

Shortening Anesthesia Duration does not Affect Severity of Withdrawal Syndrome in Patients Undergoing Ultra Rapid Opioid Detoxification

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Abstract- Ultra rapid opioid detoxification (UROD) is one of the new methods of detoxification. This method of detoxification involves putting patients under general anesthesia and actively giving them opioid antagonists. The objective of this study was to evaluate effects of anesthesia duration in UROD on severity of withdrawal syndrome. Sixty addicted patients seeking UROD procedure assigned randomly to one of the 2hr, 4hr or 6hr anesthesia duration groups. Premedication and anesthesia procedure (induction and maintenance) were the same for three groups. Detoxification was done for all patients with 50 mg oral naltrexane (prior to induction) and 20 mg intravenous naloxane (8 mg/bolus and 12 mg/infusion). Blood pressure, heart rate and respiratory rate were automatically measured and recorded every 5 minutes. The severity of withdrawal syndrome was measured and recorded every one hour during anesthesia, 2hours post-anesthesia, and 12 and 24 hours following the induction of anesthesia according to the Wang Scale modified by Lomier (WSMBL). Patients aged 20-58 in three groups. Three cases experienced delirium after detoxification that lasted 24 hours in one. Severity of withdrawal syndrome in patients of groups 2, 4 and 6 hour were 8.7, 7.4 and 5.1 respectively during anesthesia and 12.3, 11.1 and 13.9 after 18 hours of anesthesia. Results of this study showed that, in standard settings, UROD is a safe method for detoxification and has low complications. The withdrawal symptoms during and after anesthesia are low. Shortening the duration of anesthesia has no affect on severity of withdrawal syndrome during and after anesthesia.

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Introduction

Opioid dependence is a complex and difficult to treat condition (1), characterized by a withdrawal syndrome that occurs when opioid antagonists are administered or opioid agonists are discontinued in individuals who are opioid dependent (2,3). Addicted patients are afraid of experiencing withdrawal symptoms during a detoxification program (4), and managing withdrawal is a critical first step in encouraging many opioid dependent patients to receive treatment (5). In order to shorten the withdrawal period, ultra rapid opioid detoxification (UROD) have been developed, under which opioid dependent patients are detoxified with opioid antagonists administered either under general

anesthesia or deep sedation. This method was first developed by Loimer et al (6) with patients under anesthesia and intubations based on earlier rapid detoxification methods published by researchers at the Yale University (7,8). Subsequently, several modifications and improvements have been made in UROD. This method is described by many researchers as the most efficacious and safest procedure (5,6,9). Unless performed properly, this procedure can be dangerous due to the sympathetic outflow. However, with proper support, this danger can be mitigated (10). The future efforts must be directed toward lowering the risks. Duration of anesthesia constitutes one of these factors. Previous researchers have performed UROD under general anesthesia or deep sedation that lasts four

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to six hours (5,6,9,11). This increases the risk and cost of anesthesia (12).

Goal

The objective of this study was to compare the effects of different anesthesia durations in UROD procedure on severity of withdrawal symptoms in opioid dependent patients.

Patients and Methods

The study was approved by the local committee of ethics and research of Kurdistan University of Medical Sciences. Written consent form was obtained from all patients participating in the study after complete information regarding procedure.

The admission criteria included diagnosis of opiate addiction according to DSM-IV classification, previous well-being verified by outpatient clinical and laboratory evaluation, confirmation of high motivation by a psychological interview, and fasting for 8 hours before hospitalization. Exclusion criteria were concomitant alcohol dependence, acute infectious disease, pregnancy and American society anesthesiologist classification score of three or higher. Patients were admitted to UROD ward in Qods hospital of Sanandaj at 8.00 AM. 60 patients scheduled for UROD were randomly assigned to three treatment groups. Premedication and anesthesia protocols were the same for three groups including clonidine (100 mcg) and clonazepam (2 mg) orally 60 min prior to induction, dexamethason 8 mg, cimetidine 200 mg, methochlorpramide 10mg and lidocaine 1 mg/kg intravenously (IV), octrotide 100 mcg sub coetaneous and naltroxone 50 mg orally prior to

induction of anesthesia .Anesthesia was induced by midazolam (10mcg/kg) and propofol (2 mg/kg).

Orotracheal intubation was facilitated by Succenylcholine (1.5 mg/kg; IV). 60% nitrous oxide and 40% oxygen were added to propofol 100 mcg/kg/min and medazolam 0.1mg/kg/hour infusion for maintenance of anesthesia. Muscle relaxation was obtained with supplement doses of atracurium. Patients were monitored with an instrument showing cardiogram, respiratory frequency throat thoracic plethysmogram, indirect blood pressure, oxygen saturation, and end tidal CO₂. Patients were mechanically ventilated using a dragger (fabious) ventilator. Detoxification was carried out with the administration of naloxone bolus (4 mg) and infusion (12 mg) for two (2 hour anesthesia duration group), Four (four hour anesthesia duration group) or six (six hour anesthesia duration group) hours.

Infusion of anesthetic agents and N₂O administration were stopped after 2, 4 or 6 hour in 3 groups respectively. After return of the normal spontaneous breathing and suctioning mouth secretions, patient were extubated deeply and turned to lateral position with a nasal oxygen probe in site, while monitoring of ECG, oxygen saturation and IDBP continued .Clinical signs of withdrawal were evaluated according to the criteria of Wang et al. (Table 1) adapted to the conditions of general anesthesia (13).

The sign and symptoms were rated as present or absent and the scores were given. The total score represented the cumulative rating for the signs and symptoms exhibited and was obtained after starting the infusion of naloxone and then hourly during anesthesia, and 2, 12 and 24 hours after induction of anesthesia.

Table 1. Rating of withdrawal signs (wang modified scores)

| Signs | Present | Absent |
|-------------------------------------|---------|--------|
| Gooseflesh | 6 | 0 |
| Vomiting or gastric hyper secretion | 6 | 0 |
| Profuse sweating | 6 | 0 |
| Mydriasis | 6 | 0 |
| Restlessness | 4 | 0 |
| Lacrimation | 4 | 0 |
| Nasal congestion | 4 | 0 |
| Muscle contraction | 3 | 0 |
| Tremor | 6 | 0 |
| + Hypertension | 6 | 0 |
| ++Tachycardia | 6 | 0 |
| Total | 57 | 0 |

+10% increase in systolic blood pressure over control values.

++ 10 % increase in heart rate over control values.

Table 2. Baseline characteristics of study participants (n = 20 in each group)

| Characteristic | 2 hour | 4 hour | 6 hour |
|---|----------------------|-----------|-----------|
| Men | 19 | 19 | 20 |
| Age (year) | 28.4(5.1) | 29.1(4.5) | 29.3(5.2) |
| Employed | 13 | 15 | 15 |
| Married | 11 | 13 | 17 |
| Education | Primary | 8 | 11 |
| | Middle | 11 | 11 |
| | High | 1 | 0 |
| Substance | Opium | 16 | 15 |
| | Heroin | 4 | 5 |
| Rote of consumption | Intravenous | 3 | 3 |
| | Smoking | 3 | 5 |
| | Orally | 14 | 12 |
| | More than one method | 6 | 8 |
| Number of previous unsuccessful attempts for Detoxification | 3.6(2.3) | 3.7(2.9) | 4.1(2.9) |
| Addiction duration (year) | 9.4(5.1) | 7.9(4.4) | 8.8(4.5) |

At the end of anesthesia, patients were maintained in the UROD ward (with conditions similar to ICU) and treatment continued for 24 hours. Afterward, patients were discharged and naltrexone, 50 mg daily, was prescribed for six months and clonazepam 2 mg at bedtime for insomnia as needed. Patients were visited daily by an anesthesiologist for four days and by a psychiatrist weekly thereafter for six months. Urine analysis for morphine was performed at day ten, one and six months.

Statistical analysis

For nominal data, statistical analysis was carried out using either chi-square or fisher's exact test. To compare data obtained at different time points during detoxification with post-anesthetic stoppage time unpaired Student's T test was used. $P < 0.05$ was considered statistically significant.

Results

Over a 17-month period from April 2003 to September 2004, sixty patients met the inclusion criteria. 20 of who were randomly assigned for each of 2, 4 or 6 hour anesthesia duration groups. The three groups were statistically comparable for base line characteristics (Table 2).

Fifty-eight patients were male. 39.3% of patients aged under 30. Most of the patients had average

education and 69.61% were married, out of whom 28% had domestic problems. The most common opioid misused was opium (82.1%) and the most common rout of consumption was oral. The intensity of withdrawal signs and symptoms on Wang modified scale were higher at the beginning of naloxone infusion and two hours after finishing the anesthetic infusion in all groups. No statistical differences were observed in all groups in relation to withdrawal intensity. We could not establish any correlation between withdrawal degree and age ($P= 0.6$) and drug addiction time ($P= 0.15$). Nevertheless, there were statistically significant correlations between withdrawal degree and the opioid consumed and also rout of consumption; withdrawal signs and symptoms were much more intense in opium than heroin ($P= 0.02$) and in oral consumption than intravenous injection ($P= 0.043$) or smoking ($P= 0.015$). The doses of anesthetic agents used were significantly lower in the 2h group compared to 4h ($P= 0.011$) and 6h ($P= 0.005$) groups; these values were lower in 4h group than in 6h group ($P= 0.01$).

The complication rate was low and included 3 delirium cases that lasted 24 hours in one of them, who was treated with diazepam IV. A case of cardiogenic edema developed 24 hours following completion of anesthesia in a patient with a history of chronic obstructive lung disease that needed re-intubation and mechanical ventilation for additional 6 hours. Patients were visited and underwent urine morphine test after ten

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Table 3. withdrawal signs evaluated by Wang modified score [mean (SD)]

| Group/ Time | T1 | T2 | T3 | T4 |
|-------------|-----------|------------|------------|-----------|
| 2HG | 8.4 (3.8) | 14.1 (6.3) | 11.3 (6.3) | 8.3 (4.2) |
| 4HG | 7.9 (4.1) | 13.9 (6.9) | 9.5 (4.8) | 8.1 (3.9) |
| 6HG | 5.7 (3.6) | 13.7 (5.6) | 12.1 (7.2) | 8.4 (4.4) |

T1=starting the infusion of naloxone, T2=during anesthesia, T3= 12 hour from induction of anesthesia T4= 24 hour from induction of anesthesia

Table 4. Withdrawal signs evaluated by Wang modified score [mean (SD)] in consumers of different opiates

| Group/ Time | T1 | T2 | T3 | T4 |
|-------------|------------|------------|------------|------------|
| opium | 10.4 (5.6) | 13.8 (7.6) | 11.4 (5.4) | 8.2 (3.7) |
| Heroin | 7.6 (3.2) | 13.4 (5.4) | 12.4 (6.2) | 11.3 (5.3) |

T1=starting the infusion of naloxone, T2=during anesthesia, T3= 12 hour from induction of anesthesia T4= 24 hour from induction of anesthesia

Table 5. Negative morphine test after ten days (MT1), one month (MT2) and six months (MT3) of detoxification.

| Test / group | MT1 | MT2 | MT3 |
|---------------|---------|----------|---------|
| | N(%) | N(%) | N(%) |
| 2 HG (N = 20) | 16(%80) | 13(%65) | 10(%50) |
| 4 HG (N = 20) | 18(%90) | 10(%50) | 9(%45) |
| 6 HG (N = 20) | 17(%85) | 13 (%65) | 8(%40) |

days, one month and six months under supervision of anesthesiologists. 11 of 60 patients did not come back for follow-up tests. After ten days, one month and six months, 3, 10 and 15 of the remaining 49 patients respectively relapsed into addiction. No statistically significant differences were seen among groups in relation to recurrence of addiction.

Discussion

A reliable method in assessing the adequacy of withdrawal is the reinjection of high dose naloxone (20–30 mg; IV). If the patient does not show exacerbation of the withdrawal signs, detoxification is considered adequate. Absence of response to a naloxone challenge may require six hours of general anesthesia with injection of high dose naloxone at repeated intervals (10).

We compared the severity of withdrawal syndrome at different time points within and between groups. The most withdrawal severity, in our study, occurred about two hours after completion of anesthesia.

These results are not compatible with those of other studies (14-17). In this study, the highest peak occurred

at the beginning of naloxone infusion and minor peak on the day after detoxification. The cause of this discrepancy may be higher levels of sedation in our patients and the use of muscle relaxants during anesthesia. This could mask symptoms of withdrawal that appear in the awakening time in recovery. Shortening anesthesia duration did not affect severity of withdrawal, but significantly lowered the costs.

We compared patients of 3 groups in relation to the type of opiate used and there were statistically significant differences in Wang scale in each group. We observed the most intense withdrawal symptoms in patients using opium orally. There were no statistically significant differences between opium (smoking) and heroin (IV or smoking). To our knowledge, no study has compared the intensity of withdrawal signs in patients consuming opium or heroin. The relapse rate in our study was about 55% overall with no significant differences between groups. This was similar to Albanese study reporting 61/111 patients (55%) with relapse-free status at the six month follow up interval (self-reported relapse-free status was confirmed by urine drug screen; (14). In our study, after six months, only one (7%) of 14 heroin users remained abstinent but 26

(56%) of 46 opium addicts remained abstinent. This difference was significant. Most studies have shown high relapse rates to heroin use (17,18). In our study, the relapse rate was 15% at day ten, 72% in the first and 92% in the sixth month in 14 heroin consumers. A report on 15 heroin users in Sydney estimated that relapse rate was 42% in one month, 77% in two months and 83% in three months (19). Another study reported that only 2 of 43 patients (5%) were at retention for six months (20).

Cucchia *et al.* (21) reported an 80% relapse rate. In the other hand Rabinowitz and coworkers reported much lower rates of relapse after naltrexone treatment than ours they reported that 60% of patient were free of heroin use six month after detoxification (22). Another study reported that 93% of patients were abstinent from opioid a month after detoxifications under sedation (22) these are in stark contrast with ours results. In conclusion, in conclusion, the results of this study showed that the intensity of withdrawal signs in UROD procedure under general anesthesia that lasts 2 hour duration was as that of 4 or 6 hour duration. We believe that shortening the anesthesia period has the advantage of lower risk and costs.

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