

# Comparing the Efficacy of Methadone and Tincture of Opium in Controlling Agitation Caused by Withdrawal Syndrome in Opium-Addicted Patients in the Intensive Care Unit: A Randomized Trial Study

Seyed Mojtaba Sohrevardi<sup>1</sup>, Mostafa Pournamdari<sup>2</sup>, Razieh Salimi<sup>2</sup>, Farhad Sarrafzadeh<sup>3</sup>, **Mehdi Ahmadinejad<sup>4</sup>**

## Original Article

### Abstract

**Background:** Few studies have been conducted regarding the comparison of the efficacy of methadone and tincture of opium (TOP) in controlling agitation induced by withdrawal syndrome. Therefore, the current randomized trial study is carried out with the aim to evaluate comparisons on the efficacy of methadone and TOP in controlling agitation caused by withdrawal syndrome in opium addicted patients in the intensive care units (ICUs).

**Methods:** This clinical trial study was conducted on 60 patients admitted to ICU of Shahid Bahonar Hospital, Kerman, Iran. After classification of the patients into two groups, the first and second groups consumed methadone syrup (5 mg/ml) and TOP (10 mg/ml), respectively. Agitation in these patients was assessed through the Richmond Agitation-Sedation Scale (RASS). Vital signs were also assessed. Paired sample t-test and independent t-test were used for data analysis.

**Findings:** In the current study, the administered dose of methadone and TOP was  $36.17 \pm 26.99$  and  $112.67 \pm 102.74$  mg, respectively ( $P < 0.010$ ). Methadone administration led to a significant decrease of the patients' vital signs, including systolic blood pressure, heart rate, respiratory rate, and Glasgow Coma Scale (GCS) ( $P < 0.05$ ). Though TOP administration decreased systolic blood pressure and GCS significantly ( $P < 0.05$ ), it had no effect on patients' diastolic blood pressure, body temperature, heart rate, and respiratory rate ( $P > 0.05$ ). In total, no significant difference was detected between two groups regarding vital signs ( $P > 0.05$ ). However, a significant difference was seen between methadone and TOP groups in terms of RASS score ( $P < 0.01$ ).

**Conclusion:** According to the results of the current study, lower dose of methadone, compared to TOP, could control agitation caused by opium withdrawal symptoms.

**Keyword:** Methadone; Opium dependence; Intensive care units

**Citation:** Sohrevardi SM, Pournamdari M, Salimi R, Sarrafzadeh F, Ahmadinejad M. **Comparing the Efficacy of Methadone and Tincture of Opium in Controlling Agitation Caused by Withdrawal Syndrome in Opium-Addicted Patients in the Intensive Care Unit: A Randomized Trial Study.** *Addict Health* 2020; 12(2): 69-76.

Received: 22.11.2019

Accepted: 18.01.2020

1- Robarts Research Institute, University of Western Ontario, Ontario, Canada AND Pharmaceutical Sciences Research Center AND Department of Clinical Pharmacy, School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

2- Pharmaceutics Research Center AND Department of Medical Chemistry, School of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

3- Department of Internal Medicine, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

4- Department of Anesthesia, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

Correspondence to: Mehdi Ahmadinejad; Department of Anesthesia, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran; Email: mehdi50@gmail.com

## Introduction

Opium is a substance extracted from opium poppy.<sup>1-3</sup> According to World Drug Report in 2015, approximately 16.5 million people use opiates, including opium and heroin.<sup>4</sup> Consumption of opium is high in many south Asian countries, especially Afghanistan and Pakistan.<sup>1</sup> Opium is readily available in Iran due to long boundary between Afghanistan and Iran.<sup>5,6</sup>

Bases on previous studies, there were more than one million opium addicts in Iran in 2003.<sup>7</sup> Opium consumption in Iran is most prevalent in northern and southern cities.<sup>5</sup> Opium intake is associated with injury, obesity, and poor quality of life (QOL).<sup>8,9</sup> Moreover, opium consumption increases the risk of bladder, lung, laryngeal,<sup>7</sup> and upper gastrointestinal cancers.<sup>5</sup>

Studies have shown that opium use cessation or reduction in the opium-dependent individuals leads to opium withdrawal syndrome.<sup>10</sup> These symptoms can be manifested some hours after the consumption of the last dosage of the drug and may last for a week or more.<sup>11</sup> The physical withdrawal symptoms often stop after 14 days.<sup>12-15</sup> Withdrawal syndrome may impress the patient's impetus for contribution in programs of addiction treatment.<sup>13</sup> Management of these symptoms can help sufferers to cope with their disease more easily.

In medically assisted opioid withdrawal, treatment with methadone prevents withdrawal symptoms and decreases or deletes craving since its dosage is gradually decreased until the medication is discontinued.<sup>16</sup> Although methadone is considered as the main pharmacotherapy for opioid dependence,<sup>17,18</sup> the cost of treatment with methadone prevents its medical usage in some parts of South-East Asia.<sup>19</sup> One of the alternative medications for the treatment of opioid dependence is tincture of opium (TOP) which is used in some Asian countries for the management of opioid withdrawal syndrome.<sup>20</sup> It is prepared from opium in alcohol and water and contains 1% morphine. It is used as a traditional medicine in some South-East Asia region. Due to its low cost, TOP is preferred over methadone.<sup>19</sup> Given that few studies comparing the efficacy of TOP and methadone in the management of opium withdrawal syndrome,<sup>21</sup> the aim of the current study is to compare the efficacy of methadone and TOP in controlling agitation of withdrawal

syndrome in opium addicted patients admitted to the intensive care units (ICUs).

## Methods

This clinical trial study was conducted on patients admitted to ICU of Shahid Bahonar Hospital, Kerman, Iran during 2011. This study was approved by the ethics committee (K-90-145) of Kerman University of Medical Sciences. In addition, it was registered in Iranian Registry of Clinical Trials (IRCT) website with number IRCT 201107011836N2.

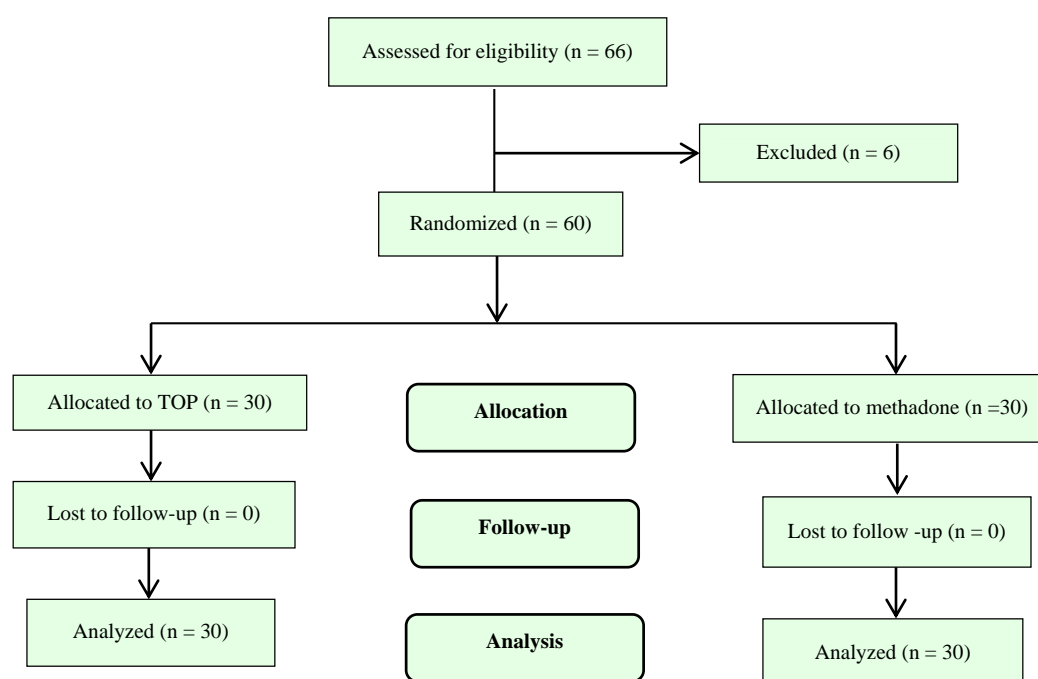
Patients in the age range 18-60 years who were addicted to opiates such as opium, opium sap, or Shireh [according to Diagnostic and Statistical Manual of Mental Disorders (DSM) -IV-TR criteria] entered the study. Moreover, the exclusion criteria were patients addicted to drugs except opium, pregnancy, lactation, and liver, heart, and kidney failure.

After taking consent from the patients or their relatives, 66 opiate addicted patients were selected from Shahid Bahonar Hospital and finally 6 patients excluded from the study (2 patients were addicted to other drugs except opium and 4 patients had heart failure). Therefore, the study was conducted on 60 patients. These patients were classified into two parallel groups using block randomization procedure ( $n = 30$ ). The first and second groups respectively consumed methadone syrup (5 mg/ml) and TOP (10 mg/ml) during hospitalization. It is noteworthy that the patients were blind in the current study. Figure 1 shows the CONSORT flow diagram of patients in Shahid Bahonar Hospital.

The type and amount of the drugs consumed were used to calculate the amount of daily morphine intake in each patient according to table 1. Then, the equivalent doses of methadone syrup or TOP were administered for each patient. Furthermore, acetaminophen (15 mg/kg) was administered every 6 hours to control pain in the patients.

The following points are essential for determining the dose of TOP and methadone.<sup>22</sup>

1. Pure opium contains about 10 % morphine.
2. Opium sap contains approximately 20 % morphine.
3. The uptake of the morphine content of opium by Vafoor is about 30%. This rate by heated-stone (Sikh-sang method) and oral method is 60% and 60%-90%, respectively.
4. One mesghal of opium is equal to 4-5 g.



**Figure 1.** Consort flow diagram of patients in Shahid Bahonar Hospital, Kerman, Iran

Determination of the dose of TOP and methadone syrup in opiate-addicted patients was calculated according to usual opium weight in consumers (Table 1).

**Table 1.** Conventional weight of opium in opium users and the amount of morphine and methadone equivalent

| Unit      | Weight used in consumer (mg) | Morphine (mg) | Methadone equivalent (mg) |
|-----------|------------------------------|---------------|---------------------------|
| 1 lentils | 24.24                        | 2.44          | 2.44                      |
| 1 Wheat   | 48.80                        | 4.88          | 4.88                      |
| 1 Pea     | 195.30                       | 19.35         | 19.35                     |
| 1 Mesghal | 4687.50                      | 468.75        | 468.75                    |

Since the half-life of methadone is long, people taking methadone received it twice a day, but the frequency of TOP use was equal to that of opium.

Agitation in these patients was assessed through Richmond Agitation-Sedation Scale (RASS) which is shown in table 2.<sup>23</sup>

In addition, vital signs including heart rate, body temperature, systolic and diastolic blood pressure, and respiratory rate were checked in each patient.

Data were entered the SPSS software (version 19, SPSS Inc., Chicago, IL, USA). Paired sample t-test was used to compare the variables before and after treatment and the independent t-test was used to compare the two groups.

**Table 2.** Richmond Agitation-Sedation Scale (RASS)

| Score | Terms             | Description   |
|-------|-------------------|---|
| +4    | Combative         | Overtly combative or violent; immediate danger to staff   |
| +3    | Very agitated     | Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff              |
| +2    | Agitated          | Frequent non-purposeful movement or patient-ventilator dyssynchrony                             |
| +1    | Restless          | Anxious or apprehensive but movements not aggressive or vigorous                                |
| 0     | Alert and calm    | Alert and relaxed; spontaneously pays attention to caregiver                                    |
| -1    | Drowsy            | Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice |
| -2    | Light sedation    | Briefly (less than 10 seconds) awakens with eye contact to voice                                |
| -3    | Moderate sedation | Any movement (but no eye contact) to voice  |
| -4    | Deep sedation     | No response to voice, but any movement to physical stimulation                                  |
| -5    | Unarousable       | No response to voice or physical stimulation  |

## Results

The mean daily intake of opium was  $2.10 \pm 0.54$  times per day. The mean adsorbed morphine was  $28.30 \pm 25.70$  mg/day. In addition, the mean consumed drug was  $1.80 \pm 2.38$  g/day.

Table 3 shows the frequency distribution of patients in terms of gender, age, type of drug, method of consumption, and administration of drug.

**Table 3.** Frequency distribution of patients in terms of gender, age, job status, marital status, type of drug, method and administration of drug

| Parameters                             | n (%)     |
|--|-----------|
| Gender                                 |           |
| Men                                    | 48 (80.0) |
| Women                                  | 12 (20.0) |
| Age                                    |           |
| < 20                                   | 3 (5.0)   |
| 20-40                                  | 28 (46.7) |
| > 40                                   | 29 (48.3) |
| Job Status                             |           |
| Unemployed people                      | 25 (41.7) |
| Employed people                        | 35 (58.3) |
| Marital status                         |           |
| Single                                 | 18 (30.0) |
| Married                                | 42 (70.0) |
| Type of drug                           |           |
| Opium                                  | 53 (88.3) |
| Opium sap                              | 7 (11.7)  |
| Method                                 |           |
| Opium pipe (locally named Vafoor)      | 11 (18.3) |
| Oral                                   | 36 (60.0) |
| Heated-stone (locally named Sikh-sang) | 13 (21.7) |
| Administered medication                |           |
| Methadone                              | 30 (50.0) |
| TOP                                    | 30 (50.0) |

TOP: Tincture of opium

Comparison of patients in the two groups in terms of demographic data showed that there was no significant difference between the two groups regarding the demographic data ( $P > 0.05$ ).

Frequency distribution of patients in the two

groups in terms of RASS score is shown in table 4.

As shown in table 4, 56.7% of patients in methadone group had RASS score 0, while 80.0% of the patients in the TOP group had RASS score 0.

Moreover, a significant difference was seen in the frequency distribution of patients in methadone group in terms of RASS score ( $P < 0.010$ ). In addition, there was a significant difference in the frequency distribution of patients in the TOP group regarding RASS score ( $P < 0.010$ ).

**Table 4.** Frequency distribution of patients in the two groups in terms of Richmond Agitation-Sedation Scale (RASS) score

| Medications |   | RASS score |      |      |     |     | P       |
|-------------|---|------------|------|------|-----|-----|---------|
|             |   | -1         | 0    | 1    | 2   | 3   |         |
| Methadone   | n | 6          | 17   | 5    | 1   | 1   | < 0.001 |
|             | % | 20         | 56.7 | 16.7 | 3.3 | 3.3 |         |
| TOP         | n | 2          | 24   | 4    | 0   | 0   | < 0.001 |
|             | % | 6.7        | 80.0 | 13.3 | 0   | 0   |         |

TOP: Tincture of opium

The effects of methadone on variables including GCS score, respiratory rate, body temperature, systolic and diastolic blood pressure, and heart rate are shown in table 5.

According to table 5, methadone decreased systolic blood pressure, heart rate, respiratory rate, and GCS ( $P < 0.050$ ), but it had no effect on diastolic blood pressure and body temperature ( $P > 0.050$ ).

Table 6 shows the effect of TOP on variables including systolic and diastolic blood pressure, heart rate, respiratory rate, and GCS.

Given table 6, TOP decreased systolic blood pressure and GCS ( $P < 0.050$ ), but it had no effect on diastolic blood pressure, body temperature, heart rate, and respiratory rate ( $P > 0.050$ ).

Comparison of the two groups (methadone and opium groups) regarding the variables including medication dose, systolic and diastolic blood pressure, body temperature, heart rate, respiratory rate, and GCS are shown in table 7.

**Table 5.** Effect of methadone on variables

| Variables                       | Before treatment   | After treatment    | P     |
|---------------------------------|--------------------|--------------------|-------|
|                                 | Mean $\pm$ SD      | Mean $\pm$ SD      |       |
| Systolic blood pressure (mmHg)  | 139.73 $\pm$ 19.78 | 133.63 $\pm$ 22.31 | 0.041 |
| Diastolic blood pressure (mmHg) | 85.23 $\pm$ 10.43  | 85.47 $\pm$ 12.24  | 0.927 |
| Body temperature (Centigrade)   | 37.42 $\pm$ 0.56   | 37.29 $\pm$ 0.57   | 0.255 |
| Heart rate/min                  | 79.10 $\pm$ 13.66  | 73.20 $\pm$ 18.25  | 0.044 |
| Respiratory rate                | 22.07 $\pm$ 5.99   | 19.30 $\pm$ 6.09   | 0.017 |
| GCS                             | 11.25 $\pm$ 2.87   | 12.32 $\pm$ 3.019  | 0.033 |

SD: Standard deviation; GCS: Glasgow Coma Scale

**Table 6.** Effect of tincture of opium (TOP) on variables

| Variables                       | Before treatment   | After treatment    | P       |
|---------------------------------|--------------------|--------------------|---------|
|                                 | Mean $\pm$ SD      | Mean $\pm$ SD      |         |
| Systolic blood pressure (mmHg)  | 130.27 $\pm$ 32.31 | 127.07 $\pm$ 20.79 | 0.041   |
| Diastolic blood pressure (mmHg) | 79.63 $\pm$ 16.19  | 76.53 $\pm$ 13.45  | 0.192   |
| Body temperature (Centigrade)   | 37.57 $\pm$ 0.57   | 37.40 $\pm$ 0.17   | 0.123   |
| Heart rate/min                  | 89.17 $\pm$ 18.22  | 84.64 $\pm$ 15.27  | 0.191   |
| Respiratory rate                | 19.43 $\pm$ 4.45   | 18.70 $\pm$ 4.46   | 0.441   |
| GCS                             | 11.10 $\pm$ 2.83   | 12.90 $\pm$ 2.04   | < 0.001 |

SD: Standard deviation; GCS: Glasgow Coma Scale

As shown in table 7, there was no significant difference between the two groups in terms of the systolic and diastolic blood pressure, GCS score, body temperature, heart rate, and respiratory rate ( $P > 0.050$ ). However, significant a difference was observed between the two groups regarding the dose of medication ( $P < 0.010$ ). Furthermore, comparison of patients in the two groups in terms of side effects showed that gastrointestinal complications were observed in 3.3 % of patients in the TOP group.

### Discussion

After hospitalization, patients treated with opioids suffer from opium withdrawal syndrome due to discontinuation of opium.<sup>24</sup> Feeling restlessness in hospitalized patients delays recovery, increases length of hospital stay, and ultimately increases morbidity and mortality. It is desirable to use a suitable alternative drug that can control the symptoms of restlessness with lower doses and least side effects. Several studies have shown the role of morphine and methadone in controlling opium withdrawal syndrome in patients addicted to opium.<sup>25,26</sup> The use of morphine is not desirable because of the need for an infusion pump device and continuous administration, low half-life, and drug accumulation in the body.<sup>25,26</sup>

To treat opium withdrawal syndrome, injectable methadone is mainly used. However, in the present study, oral forms of the two medications (oral methadone and TOP) were used because the injection process was thought to be aggressive.

Considering the RASS score, the findings of the current study showed a significant difference between the two groups after treatment. It seems that both drugs improved patients' restlessness. Although methadone and TOP could improve vital signs in patients, no significant difference was observed between the two groups in this regard. It can be claimed that the effect of the two drugs on the vital signs was almost similar. However, a significant difference was seen between the two groups in terms of medication dose. It was found that the lower dose of methadone, in comparison with TOP was needed to control patients' restlessness and vital signs.

In a study by Aghdaie et al., injectable methadone was used for the treatment of opium addicted patients hospitalized in ICUs. The findings showed that symptoms of opium withdrawal syndrome were controlled in 80.8% of patients.<sup>24</sup> Additionally, Dyer et al. reported that methadone was effective for controlling withdrawal syndrome in heroin addicted patients.<sup>27</sup>

Most studies compared the effect of morphine and methadone on agitation of withdrawal syndrome. For example, Mirinezhad et al. assessed the effect of morphine and methadone on pulmonary function of patients who were hospitalized in ICU and observed that the use of methadone was preferred to morphine since it caused no dependency on medication after being discharged from ICU and it was associated with easy ambulation.<sup>25</sup>

**Table 7.** Comparison of the two groups regarding variables

| Variables                        | Methadone group (Group 1) | Opium group (Group 2) | P       |
|----------------------------------|---------------------------|-----------------------|---------|
|                                  | Mean $\pm$ SD             | Mean $\pm$ SD         |         |
| Medication dose (mg)             | 36.17 $\pm$ 26.99         | 112.67 $\pm$ 102.74   | < 0.001 |
| Systolic blood pressure (mm Hg)  | -6.10 $\pm$ 15.65         | -3.20 $\pm$ 21.13     | 0.548   |
| Diastolic blood pressure (mm Hg) | 0.23 $\pm$ 13.74          | -3.10 $\pm$ 12.70     | 0.333   |
| Body temperature (centigrade)    | -0.13 $\pm$ 0.63          | -0.17 $\pm$ 0.58      | 0.816   |
| Heart rate/ min                  | -5.90 $\pm$ 15.36         | -4.53 $\pm$ 18.54     | 0.757   |
| Respiratory rate                 | -2.77 $\pm$ 6.00          | -0.73 $\pm$ 5.14      | 0.164   |
| GCS                              | 1.07 $\pm$ 2.52           | 1.80 $\pm$ 2.43       | 0.267   |

SD: Standard deviation; GCS: Glasgow Coma Scale



Ripamonti et al. investigated the effect of morphine and oral methadone on the treatment of pain and observed a strong linear positive relationship between morphine and methadone equianalgesic doses. The findings showed that oral methadone was stronger than morphine.<sup>28</sup> On the other hand, Pollock et al. compared methadone and morphine efficacy and reported a lack of consensus for replacing morphine with methadone.<sup>29</sup>

Lainwala et al. compared the effect of methadone and morphine administration on length of hospital stay and reported no significant difference.<sup>30</sup>

Few studies evaluated the role of TOP and methadone in controlling patient's agitation because of withdrawal syndrome. Tabassomi et al. compared the impact of methadone syrup and TOP on the management of opium withdrawal syndrome. Although they observed no significant difference between the two groups regarding opioid withdrawal scale, TOP was considered as a potential alternative to methadone syrup for suppressing opium withdrawal symptoms with minimal adverse effects.<sup>31</sup> The findings of the present study were not consistent with those revealed by Tabassomi et al.<sup>31</sup> Jittiwutikarn et al. reported that TOP was not as good as methadone

for preventing withdrawal syndrome,<sup>19</sup> which was not consistent with the current study.<sup>31</sup> However, it was specified that substitution of opium by methadone syrup and TOP could prevent toxicity of opium due to impurities, including lead.<sup>32</sup>

## Conclusion

According to the results of the current study, lower dose of methadone, compared to TOP, could control agitation caused by opium withdrawal symptoms.

## Conflict of Interests

The authors have no conflict of interest.

## Acknowledgements

The authors would like to appreciate the staff of ICU of Shahid Bahonar Hospital of Kerman for their support and contribution to this study.

## Authors' Contribution

SMS and MA designed current study. MP and RS and FS collected data and played a main role in writing of manuscript.

## References

1. Fallahzadeh MA, Salehi A, Naghshvarian M, Fallahzadeh MH, Poustchi H, Sepanlou SG, et al. Epidemiologic study of opium use in Pars Cohort Study: A study of 9000 adults in a rural southern area of Iran. *Arch Iran Med* 2017; 20(4): 205-10.
2. Heydari M, Hashempour MH, Zargarani A. Medicinal aspects of opium as described in Avicenna's Canon of Medicine. *Acta Med Hist Adriat* 2013; 11(1): 101-12.
3. Pasternak GW, Pan YX. Mu opioids and their receptors: Evolution of a concept. *Pharmacol Rev* 2013; 65(4): 1257-317.
4. United Nations Office on Drugs and Crime. *World Drug Report 2015*. New York, NY: United Nations; 2015.
5. Naghibzadeh TA, Khanjani N, Yazdi F, Varzandeh M, Haghdoost AA. Opium as a risk factor for upper gastrointestinal cancers: A population-based case-control study in Iran. *Arch Iran Med* 2014; 17(1): 2-6.
6. Meysamie A, Sedaghat M, Mahmoodi M, Ghodsi SM, Eftekhari B. Opium use in a rural area of the Islamic Republic of Iran. *East Mediterr Health J* 2009; 15(2): 425-31.
7. Akbari M, Naghibzadeh-Tahami A, Khanjani N, Baneshi MR, Kamali E, Hesampour M, et al. Opium as a risk factor for bladder cancer: A population-based case-control study in Iran. *Arch Iran Med* 2015; 18(9): 567-71.
8. Chaturvedi HK, Mahanta J, Bajpai RC, Pandey A. Correlates of opium use: Retrospective analysis of a survey of tribal communities in Arunachal Pradesh, India. *BMC Public Health* 2013; 13: 325.
9. Arab M, Kohan M, Ranjbar H, Arab N, Rayani M, Mirrashidi SS, et al. Quality of life, social desirability and their relationship in opium addicted persons in southeast of Iran. *Glob J Health Sci* 2014; 6(3): 97-103.
10. World Health Organization. *Clinical guidelines for withdrawal management and treatment of drug dependence in closed settings*. Geneva, Switzerland: WHO; 2009.
11. Esmaeili F, Moshtaghi-Kashanian G. Activity of t-helper lymphocytes in opium dependent and non-dependent individuals. *Kerman Univ Med Sci* 2005; 11(1): 39-49. [In Persian].
12. Solhi H, Salehi B, Alimoradian A, Pazouki S, Taghizadeh M, Saleh AM, et al. Beneficial effects

- of *Rosmarinus officinalis* for treatment of opium withdrawal syndrome during addiction treatment programs: A clinical trial. *Addict Health* 2013; 5(3-4): 90-4.
13. Sadock BJ, Sadock AV. Kaplan and Sadock's synopsis of psychiatry: behavioral sciences/clinical psychiatry. 10<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2007.
  14. Norouzi M, Eskandarion M R, Zargar Y. Death due to acute poisoning with high dose of lead in an opium addict: A case report. *Iran J Forensic Med* 2017; 23(2): 142-6. [In Persian].
  15. Beigmohammadi MT, Mohammadi M, Mahmoudpour A, Karvandian K, Aghdashi M. Quadriplegia due to lead-contaminated opium: A case report. *Tehran Univ Med J* 2008; 66(7): 521-4. [In Persian].
  16. Seligman NS, Rosenthal E, Berghella V. Overview of management of opioid use disorder during pregnancy. UpToDate 2019 [Online]. [Cited 2019]; Available from: URL: <https://www.uptodate.com/contents/overview-of-management-of-opioid-use-disorder-during-pregnancy>
  17. Somogyi AA, Larsen M, Abadi RM, Jittiwutikarn J, Ali R, White JM. Flexible dosing of tincture of opium in the management of opioid withdrawal: Pharmacokinetics and pharmacodynamics. *Br J Clin Pharmacol* 2008; 66(5): 640-7.
  18. Ward J, Hall W, Mattick RP. Role of maintenance treatment in opioid dependence. *Lancet* 1999; 353(9148): 221-6.
  19. Jittiwutikarn J, Ali R, White JM, Bochner F, Somogyi AA, Foster DJ. Comparison of tincture of opium and methadone to control opioid withdrawal in a Thai treatment centre. *Br J Clin Pharmacol* 2004; 58(5): 536-41.
  20. Ashby M, Fleming B, Wood M, Somogyi A. Plasma morphine and glucuronide (M3G and M6G) concentrations in hospice inpatients. *J Pain Symptom Manage* 1997; 14(3): 157-67.
  21. Auriacombe M, Grabot D, Daulouede JP, Vergnolle JP, O'Brien C, Tignol J. A naturalistic follow-up study of French-speaking opiate-maintained heroin-addicted patients: effect on biopsychosocial status. *J Subst Abuse Treat* 1994; 11(6): 565-8.
  22. Hojjat S, Rezaei M, Mohamadipoor M, Norozi Khalili M, Danesh M, Hatami S. The comparison of retention in three methods with methadone, opium and buprenorphine in patients admitted to addiction treatment centers. *J North Khorasan Univ Med Sci* 2016; 8(2): 245-56. [In Persian].
  23. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The Richmond Agitation-Sedation Scale: Validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002; 166(10): 1338-44.
  24. Aghdaie N, Farasatkish R, Mollasadeghie G, Heidarpour E. Methadone: A safe effective drug in opium addict coronary artery bypass graft (CABG) cases. *Razi J Med Sci* 2003; 9(31): 545-50. [In Persian].
  25. Mirinezhad SM, Aidi M, Kolahdouzan K. Comparison between effects of morphine infusion and IM injection of methadone on pulmonary functions after cardiac surgery in Tabriz Shahid Madani Hospital ICU. *J Pharm Sci Tabriz Univ Med Sci* 2005; 10(2): 13-20. [In Persian].
  26. Facts and Comparisons. Drug Facts and Comparisons 2011. Lippincott Williams and Wilkins; 2011. p. 553-7.
  27. Dyer KR, Foster DJ, White JM, Somogyi AA, Menelaou A, Bochner F. Steady-state pharmacokinetics and pharmacodynamics in methadone maintenance patients: Comparison of those who do and do not experience withdrawal and concentration-effect relationships. *Clin Pharmacol Ther* 1999; 65(6): 685-94.
  28. Ripamonti C, Groff L, Brunelli C, Polastri D, Stavrakis A, De Conno F. Switching from morphine to oral methadone in treating cancer pain: What is the equianalgesic dose ratio? *J Clin Oncol* 1998; 16(10): 3216-21.
  29. Pollock AB, Tegeler ML, Morgan V, Baumrucker SJ. Morphine to methadone conversion: An interpretation of published data. *Am J Hosp Palliat Care* 2011; 28(2): 135-40.
  30. Lainwala S, Brown ER, Weinschenk NP, Blackwell MT, Hagadorn JI. A retrospective study of length of hospital stay in infants treated for neonatal abstinence syndrome with methadone versus oral morphine preparations. *Adv Neonatal Care* 2005; 5(5): 265-72.
  31. Tabassomi F, Zarghami M, Shiran MR, Farnia S, Davoodi M. Opium tincture versus methadone syrup in management of acute raw opium withdrawal: A randomized, double-blind, controlled trial. *J Addict Dis* 2016; 35(1): 8-14.
  32. Ahmadinejad M, Ahmadipoor M, Divsalar K. Blood lead level in opiate addicts hospitalized in the intensive care unit of a trauma referral center in Kerman, Iran. *Addict Health* 2019; 11(1): 11-7.

## مقایسه اثربخشی متادون و تنتور تریاک در کنترل بی‌قراری ناشی از سندرم ترک در بیماران معتاد به تریاک در بخش مراقبت‌های ویژه: یک کارآزمایی تصادفی

سید مجتبی سهروردی<sup>۱</sup>، مصطفی پورنمداری<sup>۲</sup>، راضیه سلیمی<sup>۲</sup>، فرهاد صراف‌زاده<sup>۳</sup>، مهدی احمدی‌نژاد<sup>۴</sup>

### مقاله پژوهشی

### چکیده

**مقدمه:** با توجه به این که مطالعات کمی با هدف مقایسه کارایی متادون و تنتور تریاک (Tincture of opium یا TOP) در کنترل بی‌قراری ناشی از سندرم ترک انجام شده است، هدف از انجام پژوهش حاضر، ارزیابی مقایسه تأثیر متادون و TOP در کنترل بی‌قراری ناشی از سندرم ترک در بیماران معتاد به تریاک در بخش مراقبت‌های ویژه (ICU یا Intensive care unit) بود.

**روش‌ها:** این تحقیق از نوع کارآزمایی بالینی بود که بر روی ۶۰ بیمار بستری در بخش ICU بیمارستان شهید باهنر کرمان انجام شد. پس از تقسیم بیماران به دو گروه، در گروه اول شربت متادون (۵ میلی‌گرم در میلی‌لیتر) و در گروه دوم TOP (۱۰ میلی‌گرم در میلی‌لیتر) مورد استفاده قرار گرفت. درجه اضطراب در این بیماران به وسیله مقیاس بی‌قراری- آرامش (Richmond Agitation-Sedation Scale) Richmond یا (RASS) ارزیابی گردید. علایم حیاتی نیز مورد بررسی قرار گرفت. به منظور تجزیه و تحلیل داده‌ها، از آزمون‌های Paired t و Independent t استفاده شد.

**یافته‌ها:** دز تجویز متادون و TOP به ترتیب  $26/99 \pm 36/17$  و  $102/74 \pm 112/67$  میلی‌گرم بود ( $P < 0/010$ ). تجویز متادون منجر به کاهش معنی‌دار علایم حیاتی بیماران از جمله فشار خون سیستولیک، ضربان قلب، ضربان تنفسی و مقیاس اغمای (Glasgow Coma Scale) Glasgow یا (GCS) شد ( $P < 0/050$ ). اگرچه تجویز TOP فشار خون سیستولیک و GCS را به میزان قابل توجهی کاهش داد ( $P < 0/050$ )، اما هیچ تأثیری بر فشار خون دیاستولیک بیماران، درجه حرارت بدن، ضربان قلب و ضربان تنفسی بیماران نداشت ( $P > 0/050$ ). در مجموع، از نظر علایم حیاتی بین دو گروه اختلاف معنی‌داری مشاهده نشد ( $P > 0/050$ )، اما از نظر نمره RASS اختلاف بین گروه متادون و TOP معنی‌دار بود ( $P < 0/010$ ).

**نتیجه‌گیری:** با توجه به نتایج، دز کمتری از متادون در مقایسه با TOP، می‌تواند باعث کنترل بی‌قراری ناشی از علایم ترک تریاک شود.

**واژگان کلیدی:** متادون؛ اعتیاد به تریاک؛ واحد مراقبت‌های ویژه

**ارجاع:** سهروردی سید مجتبی، پورنمداری مصطفی، سلیمی راضیه، صراف‌زاده فرهاد، احمدی‌نژاد مهدی. مقایسه اثربخشی متادون و تنتور تریاک در کنترل بی‌قراری ناشی از سندرم ترک در بیماران معتاد به تریاک در بخش مراقبت‌های ویژه: یک کارآزمایی تصادفی. مجله اعتیاد و سلامت ۱۳۹۹؛ ۱۲ (۲): ۷۶-۶۹

تاریخ پذیرش: ۱۳۹۸/۱۰/۲۸

تاریخ دریافت: ۱۳۹۸/۹/۱

- ۱- پژوهشکده تحقیقاتی Robarts، دانشگاه انتاریو غربی، اونتاریو، کانادا و مرکز تحقیقات علوم دارویی و گروه داروسازی بالینی، دانشکده داروسازی، دانشگاه علوم پزشکی شهید صدوقی، یزد، ایران
  - ۲- مرکز تحقیقات دارویی و گروه شیمی پزشکی، دانشکده داروسازی، دانشگاه علوم پزشکی کرمان، کرمان، ایران
  - ۳- گروه داخلی، دانشکده پزشکی، دانشگاه علوم پزشکی کرمان، کرمان، ایران
  - ۴- گروه بیپوشی، دانشکده پزشکی، دانشگاه علوم پزشکی کرمان، کرمان، ایران
- نویسنده مسؤول:** مهدی احمدی‌نژاد؛ گروه بیپوشی، دانشکده پزشکی، دانشگاه علوم پزشکی کرمان، کرمان، ایران

Email: mehdi50@gmail.com