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Comparison of the Side Effects of Intrathecal Lidocaine without Additional Anesthetics and the Combination of Sufentanil and Lidocaine in Cesarean Section

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ABSTRACT

The Investigation of new agents with ability to produce long lasting analgesic period and minimal side effects are considered as crucial issues to drug researchers. The current study was conducted to compare the incidence of some common side effects including headache, pruritus, hypotension, nausea and respiratory depression under spinal anesthesia induced by lidocaine alone and in combination with sufentanil in caesarean section. This is a randomized, double-blind clinical trial and the samples were 100 healthy pregnant women referring to Tehran Javaheri hospital from April 2011 to April 2012. They were randomly divided into two groups. The first group was injected intrathecal 1/5 ml lidocaine 5% and the second one received 1 ml lidocaine 5% in combination with 1 ml sufentanil, (containing 5-µg sufentanil). Some common side effects such as headache, pruritus, hypotension, nausea and respiratory depression were recorded in the patients, during the surgery and 1, 3, 6, 24 hours after the operation. A checklist and a questionnaire were used for data collection. The data were analyzed by computer software SPSS, chi-square, and ANOVA tests. The side effects were more significant in the sufentanil group. It can be concluded that, the combination of lidocaine and sufentanil can induce more side effects than merely lidocaine.

KEYWORDS: Lidocaine; Sufentanil; Spinal anesthesia; Cesarean section, Side effect of drugs

INTRODUCTION

Subarachnoid block is a widely used technique for cesarean section. Lidocaine, Tetracaine, Bupivacaine and Ropivacaine are the common drugs preferred in this technique. Compared to another prescribed drugs Lidocaine is more easily available and economical. This can be a reason for choosing lidocaine in this procedure although Bupivacaine is more common than the others. The average dose of lidocaine for abdominal surgery is 75-100 mg and for deeper anesthesia is 100-150 mg. The analgesic effect starts 2-3 minutes after the injection and last for 20-30 minutes. In some cases, lidocaine has been used with other agents to prolong the analgesic period [1]. The combinations of intrathecal opioids and local anesthetics together have a potent synergistic effect on improving the quality of intraoperative and postoperative analgesia [2]. The addition of fentanyl 10 µg to local anesthetic increases the intraoperative and early postoperative quality of subarachnoid block [3]. Highly lipid-soluble synthetic opioids such as sufentanil and fentanyl are being increasingly used

along with very low concentrations of local anesthetic agents such as lidocaine to provide excellent pain relief during labor [4]. It has been reported that the combination of lidocaine and sufentanil has more effective analgesia during cesarean section [5]. Hypotension and nausea are common side effects of subarachnoid block. The hypotension as an auto-regulation-mechanism can directly affect fetus blood circulation when uterus blood circulation decreases [6]. Although, addition of sufentanil to lidocaine can prolong analgesic period, some adverse reactions have been reported by intrathecal injection of sufentanil, for example respiratory depression, apnea [7], hypotension [8], skeletal muscle rigidity [9], nausea and vomiting [10] and transient neurological symptoms [11]. The current study was conducted to compare the incidence of some common side effects including headache, pruritus, hypotension, nausea and respiratory depression induced by lidocaine alone and in combination with sufentanil in caesarean section during and after the spinal anesthesia.

PATIENTS AND METHODS

This is a randomized, double-blind clinical trial and all procedures of the current study were approved by the Local Ethics Committee (University of Tehran Medical Sciences). One hundred healthy pregnant women were randomly selected for elective cesarean section with spinal anesthesia. The main goal of the study was explained to each patient and the signed informed consent sheets were obtained from all of them. The exclusive criteria were uncooperative patients, the patients with hypertension, asthma, diabetes, cardiovascular diseases and renal disorders or other established contraindications of spinal anesthesia. The volunteers were NPO (nothing per oral) overnight and received nomedication preoperatively. At least 500 ml of lactated Ringer's solution (20 mL/kg) was used for intravenous (IV) hydration. With the patient in the sitting position, a 26-gauge needle was inserted in the subarachnoid space at the third or fourth lumbar inter space. The procedure was assisted by an anesthetic nurse, who was not otherwise involved in the study or care of the patients. Neither the anesthesiologist nor the patient herself was aware of the dose administered. Randomization was done according to systemic random sampling; the patients were divided into two groups (50 in each group). They received the doses and volumes as follows: Group 1 (Lidocaine) was administered 1/5 ml of lidocaine 5% (75 mg) and patients in Group 2 (lidocaine+sufentanil) were received 1 ml of lidocaine 5% (75 mg) and 5 micrograms (1 ml) sufentanil. After the intrathecal injection, the patient returned to the supine position with a left lateral tilt to accomplish a left uterine displacement. Systolic blood pressure was recorded every one minute; further heart rate and arterial oxygen saturation were also assessed. Hypotension was defined as a systolic blood pressure below 100 mm Hg or a decrease in systolic pressure of more than 30% of the baseline value. The 2-4 L/min oxygen was used through a nasal cannula. The oxytocine Infusion (30 IU) was administered to patients as soon as the baby was delivered. In the recovery room, the patients were carefully monitored, and their blood pressure was checked every 3 minutes. In addition, adverse reactions such as headache, Pruritus, hypotension, nausea and respiratory depression, and other possible side effects, as well their treatments were recorded during the surgery and at the intervals of 1,3,6,24 hours after operation. Respiratory depression was considered as a respiratory rate below 8 per minute. A checklist and a questionnaire were used for data collection, and then the data were analyzed by computer software SPSS, chi-square, and ANOVA tests. The p value < 0.05 was considered significant.

RESULTS

The patient variables are depicted in Table 1; as can be seen, there are no significant differences between Group 1 and Group 2, except for the weight of the patients. The mean value for weight in Group 1 (lidocaine) was 83 ± 3.1 kg 56% of patients were in the range of 70-80 kg and 28% were in the range of 80-90. A further 16% of the patients in this group weighed more than 90 kg. In Group 2 (lidocaine + sufentanil), 32% of the patients weighed lower than 70 kg. 52% of patients were in the range of 70-80 kg and 12% were in the range of 80-90 kg. Also 4% was more than 90 kg.

Table 1: Demographic date

Patients variables	Group 1	Group 2	P- value
Age (year)	26.1±3.71	26.6±4.35	0.69
Height (cm)	165±6.14	162±9.25	0.71
Weight (kg)	83±3.1	75±2.8	0.04
Parity	1.3	1.5	0.56
Duration of surgery	59.8±19	61.8±15	0.33

The evaluated side effects during and after the cesarean section are shown in Table 2. As can be seen, the addition of sufentanil to lidocaine was associated with some side effects. Pruritus and respiratory depression were observed in 8 % and 12% of the patients, respectively in the recovery room. Nausea and headache were recorded in both groups; however, the side

effects were more in Group 2.

Table 2: The evaluated side effects during and after the operation in the patients

Patients variables	Group 1		Group 2		P- value
	During	After	During	After	
Pruritus	Zero	Zero	Zero	8%	0.04
Respiratory depression	Zero	Zero	Zero	12%	0.03
Nausea	Zero	12%	4%	44%	0.01
Headache	Zero	24%	Zero	60%	0.03

The measured blood pressure during and after the cesarean section in the patients is presented in Table 3. As can be seen, the addition of sufentanil to lidocaine was found to be hypotensive. In Group 1, the mean for the participants blood pressure before and during the operation was 121 mmHg; however, in the recovery room, it decreased to 118 mmHg. In Group 2, the patients had a mean blood pressure of 119 mmHg. During the operation, it dropped to 94 mmHg and after the surgery elevated to 107 mmHg.

Table 3: The measured blood pressure during and after the operation in the patients

Blood pressure (mmHg)	Group 1		Group 2		P- value
	During	After	During	After	
80-100	48%	4%	92%	40%	0.01
100-120	48%	76%	4%	60%	0.01
120-140	4%	20%	4%	Zero	0.03

DISCUSSION

Investigation of new agents with ability to produce long lasting analgesic period and minimal side effects are the issues of considerable interest to drug researchers.

“Combination Wisdom” allows the use of a lower dose of the local anesthetic agent with adjuvants, which offer hemodynamic stability. Opioids in conjunction with local anesthetics improve the quality of intraoperative analgesia and prolong the duration of postoperative analgesia [2,11]. In the recent study, it has been demonstrated that addition of sufentanil to lidocaine 5% provided more duration of analgesia for cesarean delivery [5]. Similarly, It has been well established that a combination of bupivacaine with fentanyl or sufentanil has a synergistic analgesic effect when used intrathecally [12-14]. Despite the impressive perspective of the prolonged analgesia, the addition of opioids to local analgesics can induce side effects, varying from moderate to life threatening. In the current study, we evaluated the incidence of side effects by addition of sufentanil to local analgesic, lidocaine 5%. Since sufentanil is much more lipid soluble than morphine (approximately 800 folds) and therefore its rapid onset of action [15], we chose to use this opioid in combination with lidocaine. Further, morphine will exhibit slower onset and longer duration of Antinociception and a higher incidence of some side effects [15]. We observed that, the addition of sufentanil to lidocaine could result in pruritus in 8% of patients; this finding is in line with previous studies [16]. However, the mechanism of the pruritus has not been completely described yet. As we showed, sufentanil could considerably induce respiratory depression. This aspect of our results is consistent with the previous reports [17,5]. Contrary to our findings, it has been claimed that, sufentanil has no effect on peripheral O2 saturation during spinal anesthesia [18].

The risk factors for development of “respiratory depression” include increasing age, the concomitant use of long-acting sedatives and co-existing respiratory disease. The combination of opioid analgesics during the first 12–24-hours after intrathecal anesthesia has long been a concern regarding the development of early and late onset respiratory depression, but large scale prospective surveys have refuted this claim [19]. It is well documented that opioids can induce nausea and

vomiting [19]. Our observation of increased nausea by sufentanil is supportive of this fact. Interestingly, we found that sufentanil can cause headache. Consistently, it is reported that opioids can induce abnormal pain sensitivity [20]. Our data show that, the majority of the patients experience low blood pressure during the operation. Parallel with our observations, a dose dependent reduction of blood pressure has been previously reported by sufentanil [5]. However, there are some studies suggesting that, sufentanil not induce hypotension during and after spinal anesthesia [21,22]. The incidence and risk factors for hypotension after spinal anesthesia are correlated with age, weight, height, body mass index, amount of colloid infusion before puncture, chronic alcohol consumption, spinal anesthesia physical status (spinal deformity, chronic lower back pain and etc.), history of hypertension, urgency of surgery, surgical department (inexpert operators, severe bleeding during the operation), sensory block height of anesthesia and frequency of puncture (lumbarpuncture has been associated with intracranial subdural collections. This has also been hypothesized to be secondary to intracranial hypotension and downward descent of the brain) [23,24].

However, in our study the demographic data were the same for both groups. In the current work, we found that, the addition of sufentanil to lidocaine is associated with the increased incidence of some side effects particularly respiratory depression and hypotension. Since, such side effects can be life threatening; more care should be taken into consideration for the management of these complications during spinal anesthesia.

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