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Research Article

Failed spinal anesthesia in addicts: Is it an incidence or coincidence?

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KEYWORDS

Regional intrathecal anesthesia;
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Abstract *Background:* Drug addiction remarkably increases morbidity and mortality among patients. Several cases of failed spinal anesthesia have been discovered in the clinical practice among addict patients. Different causes of failed spinal blocks have been mentioned in the literature.
The aim of the study was to compare the success rate of spinal anesthesia in adult addicts and non-addicts.
Methodology: The study was conducted in Kasr al Ainy teaching hospital, Cairo University, Egypt. One hundred patients aged 20–50, ASA 1-2, both genders, undergoing lower abdominal or limbs surgeries under regional anesthesia, were included in the study. They were divided into 2 equal groups, relative to the addiction history to Marijuana, Cannabis, Tramadol, and Clonazepam. Group [NAD] non-addicts ($n = 50$); and Group [AD] addicts ($n = 50$). The success rate, onset, duration of sensory and motor blocks were evaluated. Hemodynamic data were collected, and any complications due to the drugs used or due to spinal anesthesia were recorded.
Results: The incidence of failure of the spinal anesthesia was higher in Group [AD] (33%) than Group [NAD] (4%), ($p < 0.05$). There was delay in the onset time and decreased duration of both sensory and motor blocks in the addict groups compared to non-addicts. All previous findings showed statistical significant difference ($P < 0.05$). Hypotension ($p < 0.05$) and nausea occurred more in addict groups than in non-addicts. No other complications were encountered in the study.
Conclusion: The incidence of failure of the intrathecal anesthesia seemed to be higher in the addict than in non-addict patients. Redo intrathecal injection with a top up 1/2 of the initial dose resulted in success of the block in all failed cases. There was a slower onset and decreased duration of both

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sensory and motor blocks, with higher incidence of hypotension and nausea more in the addict patients than in non-addicts.

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1. Introduction

Over the last 5 years, drug addiction has become a more common problem worldwide. In many countries drug abuse is rapidly increasing among young generations [1,2]. By taking routine preoperative history, it has been noticed that there is a high percentage of patients who were addicted to different types of drugs. Drug addiction remarkably increases morbidity and mortality among patients [2–4]. There are many circumstances which subjected them to surgeries in lower abdominal or lower limbs under regional anesthesia. In the recent clinical practice, several cases of failed spinal anesthesia have been discovered among addict patients, most probably, without any other apparent causes. Different causes of failed spinal blocks have been mentioned in the literature [5,6]. However, there was no reference to any correlation with addiction.

In the present study, it was hypothesized that there was a relation between failed spinal anesthesia and addiction. In reviewing the literature on this relation, it was found that only two studies were discussing the effect of addiction on intrathecal anesthesia [7,8].

Within this framework, the aim of the present study was to compare the success rate of spinal anesthesia in adult addicts and non-addicts, and to compare the onset, duration of the block, the presence of any local or systemic complications due to the use of drugs in the study.

2. Methodology

This case-control observational study was conducted in Kasr al Ainy teaching hospital, Cairo University, Egypt, from December 2012 to June 2013. After approval of the local ethical committee, and written informed Consents from the patients, 100 patients aged 20–50, ASA 1-2, both genders, undergoing elective lower abdominal or lower limbs surgeries under regional anesthesia, were enrolled in the study. They were divided into 2 equal groups, 50 each according to the presence or the absence of history of addiction to Marijuana, Cannabis, Tramadol, and Clonazepam. Group [NAD], non-addicts (n = 50); and Group [AD], addicts (n = 50) to one or more of the previously mentioned drugs. The anesthetist who got the medical history of the involved subjects did not share in the anesthetic management of these patients. The anesthetist in charge in the operating room (OR), was informed not to take history of the patients as they are candidate of a special study.

In addition to the previous criteria, patients with body weight: 70–100 kg; height: 160–175 cm; for Group [AD], history of addiction to different drugs (single drug addiction or addiction to a combination of 2 or more) such as Cannabis, Tramadol, Marijuana, and Clonazepam; and duration of addiction >1 year; but for Group [NAD], the absence of history of addiction to any drug were included in the study.

Furthermore, patient's refusal; patients with any coagulation disorder; patients on anticoagulants, INR > 1.5; local skin disease, infection or disturbed anatomy at the site of injection; unstable cardiac condition; and active chest disease were excluded from the study.

In the preoperative preparation room, midazolam 0.02 mg/kg was injected intravenously to the patient, followed by 500 ml of ringer solution as a preload. In the operating room the patient was fully monitored by non-invasive blood pressure (NIBP), electrocardiogram (ECG), and pulse oximetry. The patient was held in the sitting position. The back was scrubbed with an antiseptic solution. Under complete aseptic conditions, the level of L3-4, or L4-5 intervertebral space was identified. Using a 3 ml syringe, 23G, 2 ml lidocaine was injected subcutaneously along the track of puncture of the spinal needle. With the patients' feet placed on a stool, the patient was asked to curve the back in order to open the intervertebral spaces, and to flex the neck, with the chin touching the chest. Then, 25G spinal needle was introduced at the selected level until clear CSF came out. If the CSF was bloody, the case was excluded from the study, and replaced by a new case. All patients were injected intrathecally with a mixture of 3 ml bupivacaine 0.5% + 0.5 ml (25 μg) Fentanyl. Then, the patient was repositioned immediately in the supine position. The success rate, onset, duration of sensory and motor blocks were evaluated. Hemodynamic data were also collected at specific time intervals, preoperatively **(T0)**, at the onset of sensory block **(T1)**, and at 2 segment regression of sensory block for each patient **(T2)**. Any complications that might occur due to the drugs used or due to the spinal anesthesia were also assessed.

The onset of sensory block was defined as the time elapsed from intrathecal injection of the drug until reaching the level of T10 sensory loss. The level of the sensory loss was examined by needle prick, and loss of sensation to cold using an alcohol swab at the midclavicular line and midaxillary line bilaterally.

The onset of motor block was defined as the time starting from the intrathecal injection till complete motor block (score 3). The motor block was examined using ***Modified Bromage Scores*** [9] where score 0: no motor loss; score 1: inability to flex the hip; score 2: inability to flex the knee; score 3: inability to flex the ankle or complete motor block. The onset of motor block was recorded when Modified Bromage Score was 3, or there is complete motor block.

The success rate was defined as the number of patients experiencing adequate sensory loss reaching T10 dermatomal level and complete motor block (Modified Bromage Score 3) within 15 min recorded from the time of injection. If the sensory loss failed to reach the T10 dermatomal level and or inadequate motor block (Modified Bromage Score <3) after 15 min, the block was considered as failed. When this happened, the patient was held again in the sitting position; a redo of spinal anesthesia with 1/2 of the initial dose under complete aseptic conditions was performed. Then the patient was repositioned. Assessment of the sensory and motor blocks was performed as before. After adequate satisfactory block, the highest level of sensory block was demarcated on the patient's skin, and then the surgery was allowed to proceed.

The duration of the sensory block was also recorded from the time of injection of local anesthetic until the time of 2

segment regression in the sensory level. This was tested frequently after 1.5 h at a 5 min interval, return of sensation to alcohol swab below the demarcated highest level of sensory loss. If sensation was regained at 2 segments lower down, this was confirmed by needle prick and was considered to be the duration of the sensory block.

The duration of motor block was recorded from the time of injection until when Modified Bromage Score became 0 or no limitations of movements at all.

The mean arterial blood pressure, and mean heart rate were recorded preoperatively (T0), then recorded regularly at 5 min intervals with a special record at the onset of sensory block (T1), and at 2 segment regression of sensory block for each patient (T2).

3. Statistical analysis

Data were collected and analyzed using SPSS19.09. The 2 main groups were compared together using independent samples *t*-test. Within same group measurements were compared together using paired *t*-test and repeated measures ANOVA. Categorical data were compared together using Chi square test. Ordinal data were expressed as Mean ± SD while categorical data were expressed as number (%). $P < 0.05$ is considered to be statistically significant.

4. Results

A total of 102 patients were enrolled in the study. Two patients showed bloody CSF, and thus were excluded from the study and replaced by two new cases according to their own group, in order to keep the total sample size of the study at 100 patients. The patients were classified by computer into 2 groups according to the presence or the absence of addiction history. The demographic characteristics are presented in Table 1.

In Group [NAD] there were 35 (70%) male patients and 15 (30%) female patients while Group [AD] was composed of 45 (90%) male and 5 (10%) female patients. This was statistically significant ($p = 0.012$). However, this was clinically insignificant. Otherwise there was no statistical significant difference between studied groups regarding the demographic characteristics (Table 1).

The mean onset of sensory and motor blocks showed statistically significant delay in the mean onset time in Group [AD] more than in Group [NAD]. This finding was significant ($p < 0.05$).

Regarding the incidence of failure in spinal block, two (4%) patients in Group [NAD] and 17 (34%) patients in Group [AD] failed to reach the T(10) level of sensory loss and or inadequate motor block (Modified Bromage Score < 3) within 15 min. This finding was statistically significant ($p < 0.05$) (Fig. 1, Table 1). The failed cases from both groups were included into two subgroups Group [NAD] F, and Group [AD] F and then compared with each other.

In failed cases, after redo spinal anesthesia, *there was delay in the mean onset of sensory and motor blocks* in Group [AD] F more than in Group [NAD] F. The mean onset of motor block was statistically significant ($P = 0.015$) (Table 3).

The mean duration of sensory and motor block was shorter in the addict groups, Group [AD], [AD] F than in the non-addict groups, Group [NAD], [NAD] F. There was a statistically significant decrease in the mean sensory ($p = 0.005$) and motor ($p < 0.05$) duration in Group [AD], Group [AD]F more than Group [NAD]and Group [NAD]F (Tables 2 and 3).

Concerning the hemodynamic changes, preoperatively (T0) there was no statistical significant difference between studied groups. At the onset of the sensory block (T1), the mean of MBP, and MHR was lower in Group [AD] compared to Group [NAD]. This was statistically significant ($p = 0.009$) and ($p = 0.004$) respectively between Group [NAD] and Group [AD]. In the redo cases, at the onset of sensory block (T1), the mean of MBP showed no significant difference when both groups were compared together (Table 4). If the MBP decreased to ⩽60 mmHg or by ⩾20% of the initial preoperative state ephedrine (30 mg diluted in 10 ml saline) was used in increments to stabilize the BP together with intravenous fluids. The heart rate (HR) also decreased with the onset of the block. If the HR decreased < 60 b/min, a bolus dose of atropine, 0.01–0.02 mg/Kg body weight was given to increase heart rate. At 2 segment regression (T2), the mean of MBP, and MHR was also lower in Group [AD] when compared to Group

Table 1 Demographic characteristics and incidence of failure.

	Group [NAD] ($n = 50$)	Group[AD] ($n = 50$)
Age [y]	35.2 ± 8.95	32.6 ± 5.58
Body weight (kg)	79.7 ± 7.35	76.2 ± 5.44
Height [cm]	167.9 ± 4.70	168.2 ± 4.74
Sex: *n* (%)		
M	35 (70%)*	45 (90%)*
F	15 (30%)*	5 (10%)*
Failure rate *n* (%)	2 (4%)*	17 (34%)*

Ordinal data are expressed as Mean ± SD; categorical data are expressed as frequency (%).
* $P < 0.05$ is considered significant when both groups were compared together.

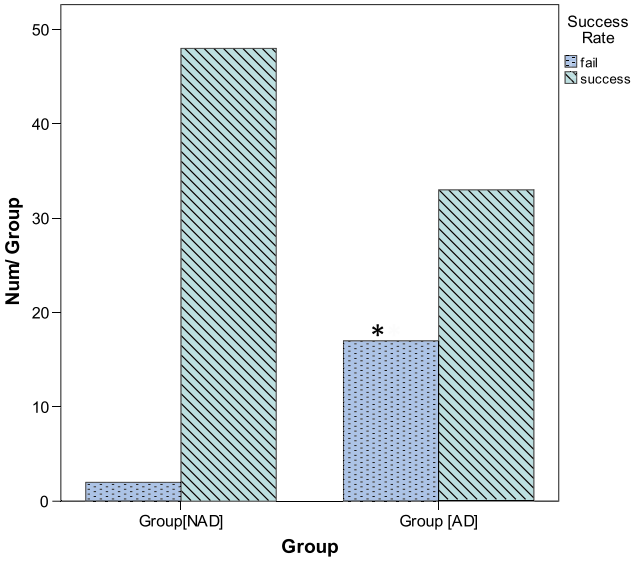

Figure 1 Success rate of spinal block. There was statistical significant difference between the two groups regarding the number of failed cases. *$P < 0.05$.

Table 2 Onset, duration, complications of the block.

	Group [NAD] (n = 48)	Group [AD] (n = 33)	p
Onset of block [min]			
Sensory	5.9 ± 1.08*	7.9 ± 1.01*	(<0.05)
Motor	7.8 ± 0.78*	10.1 ± 1.42*	(<0.05)
Duration of block (min)			
Sensory	163.4 ± 16.44*	133.6 ± 15.16*	(0.005)
Motor	142.8 ± 24.16*	114.1 ± 8.33*	(0.009)
Complications n (%)			
Nausea	2 (4.2%)	4 (12.1%)	–
Hypotension	3 (6.3%)*	8 (24.2%)*	(0.020)

Ordinal data are expressed as Mean ± SD; categorical data are expressed as frequency (%).
* $P < 0.05$ is considered significant when both groups were compared together.

Table 3 Onset, duration, and complications in redo (failed) cases.

	Group [NAD] F (n = 2)	Group [AD] F (n = 17)	p
Onset of the block (min)			
Sensory	4.7 ± 0.35*	6.8 ± 1.25*	(0.041)
Motor	6.5 ± 0.71*	8.7 ± 1.15*	(0.015)
Duration of the block (min)			
Sensory	165.1 ± 21.23*	135.9 ± 11.21*	(0.005)
Motor	145.2 ± 7.07*	120.6 ± 12.85*	(0.019)
Complications n (%)			
Nausea	1(50%)	3(17.6%)	–
Hypotension	2(100%)*	5(29.4%)*	(0.049)

Ordinal data are expressed as Mean ± SD; categorical data are expressed as frequency (%).
* $P < 0.05$ is considered significant when both groups were compared together.

[NAD]. This finding was statistically significant (p0.032), and (p0.008) respectively. However they were comparable in the redo cases. Regarding Group [NAD] and Group [AD], within same group comparison showed statistical significant decrease in the MHR and MBP at T(1) and T(2) when compared to T(0). Furthermore, there was statistical significant increase in both MHR and MBP when data collected at T(2) were compared to T(1) data, ($p < 0.05$). Regarding Group [NAD]F and Group [AD]F, within same group comparison showed no statistical significant differences in the MHR and MBP at T(1) and T(2) (Table 4).

Any complications related to the block were also recorded. The incidence of hypotension (26%) and nausea (14%) was higher in addict groups, Group [AD], and Group [AD]F than in the non-addict groups, Group [NAD], and Group [NAD]F. Each symptom was treated accordingly. No other complications were encountered in the study, (Tables 2 and 3)

5. Discussion

There is an increased incidence of drug addiction in our country especially among young population [1,2]. In the last few

Table 4 Hemodynamic changes in different groups.

	Group [NAD]	Group [AD]	p	Group [NAD] F	Group [AD] F	p
Prep(T0)						
M(MBP)	78.1 ± 7.22[a]	74.2 ± 5.19[a]	–	–	–	
MHR	75.1 ± 6.72[a]	75.6 ± 5.01[a]	–			
Onset(T1)						
M(MBP)	67.4 ± 5.46*,a,‡	63.9 ± 6.38*,a,‡	0.009	61.5 ± 4.94	63.1 ± 6.32	–
MHR	66.1 ± 4.13*	63.4 ± 3.61*,a	0.004	66.5 ± 4.95	64.6 ± 7.24	–
2 Seg Reg (T2)						
M(MBP)	71.6 ± 3.84*,a,‡	69.5 ± 4.89*,a,‡	0.032	72.1 ± 5.65	66.1 ± 4.33	–
MHR	69.1 ± 4.33*,a	66.2 ± 5.12*,a	0.008	70.5 ± 7.77	64.4 ± 4.62	–

Ordinal data are expressed as Mean ± SD.
* $P < 0.05$ is considered significant when both groups are compared together at the same time interval.
[a] $p < 0.05$ is considered significant when within same group data in Group [AD] and [NAD] at T(1) and T(2) were compared with T(0) data.
‡ $p < 0.05$ is considered significant when within same group data in Group [AD] and [NAD] were compared between T(1) and T(2).

years, considerable cases of failed spinal anesthesia were observed among addicts. In general, many factors might be accused in the failure of spinal anesthesia, as problems in the technique, or anatomical disturbances in the subarachnoid space leading to patchy or unilateral block [5,6]. By excluding most of these factors, especially those which were related to the technique itself, no patient showed patchy or unilateral block. These patients had no other apparent causes affecting the success rate of the procedure. After repeated exposure to high doses of drugs, some receptors develop a state of tolerance to overcome the chronic exposure to drugs, thus leading to decrease response to the same dose and concentration of the drug [10].

Many mechanisms might be involved in the production of the tolerance. Downregulation of the receptors' number decreases the response to the drug, the receptor function, and the affinity for agonists. Tolerance might also result due to uncoupling between the receptor and intracellular second messengers by increasing adenylyl cyclase activity [11]. The excessive exposure to exogenous drugs has resulted in variability in the release and function of the endogenous peptides thus leading to lessening of pain threshold and increase in the response to pain stimuli [8,12,13]. So, based on the previous theories, there would be decrease in the duration of spinal anesthesia in the addict patients more than in non-addicts, thus compelling the anesthetist to increase the dose of analgesics in order to relief the patient's complaint [8,12,13]. Narcotic compounds not only affect mu, kappa, and delta receptors but also, can influence many receptors centrally and peripherally in the nervous system including receptors responsible of local anesthesia [13].

Tolerance to some opioids as morphine might occur rapidly. This can be accomplished by receptor desensitization or decoupling of the opioid receptor from the G protein, which results in "nonanalgesic" G protein, thus leading to decreases in analgesic activity [14]. However there might be cross-tolerance among most receptor subtypes. Sufentanil is the least narcotic in producing tolerance. Tolerance can be overcome initially by increasing the dose of the drug [15].

Some opioids exert a local anesthetic effect on the peripheral nerves. This might be achieved by blocking sodium channels in the peripheral nerve roots [16,17]. Opioids might produce their local anesthetic effect on the excitable cell membrane itself [18].

The receptors involved in spinal anesthesia are comparable in constitution and function to opioid receptors in certain parts of the body such as the spinal cord, making them affected by the prolonged exposure to opioids [19]. Therefore, correlating the findings of our study, the interaction between local sedatives and opioid receptors, and the decreased pain threshold in addicts, all explain that tolerance can occur to opioid receptors as well as local anesthetic receptors especially in the spine [13]. Tolerance and resistance to local anesthetic drugs are translated to the body as delay in the onset, decrease in the duration of spinal anesthesia or even complete failure of response to the usual dose of the local anesthetic, thus needing to increase the dose of local anesthetic to overcome the state of tolerance.

Regarding the ***incidence of failure*** *of spinal block*; in the present study, two (4%) in Group [NAD] ($n = 50$), and 17 (34%) in Group [AD] ($n = 50$) failed to reach the level of T10 sensory reach the T(10) level of sensory loss and or inadequate motor block (Modified Bromage Score < 3) within 15 min from intrathecal injection. This was statistically significant. However all failed cases had succeeded after redo intrathecal injection with 1/2 the initial dose to provide adequate anesthesia [5] In consistence with our findings Nagata [20] found a cluster of 3 cases of complete failure of spinal anesthesia, and 5 others of incomplete failure of spinal block. They thought that the problem was in the drug used. However, the drug met all the manufacturer specifications. In a prospective study by Fuzier et al [21], the incidence of failed spinal was 3.2% (39 cases) of which 41% were complete spinal failure. The possibility of resistance to the used local anesthetics, or the occurrence of mutation at the level of sodium channel was discussed in the literature [22].

Andrea and Trescot [23] published an interesting case report on the internet explaining that a patient was suffering from COPD and addiction. He had failed spinal block. Then after 15 min, a redo spinal was done again due to its bad chest condition. The anesthetist figured a second time failure. However the onset of spinal anesthesia started after 45 min from the first injection. The author explained that the problem was due to low PH of the CSF, or low PH of the injected drug which leads to delayed onset of blockade. The slow onset of anesthesia was due to decrease in the diffusion rate of the reduced uncharged base form of the drug across the nerve membrane. However many cases were reported to fail due to local anesthetic resistance or due to anatomical variations, channel mutation or drug failure [24].

Only two studies were discussing the effect of addiction on intrathecal anesthesia [7,8]. In opposition to our study, in the study done by Farzan et al. [7] comparing the success rate of the spinal anesthesia in addicts and non-addict patients, they did not find any difference in the success rate of spinal anesthesia between both studied groups. The addicts who claimed pain sensation at the surgical site were malingerers trying to take more opioids. Their results might be due to small sample size, the addiction to different drug types. However, in the present study, the sample size was increased and the duration of addiction was considered longer than 1 year to give more time for receptor exposure to the drug effect, and hence more chance to the development of tolerance.

The mean onset of sensory and motor block was more delayed in the Group [AD] more than in Group [NAD]. This finding was statistically significant ($p < 0.05$). Within the redo cases, the onset of the sensory block was slightly accelerated in Group [NAD] more than in Group [AD]. This finding was also statistically significant ($P < 0.05$). Regarding non-addict groups, our findings were consistent with a study done by Poonam et al. [25] showing harmonious onset times. In contrast to our study, Sarvela et al. [26] were comparing plain with hyperbaric bupivacaine, and found that the onset of sensory block was 19 min and that of motor block was 7–10 min. The onset time end point was recorded at the highest dermatome level, mostly T4, compared with our study where the onset time was recorded at T10 sensory loss. Usually in the cesarean sections, a level of T4 sensory block is recommended to produce adequate anesthesia for surgery.

As regards the mean duration of sensory and motor block, in the present study, there was a significant decrease in the duration of both sensory and motor block in Group [AD], and in Group [AD] F. Our observations resembled the study by Mansourian et al. [8] in which they compared the duration

of spinal block in the addicts and in non-addicts. They found that the addicts had shorter sensory and motor duration of action, even with addition of epinephrine.

As regards complications, hypotension occurred in 13 (26%) of the 50 patients in both Group [AD], and Group [AD] F, while it occurred in 5 (10%) of patients in both Group [NAD] and Group [NAD] F. This was statistically significant ($p < 0.05$). This finding is mostly explained by the state of relative dehydration in most of the addicts, due to their eager for the drugs with negligence to food and fluid intake. The preoperative fasting made the dehydration worse. The replacement with only 500 cc of IV fluids was insufficient to treat hypovolemia prior to anesthesia. With the onset of spinal block, sympathetic block also occurred, resulting in vasodilatation and more hypotension. No other complications were recorded in all groups. In the present study, hypotension occurred in 18 (18%) patients from a total of 100 patients. In agreement with our study, in Tarkkila and Isola. [27] hypotension occurred in 15% of patients. However, on the contrary to our results, Brenck et al.'s [28] study showed that hypotension occurred in (56.5%) of cases. In our study, hypotension was accompanied in some cases with nausea. In Abouleish et al. [29] nausea occurred in 41.7% of cases and was reduced significantly after ondansetron administration to the patients. These findings were incongruous to our results.

To sum up, many opioids were found to have a local anesthetic effect by blocking sodium channel receptors at the peripheral nerve endings [16–18]. Similar to opioid receptors, these receptors might, by time, develop tolerance to the opioids as well as to the local anesthetics. By consequences, the usual dose of local anesthetic might be needed to be increased in order to produce the same targeted effect. The duration time of addiction, the type of drug abuse, and the number of drug intake per week, might also play a role in the occurrence of tolerance. Many people become addicted to more than one type of these drugs. So the different receptors for these drugs might show drug interaction, mutation, tolerance, or cross-tolerance [30].

On the other hand, there were limitations to our study; first, the small sample size relatively to the increased incidence of addiction, second, the sample enrolled in the study was not addict to one specific type of drug but mostly to several types of drugs. This makes the diagnosis and specification of the causes of failure became more difficult. We recommend the performance of several separate researches to study the incidence of failure on a sample population addicted to only one drug type at a time. Further studies are needed, on a larger sample of population to investigate the main causes of increased incidence of failed spinal anesthesia among addicts, especially on the cellular and receptor level to concur our results.

6. Conclusion

We concluded that the incidence of failure of the intrathecal anesthesia seemed to be higher in the addict than in non-addict patients. Redo intrathecal injection with a top up 1/2 the initial dose resulted in success of the block in all failed cases. There was a slower onset and decreased duration of both sensory and motor block in addict patients, with higher incidence of hypotension and nausea than non-addict patients.

Conflict of interest

No conflict of interest.

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