agrees with Bresil et al³.

It was shown that IM lidocaine or bupivacaine decreased the induction and maintenance doses of propofol which was examined by BIS monitorization⁹. In our work, with infusion of lidocaine there is no statistically significant difference between two groups when duration of anesthesia and surgery were compared ($p > 0.05$). Desflurane dose level was 105.31 ± 21.25 ml in lidocaine group where it was 99.22 ± 25.79 ml in control group. Therefore, there is no statistically significant difference between two groups when desflurane dose level was compared ($p > 0.05$). Also eye opening time and extubation time were not significantly different in these two groups ($p > 0.05$).

Lidocaine that we used an amino amide type local anesthetic drug. Recommended doses of local anesthetics were examined in several articles in literature. In these studies maximum lidocaine dose was reported as 7 mg.kg^{-1} ^{10,11}. Mean lidocaine dose in our paper is 35.10 ± 6.86 mg. This dose is lower than the level reported in those studies and no local anesthetic toxicity or other side effects were observed in our patients.

Analgesic and antihyperalgesic effect of perioperative lidocaine was examined in several studies and the decrease in postoperative analgesic demand was reported^{14,15}. Cui et al¹⁵ referred that postoperative morphine usage and propofol dosage given by infusion pump during intubation, extubation, lung resection and during closure of chest wall were lower in patients who had been

given lidocaine infusion in thorax surgery with propofol-remifentanyl anesthesia. In our study, higher levels of dolantine usage in lidocaine group patients is interesting. But there is no statistically significant difference between two groups when dolantine, paracetamol and novalgine doses used in patients were compared ($p > 0.05$). This indifference between two groups, especially for narcotic analgesics may be due to less demand of analgesics during postoperative period in hypophyseal surgery when compared with thorax surgery. Martin et al¹⁷ also reported that IV lidocaine has no effect on analgesia, functional recovery and nociceptive pain threshold and this result supports our study in this manner.

Proper anesthetic regimen for endoscopic endonasal transsphenoidal surgery was examined in several researches. Cafiero et al¹⁸ found that faster recovery was seen with sevoflurane-remifentanyl combination when compared with propofol-remifentanyl infusion. Thus, we've chosen desflurane-remifentanyl combination for maintenance of anesthesia. No study is found in literature examining the effect of perioperative lidocaine infusion on remifentanyl dosage used in hypotensive anesthesia.

Conclusions

Mean remifentanyl dose was 25.48 ± 11.47 (median = 21.7) in lidocaine group and 26.77 ± 14.53 (median = 30.0) in control group. There was no statistically significant difference between the two groups when remifentanyl doses were compared ($p > 0.05$).

Conflict of Interest

The Authors declare that they have no conflict of interests.

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