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STUDY OF THE EFFECTS OF SEDATION WITH MIDAZOLAM ON ARTERIAL OXYGEN SATURATION DURING SPINAL ANAESTHESIA IN LOWER ABDOMINAL SURGERY

Anaesthesiology

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ABSTRACT

A variety of systemic and intrathecal adjuvants to local anesthetics have been found to expand the duration and improve the quality of spinal block and decrease pain after surgeries. **Aims and Objectives:** The aim of this study was to evaluate the effect of the addition of midazolam to lidocaine for spinal anesthesia in lower abdomen surgeries. **Patients and Methods:** In a prospective, randomized, double blind study, 40 patients aged 20 to 60 years, and American Society of Anesthesiologists (ASA) I or II, were randomly allocated to receive either intravenous midazolam (30 µg/kg) or placebo in spinal anesthesia. Level of sensory block, time to achieve maximum motor and sensory block, duration of sensory and motor block, recovery time, side effects, heart rate, blood pressure, arterial oxygen saturation and sedation score were measured and analyzed using the SPSS software version 15 by t-test and ANOVA. Data were considered significant at 0.05. **Results:** The motor block duration in midazolam and control group was 82.9 ± 27.3 and 59.1 ± 26.5, respectively (P = 0.01). However the duration of sensory block was not different between the two groups (P = 0.07). The median of sensory block level was at T8 and T10 in midazolam and control group (P = 0.02). Recovery time was more prolonged in the midazolam group (P = 0.002). Hemodynamic indices did not show any significant differences between the two groups. **Conclusions:** Addition of 30 µg/kg midazolam to lidocaine for spinal anesthesia improved duration of motor block and increased intraoperative sedation score without causing side effects in patients' requiring lower abdomen surgery.

KEYWORDS

Midazolam, Spinal Anaesthesia, Lower Abdominal Surgery

INTRODUCTION

The first spinal anesthesia was carried out by Dr August Bier in 1899 and his anesthetic technique has become the standard practice for lower extremity and abdominal surgery worldwide [1]. Nowadays, the most commonly used drugs for spinal anesthesia are local anesthetics. However, a major disadvantage of single injection spinal anesthesia is its limited duration of action. In clinical practice, a number of adjuvants have been added to intrathecal local anesthetics for supplementation of intraoperative anesthesia and postoperative analgesia. They have advantages as they reduce the dose of local anesthetic; provide long lasting postoperative analgesia with reduced incidence of central nervous system depression, motor effects or hypotension [2].

Midazolam, synthesized by Walsar and colleagues in 1976, was the first clinically used water soluble benzodiazepine [3]. It is also the first benzodiazepine that was produced primarily for use in anesthesia [4]. In 1986, Faull and Villiger demonstrated that there is a high density of benzodiazepine (*GABA-A*) receptors in lamina II of the dorsal horn in the human spinal cord, suggesting a possible role in pain modulation [5]. One year later, Goodchild and Serrao reported that benzodiazepines might have analgesic effects at the spinal cord level in animals [6]. In 1990s, analgesic efficacy of intrathecal midazolam in humans has been demonstrated [7-9]. Naltrindole, a δ-selective opioid antagonistic agent, suppresses the antinociceptive effect of intrathecal midazolam, suggesting that intrathecal midazolam is involved in the release of an endogenous opioid acting at spinal δ receptors [10].

Aims and Objectives

The aim of this study was to evaluate the effect of the addition of 30 µg/kg midazolam to lidocaine for spinal anesthesia in patients requiring lower abdomen surgery.

Patients And Methods

This double blind clinical trial included 40 patients aged 20 to 60 years with American Society of Anesthesiologists (ASA) class I or II, who were scheduled for elective lower abdomen surgery. After obtaining the approval of the ethics committee, the study protocol was explained for patients and written informed consent was taken from all patients.

The participants were randomized into two groups of 20 patients each by randomization software. Patients, who had used benzodiazepine before the surgery, had a history of alcohol or other substance abuse, benzodiazepine hypersensitivity reaction, and any regional anesthesia contraindication, were excluded from the study. The participants were allowed to leave the study whenever they wished. In the operating room, after routine monitors including non-invasive blood pressure monitor, electrocardiogram, and pulse oximeter were attached to the patients, baseline vital signs were recorded. All patients received 10 cc/kg of Ringer's lactate serum. Spinal anesthesia was performed by 2 mL of 5% lidocaine in sitting position at L3 - L4 or L4 - L5 levels using a 23 G Quincke type needle.

The subjects in the first group received 0.03 mg/kg of midazolam and 1 µg/kg of fentanyl, five minutes after midazolam, intravenously. The second group was considered as control and received normal saline (2 cc) plus 1 µg/kg fentanyl, five minutes after normal saline injection. An anesthesiologist not involved in the study prepared the study solutions so both patient and investigators were blinded to the patient group assignment.

After completion of spinal anesthetic drug administration, level of sensory block was assessed by pinprick testing, every two minutes, until the highest dermatomal level of sensory blockade was achieved. Time to achieve maximum motor and sensory block, duration of sensory and motor block, any side effect (regarding hypotension, nausea and vomiting) and recovery duration were recorded by another anesthesiologist not involved in the study.

Heart rate, systolic and diastolic blood pressure, arterial oxygen saturation (SaO_2) and sedation score were monitored five minutes before surgery and every five minutes during the surgery. Assuming a 5% significance level ($\alpha = 0.05$) and power of 80% ($\beta = 0.20$), to detect seven minutes sedation time differences in two groups, a sample size of 20 patients per group was required. Data were analyzed using the SPSS software version 15. Student's t-test and repeated measure ANOVA (RMA) was used for comparing the two groups' quantitative variable, while the chi-square test was used to evaluate categorical data. P value of < 0.05 was considered statistically significant.

RESULTS

We studied a total of 40 patients, 20 in each group with a mean age of 44.9 ± 14.4 years and mean weight of 72.1 ± 9.3 kg. All patients had successful spinal anesthesia and no one was excluded because of technical failure. Twenty-five participants (74.2%) were male and fifteen were female (29.8%). Demographic and baseline data were similar between the two groups Table 1.

As assessed by Student's t-test, the motor block duration was 83.9 ± 28.3 and 59.1 ± 26.5 minutes for the midazolam and control group, respectively (P = 0.01). However, the duration of sensory block was not different between the two groups (P = 0.07). The median of sensory block level was at T8 for the midazolam group and at T10 for the control group (P = 0.02). Our results showed that the duration of

recovery was more prolonged in the midazolam group compared with the control group (P = 0.002).

Based on the participants' vital signs, as shown in Table 1, systolic and diastolic blood pressure and heart rate did not show any significant changes within or among the groups. The mean of SaO_2 change was not significantly different between and within groups although in measurements at 25 and 30 minutes after inducing spinal anesthesia, the midazolam group had lower saturation level compared with the control group. There was a trend for progressively higher sedation scores over time in the midazolam group (P < 0.001). In addition, postoperative sedation score values were significantly higher in the midazolam group compared with the control group (P = 0.04). One patient in the midazolam group and two in the control group required opioid for postoperative pain (P = 0.99).

No adverse effect was seen throughout the study period in either group; only three patients had nausea that required antiemetic treatment, among which two were from the midazolam group (P = 0.04). None of the patients from either group had vomiting or respiratory distress.

Table 1: Demographic Data, Vital Sign And Physiologic Variables Of Participants

Variables	Midazolam Group	Control Group	P Value
Age, y	46.6 ± 16.7	45.3 ± 13.4	0.75
Weight, kg	72.8 ± 6.4	67.3 ± 11	0.07
Gender			0.45
Male	15 (77.8%)	12 (66.7%)	
Female	5 (23.2%)	8 (34.3%)	
Sensory block duration, min	75.1 ± 28	58.8 ± 23.3	0.06
Motor block duration, min	82.9 ± 27.3	59.1 ± 26.5	0.01
Recovery duration, min	116.1 ± 29.6	87.8 ± 21.4	0.002
Systolic blood pressure, mmHg	125.9 ± 17.6	126.1 ± 16.7	0.96
Diastolic blood pressure, mmHg	72.6 ± 18.6	71.5 ± 14.4	0.76
Heart rate, beat/min	81.9 ± 15.9	86.7 ± 17.6	0.35
SaO_2	97.4 ± 3.3	97.9 ± 2.8	0.20
Sedation score	2.16 ± 0.06	0.46 ± 0.06	< 0.001

[a]No. = 20
[b]Data are presented as Mean ± SD.

DISCUSSION

Spinal anaesthesia with hyperbaric tetracaine decreases HR and arterial pressure by depressing sympathetic activity, and increases parasympathetic neural tone to produce a vagotonic cardiac autonomic nervous system'. We showed that intravenous midazolam of 0.05 mg/kg made the cardiac autonomic nervous system further vagotonic as shown by the changes in the spectral components superimposed on a vagotonic condition produced by spinal anaesthesia. Midazolam suppresses catecholamine concentrations'2 , and abolishes response to command in unpremedicated patients at an ED50 of 0.26 mg/kg'l. Ventilatory depression is demonstrable by CO2 response at a dose of 0.2 mg/kg, although no serious depression has been reported at about 0.05-0.075 mg/kg'4.'5 . The primary effect of midazolam is to decrease tidal volume'6 , with a 500/0 reduction within 2 minutes at 0.1 mg/kg17. Our study demonstrates that a dose of midazolam as small as 0.05 mg/kg would enhance cardiac autonomic nervous system vagotonia when given during surgery under spinal anaesthesia. It was believed that the nature of the cardiac autonomic nervous system would have been different individually. We could not determine whether there was sympathetic activity, and increases parasympathetic neural tone to produce a vagotonic cardiac autonomic nervous system'. We showed that intravenous midazolam of 0.05 mg/kg made the cardiac autonomic nervous system further vagotonic as shown by the changes in the spectral components superimposed on a vagotonic condition produced by spinal anaesthesia. Midazolam suppresses catecholamine concentrations'2 , and abolishes response to command in unpremedicated patients at an ED50 of 0.26 mg/kg'l. Ventilatory depression is demonstrable by CO2 response at a dose of 0.2 mg/kg, although no serious depression has been reported at about 0.05-0.075 mg/kg'4.'5 . The primary effect of midazolam is to decrease tidal volume'6 , with a 500/0 reduction within 2 minutes at 0.1 mg/kg17. Our study demonstrates that a dose of midazolam as small as 0.05 mg/kg would enhance cardiac autonomic nervous system vagotonia when given during surgery under spinal anaesthesia. It was believed that the nature of the cardiac autonomic nervous system would have been different individually.

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