Comparison of Spinal Anesthesia Quality Between Patients Addicted and Not Addicted to Opium

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Purpose: *This study aimed to compare the quality of spinal anesthesia between opium-dependent and opium-naive patients.*
Design: *A case-control study.*
Methods: *Two groups of subjects including opium-dependent and opium-naive patients (30 per group) were enrolled. Spinal anesthesia was performed using 15 mg of bupivacaine. The level of anesthesia was assessed every minute for 10 min and then every 10 min for 180 min. Motor block was recorded at 10, 60, 120, and 180 minutes. The duration of anesthesia was recorded.*
Findings: *The mean duration of spinal anesthesia was significantly shorter in opium-dependent patients (101.45 ± 28.670) than in opium-naive patients (126.14 ± 24.206) (P = .003). The mean onset of sensory block was not significantly different between the two groups (4.14 ± 1.62 vs 3.69 ± 1.36, P = .259).*
Conclusions: *Substance abuse affects the duration of spinal anesthesia, so it is recommended to use intravenous medications or higher doses of spinal marcaine for these patients.*

Keywords: *anesthesia, opium dependence, spinal anesthesia.*

SPINAL ANESTHESIA HAS lower complications than general anesthesia. Maintaining spontaneous breathing and awareness during surgery is one of the advantages, especially for those with obstructive and restrictive pulmonary disease or difficult airways who are prone to increased risks of general anesthesia. However, the duration of spinal anesthesia depends on various factors, including medication dose, the potency of local anesthetics, and the use of additives. The level of sensory block also relies on patient-related (ie, height, age, gender; cerebrospinal fluid volume; the resistance of the spine; and pregnancy) and medication-related factors.[1]

Substance abuse is one of the health, treatment, and social problems of the modern world,[2] affecting almost all communities. Addiction is also common in Iran.[3] According to the available statistics, such as those reported by the United Nations Office on Drugs and Crime, more than 2 million (3%) individuals are addicted to opioidsin Iran.[4]

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Opioids are commonly used for chronic and acute pain. However, the long-term consumption of these substances, especially in chronic pain cases, results in the development of opioid dependency, which can cause cross-tolerance between local anesthetics and opioids.[5,6] Chronic opium abuse causes a number of cellular changes in pain receptors. These changes make the opium abuser more resistant to both opioid analgesics and nonopioid analgesics (such as local anesthetics).[7] It has been observed in clinical settings that regional anesthesia duration is shorter in opium-dependent individuals; as a result, they are in a greater need for the intravenous administration of analgesic medications and sedatives. Various causes have been mentioned for the influence of opiuim in addicts in terms of duration, including the cross-tolerance between local anesthesia and opioids.[8,9]

One of the important reasons for using spinal anesthesia in substance-dependent patients is concomitant pulmonary problems.[1,10] Opium-dependent individuals are more resistant to medications and have a lower threshold of pain than opium-naive patients.[11] Some recent studies have revealed new findings on pain and its mechanism in substance-abuse patients and the interaction effect of local anesthetic receptors and opioid.[12]

With this background in mind, the present study aimed to evaluate the duration and onset of spinal anesthesia among opium-dependent and opium-native groups.

Materials and Methods

This case-control study was conducted on 60 patients admitted to the operating room of Imam Reza Hospital, Mashhad, Iran, to undergo elective lower abdominal and lower extremity surgeries. After obtaining written approval from the ethics committee of the university, participants were randomly divided into two groups of opium-dependent and opium-naive (30 cases per group) based on their medical history. The subjects in the addict group were dependent on opium for a minimum of 1 year. The opium-dependent group was questioned about daily opium dose and duration of abuse. The thin-layer chromatography (TLC) blood test methods were used to confirm the opioid use in the opium-dependent group and lack of morphine in the opium-naive group.

After explaining the research objectives to the participants, they were ensured of the confidentiality terms regarding their personal information. In addition, written informed consent was obtained from the subjects before the study. All patients were visited in the preoperative clinic before surgery, and the patients of the intervention group were encouraged to use the daily dose of substance before surgery.

Inclusion criteria included (1) willingness to undergo spinal anesthesia, (2) candidate of lower abdominal and extremity surgeries, (3) age range of 20-65 years, and (4) height of 150-185 cm. In addition, a minimum of 1-year experience of opium consumption or having opium withdrawal symptoms when stopping use was another criterion for inclusion in the opium-dependent group. On the other hand, subjects in the control group were opium-naïve (according to the patient's statement). Exclusion criteria included a history of underlying pulmonary and cardiac diseases as well as a partial or absolute contraindication for spinal anesthesia.

After complete monitoring of the patients (eg, pulse oximetry, blood pressure, and electrocardiography), 500-cc Ringer's solution was administered over 15 minutes. Spinal anesthesia was performed with the subjects in a sitting position under sterile conditions using 15-mg (3 cc) bupivacaine 0.5% and 25G spinal needle in the L4-L5 interspace. After the injection, the patient's position was immediately changed to the supine position.

The level of anesthesia was evaluated and recorded every minute in the first 10 minutes and then every 10 minutes until recovery using the pinprick test. Moreover, the motor block was assessed and level recorded at 10, 60, 120, and 180 minutes from the beginning of the injection until recovery from spinal anesthesia based on the Bromage score (grade I: full motion of the lower extremity, grade II:

Table 1. Comparison of the Case and Control Groups in Terms of the Onset and Duration of Motor Block

Time	Group	Grade I	Grade II	Grade III	P Value
Minute 10	Nonaddict	12 (41.3%)	10 (34.4%)	7 (24.1%)	.37
	Addict	17 (58.6%)	6 (20.6%)	6 (20.6%)	
Minute 60	Nonaddict	0	4 (13.7%)	25 (86.2%)	.21
	Addict	1 (3.4%)	4 (13.7%)	24 (82.7%)	
Minute 120	Nonaddict	5 (17.2%)	4 (13.7%)	20 (6.8%)	.27
	Addict	8 (27.5%)	7 (24.1%)	14 (48.2%)	
Minute 180	Nonaddict	25 (86.2%)	1 (3.4%)	3 (10.3%)	.31
	Addict	28 (96.5%)	1 (3.4%)	0	

movement of the lower leg, and grade III: lack of lower limb movement).

If discomfort was expressed by the patients, midazolam 1 mg and fentany l50 μgr were intravenously administered after evaluation of the sensory level. Patients with continued discomfort and pain underwent general anesthesia. Anesthetic failure was defined as the lack of achieving a favorable sensory level and complete motor block after 15 minutes. In addition, blood samples were drawn from the participants to perform the TLC test before anesthesia. The subjects were ensured about the confidentiality terms regarding their test results. The prepared samples were centrifuged with codes (without the patient's name). The presence of morphine in the blood serum was determined after separating the serum using the TLC technique.

Statistical Methods and Sample Size

The sample size was determined as 60 cases (30 subjects in each group) based on similar studies[13] and the sample size formula. Data analysis was performed in SPSS (version 11.5; IBM Corporation, NY) using the Fisher's exact test, *t* test (to compare the duration of anesthesia in the two study groups), Pearson's correlation coefficient (to compare the quantitative variables), χ^2 test (to compare the qualitative variables), and linear regression analysis (to control the confounding variables). A *P* value less than .05 was considered statistically significant.

Results

In total, 60 patients were entered into the study. However, two individuals were excluded from the study after performing the TLC test on blood samples and finding one positive case in the opium-naive group and one negative case in the opium-dependent group. Therefore, the study was continued with 29 (50%) healthy and 29 (50%) opium-dependent individuals. The mean ages of the participants were 50.03 ± 20 years and 50.03 ± 16 years in the nonaddict and addict groups, respectively. Results of the χ^2 test demonstrated that the two study groups were homogenous in terms of gender ($P = .16$).

Motor Block

The comparison of the case and control groups in terms of the onset and duration of the sensory block is presented in Table 1. Results revealed no significant difference between the two groups regarding the level of sensory block at 10, 60, 120, and 180 min ($P > .05$).

Sensory Block

The mean onset of sensory block was 4.14 ± 1.62 and 3.69 ± 1.36 min in the opium-naive and opium-dependent groups, respectively, with no significant difference between groups ($P = .259$). Mean duration of spinal anesthesia (defined as the time interval from the onset of anesthesia to two levels lower than the maximum block level) was 126.14 and 101.45 min in the opium-naïve and opium-dependent groups, respectively (Table 2). The duration of spinal anesthesia was significantly lower in the opium-dependent group than that in the opium-naive group ($P = .003$). In addition, the results of the *t* test demonstrated a significant difference between the study groups regarding the duration of anesthesia.

Table 2. Comparison of the Case and Control Groups in Terms of the Onset and Duration of Sensory Block

Variables	Groups		*P* Value
	Opium-Naive (N = 30) (min)	Opium-Dependent (N = 30) (min)	
Onset of sensory block (mean ± SD)	4.14 ± 1.620	3.69 ± 1.365	.259
Duration of anesthesia (mean ± SD)	126.14 ± 24.206	101.45 ± 28.670	.003

SD, standard deviation.

The frequency distribution of variables, including age, history of previous anesthesia, need for the administration of sedatives (midazolam) and analgesics (fentanyl), as well as hemodynamic stability (need for ephedrine injection) in the two groups is summarized in Table 3. The results revealed no statistically significant difference between the study groups in terms of the mentioned variables ($P > .05$). In terms of the surgeon's satisfaction with anesthesia, 96.4% and 80.8% of cases in the opium-naïve and opium-dependent groups were satisfactory, respectively. Fisher's exact test revealed no significant difference between the study groups in this respect ($P = .95$).

Based on the results of the Pearson's correlation coefficient, there was a significant relationship between the onset of spinal anesthesia and duration of anesthesia in the opium-naive group ($r = 0.49$, $P = .007$). However, no significant relationship was observed in the opium-dependent group in this regard.

The results of the linear regression model, evaluating the relationship between variables and duration of anesthesia, are illustrated in Table 4. At first, the variables were entered one by one, and at the final stage, all the important variables were entered into the model. The regression analysis demonstrated that the variable of the groups (ie, addiction and nonaddiction) had a significant impact on the duration of anesthesia, even after entering the underlying variables. Among all variables, age had an important and significant effect on the duration of anesthesia. Even controlling age did not eliminate the effect of group on the duration of anesthesia.

Discussion

Based on recent studies, reduced sodium channels in substance abusers lead to the development of tolerance to local anesthesia. In addition, the respiratory acidosis caused by chronic drug addiction might reduce the efficiency of intrathecal local

Table 3. Frequency Distribution of Variables in the Case and Control Groups

Variables	Opium-Naive N (%)	Opium-Dependent N (%)	*P* Value
Sex			
Female	7 (24.1)	3 (10.3)	.16
Male	22 (75.9)	26 (89.7)	
History of anesthesia			
Yes	16 (52.2)	11 (37.9)	.18
No	13 (44.8)	18 (62.1)	
Need to inject ephedrine			
Yes	2 (6.9)	4 (14.3)	.42
No	27 (93.1)	24 (85.7)	
Need for supplementary medication			
Yes	2 (6.9)	6 (20.7)	.25
No	27 (93.1)	23 (79.3)	
Need for general anesthesia			
Yes	0	4 (13.8)	.11
No	29 (100)	25 (86.2)	

Table 4. Results of Linear Regression Test

Coefficients					
	Unstandardized Coefficients		Standardized Coefficients		
Model	Beta	Standard Error	β	t	*P* Value
1					
Constant	177.312	21.917		8.090	.000
Group	−22.481	6.930	−0.390	−3.244	.002
Age	−0.412	0.183	−0.263	−2.249	.029
Gender	4.373	9.119	0.057	.480	.633
History of anesthesia	−9.312	6.901	−0.161	−1.349	.183
2					
Constant	184.016	16.761		10.979	.000
Group	−23.028	6.786	−0.399	−3.393	.001
Age	−0.418	0.182	−0.267	−2.297	.026
History of anesthesia	−9.637	6.818	−0.167	−1.414	.163
3					
Constant	170.837	14.054		12.156	.000
Group	−24.690	6.744	−0.428	−3.661	.001
Age	−0.400	0.183	−0.255	−2.186	.033

anesthetics.[5] In a systematic review conducted by Dabagh and Rajaei in 2016, 95 studies published within 2005-2016 on opium and anesthesia were extracted from PubMed.[7] The systematic review evaluated the problems related to anesthesia in the addicts. The study revealed that pain receptors in the brain, spinal cord, and peripheral nerves in the opium-dependent group undergo cellular and subcellular changes due to the repeated exposure of the receptors to opium, altering the receptors' responses to pain.

The opium attachment to the receptor leads to the extraction of ribonucleic acid (RNA) from an abnormal cell. This would result in the production of unnatural protein and thereby various abnormal responses such as pain intolerance, hyperalgesia, and allodynia. Moreover, the structural changes in the receptors of the addicts and other cellular alternations result in the development of resistance to opioids and local anesthetics.[7]

In a study conducted in 2014, Youssef and Abdelnaim investigated 100 patients undergoing lower extremity and lower abdominal surgeries in the Qasr El Eyni Hospital in Egypt.[14] The patient's addiction was detected only based on the medical history of the patients. However, in the current study, the patient's use of opium was investigated by collecting blood samples for performing TLC before anesthesia, along with reviewing their medical history. In the mentioned study, the mean duration of onset of sensory block in the opium-dependent group was significantly longer (1.01 ± 7.9) than that in the opium-naive group (1.08 ± 5.9).

In the present study, spinal anesthesia was initiated with a longer delay in the nonaddict group than in the addict group. However, this difference was not statistically significant. In total, 4% and 34% of the nonaddict and addict groups, respectively, experienced a block failure, revealing a significant difference.

None of the subjects of the opium-naive group required general anesthesia. Nonetheless, in the opium-dependent group, there were four cases (13.8%) needing general anesthesia. However, this difference between the study groups was not statistically significant ($P = .11$). In the study by Youssef and Abdelnaim, the duration of spinal anesthesia was significantly shorter in the opium-dependent group (11.2 ± 135.9) than that in the opium-naive group (21.2 ± 165.1), which is in line with our findings.[14]

In this study, the onset of motor block was considered as the time interval from the anesthetic injection to the complete loss of motor power in the lower extremities. In addition, the duration of motor block was regarded as the time between the injection of medication and regaining complete lower extremity movement. In the present study, the motor block was evaluated and recorded at 10, 60, 120, and 180 minutes according to the Bromage score. Although the duration of motor block was significantly shorter in the opium-dependent group than in the opium-naive group, there was no significant difference between the two groups in terms of the level of the motor block at 10, 60, 120, and 180 minutes.

In another study carried out in Tehran in 2007, Dabbagh et al performed a comparative evaluation between the two groups of addicts and nonaddicts undergoing elective lower orthopedic surgeries under spinal anesthesia with bupivacaine.[15] According to their results, the duration of spinal anesthesia was shorter in the opium-dependent individuals (86.6 ± 15.7 min) than that in the healthy subjects (162 ± 22.1 min).[15]

In the present study, the mean duration of spinal anesthesia was 126.14 and 101.45 min in the opium-naïve and opium-dependent groups, respectively, with duration of spinal anesthesia was significantly shorter in the opium-dependent individuals than that in the healthy subjects.

Farzan et al (2010) investigated the success of spinal anesthesia in the opium-dependent (n = 25) and opium-naive (n = 25) groups, who were within the age range of 25-50 years.[16] They used morphine urine test to identify addicted patients. A success rate of 100% was reported in both groups. However, five and two individuals in the addict and nonaddict groups expressed pain during the surgery, respectively. Nonetheless, this difference was not statistically significant.[16]

In the present study, four cases (13.8%) in the opium-dependent group required general anesthesia because of the short duration of anesthesia. In addition, two cases (6.9%) in the opium-naive group and six subjects (20.7%) in the addict group expressed pain and required intravenous supplementary medications, such as midazolam and fentanyl. Nevertheless, in line with the results reported by Farzan,[16] this difference was not statistically significant between the two groups.

In a randomized trial conducted by Mansourian et al in the Shahid Bahonar Hospital of Kerman, Iran, spinal anesthesia with lidocaine alone and lidocaine plus epinephrine was compared in the addict and nonaddict groups (201 male patients).[17] The duration of anesthesia was longer in the nonaddict group than that in the addict group.[17]

Furthermore, a study carried out by Tabatabaei et al (2018) in the Shahid Beheshti Hospital in Yasuj University, Iran, compared the duration of spinal anesthesia with marcaine and lidocaine plus fentanyl in addict and nonaddict patients undergoing orthopedic surgery.[11] The addict and nonaddict groups were each divided into two subgroups. For one subgroup, 3 cc of Marcaine 5% was used, and 75 mg of 5% lidocaine plus 50 μgr of fentanyl was injected in the other subgroup. They reported that the duration of decrease in sensory level in addict subgroups that received Marcaine and lidocaine plus fentanyl was lower than that among nonaddict patients ($P < .0001$). According to the results regardless of the anesthetic agent being used, the duration of spinal anesthesia was shorter in addict patients than in nonaddict ones. In the present study, similar findings were obtained.[11]

Limitations

In the present study, it was not possible to equalize the daily dose of opium and its frequency in the opium-dependent group. In addition, the effects of adding adjuvant medications to bupivacaine on the duration of anesthesia were not assessed.

Suggestion for Future Works

Further research should be undertaken to evaluate the onset time of pain and need for analgesic drugs in the postanesthesia care unit for opium-dependent patients compared with opium-naïve patients. Consequently, further studies are required to evaluate the effect of this substance on the duration of spinal anesthesia in the addict individuals. Moreover, given the prevalence of various industrial and psychotropic drug consumptions in the society, it is recommended more research be conducted on how to modify anesthetic choice to provide better anesthesia for opioid-tolerant patients.

Conclusions

As the findings of the present study indicated, the duration of spinal anesthesia was shorter in the opium-dependent group than that in the opium-naive group. Therefore, it is recommended to use intravenous supplementary medications or higher doses of spinal bupivacaine for these patients. Moreover, it is recommended that the possibility of the need for general anesthesia during surgery be considered and the necessary facilities be provided for general anesthesia before surgery.

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