Comparing the Effects of Methadone, Buprenorphine, and Opium Tincture Maintenance Therapy on Sexual Function

Ali Kheradmand1, Ahad Fazeli2, Azadeh Mazaheri Meybodi1

Abstract

Background: Opioid use disorder is a major concern to public health, and opioid maintenance treatment on methadone or buprenorphine is a widely used approach. On the other hand, in recent years, there has been more regards for the use of opium tincture for detoxification and maintenance treatment of opioid dependence in certain parts of the world. The purpose of our research was to compare sexual impairments of methadone maintenance treatment (MMT), buprenorphine maintenance treatment (BMT), and opium tincture maintenance treatment (OMT) in patients.

Methods: The study sample consisted of opium-addicted men candidates for maintenance treatment in an addiction quitting clinic in Tehran, Iran, from November 2017 to February 2018. Participants (n = 84) were randomly assigned to three groups (of the equal number), receiving either methadone tablet, buprenorphine sublingual tablet, and opium tincture. The average score for sexual function was evaluated using the Arizona Sexual Experiences Scale (ASEX) at the beginning and after 3 months after treatment.

Findings: Although there was no significant different in ASEX scores between the groups at the beginning and end of the study (P > 0.05), but the difference was significant in each group in comparing by themselves.

Conclusion: These results showed that sexual dysfunction became better after opioid substitution therapies, and no differences were observed on sexual dysfunction between the three groups.

Keywords: Methadone; Buprenorphine; Opium tincture; Sexual dysfunctions; Opioid substitution therapies

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Introduction

Opioids are of the most common substance abuse materials for which patients seek treatment. Globally the burden is estimated to be 32.4 million with an overall prevalence of 0.7%. Methadone maintenance treatment (MMT) is identified as a potent substitute therapy for opioid addiction.

Sexual dysfunctions such as erectile dysfunction (ED), ejaculatory disturbances, and lack of desire for sexual relations are often reported in a considerable number of men patients on methadone maintenance. The fundamental process may be the reaction of hypothalamus and pituitary system to heroin and methadone, and also the lower performance of dopaminergic neurons of the mesolimbic area.

Methadone’s long-term stimulation of the μ-opioid receptors changes the function of the tubero-infundibular axis and dopaminergic influences on prolactin, which can affect sexual performance. High presence of circulating prolactin inhibits gonadotropin-releasing hormone (GnRH), which decreases sex hormones including testosterone. Decrease in testosterone measures may cause low sexual desire.

In conjunction with MMT, there were studies that showed that buprenorphine maintenance treatment (BMT) was an alternative effective treatment for opioid addiction. Buprenorphine is a mixed agonist-antagonist opioid, with a low intrinsic activity and a high affinity for the μ-opioid receptor, and no intrinsic activity but a high affinity for the κ-opioid receptor.

Although animal studies showed no significant changes in the basement membrane, seminiferous tubules, Sertoli cells, interstitial tissue, or sperm compared to a group that received methadone but in humans, some studies reported more frequent sexual and ED to methadone, while other ones found no significant differences between the two maintenance treatments.

Recently MMT and opium tincture maintenance treatment (OMT) for detoxification has achieved especial attention in some parts of the world. Opium tincture also called Laudanum is a clear, reddish-brown hydroalcoholic preparation of opium with a characteristic odor and bitter taste. Morphine is the active ingredient of opium tincture with the chemical formula of C_{17}H_{19}NO_{3} and each milliliter of opium tincture contains 10 mg of morphine equivalent.

Opium tincture has gained growing popularity since its introduction in the national protocol of opioid addiction treatment in Iran in 2010, and is now widely used (64000 patients) as the second most common medication after methadone or maintenance treatment of opioid reliance.

Despite the increasing prevalence of opium tincture use as maintenance treatment in Iran, however, there is insufficient information about long-term use of opium tincture as a new option of maintenance treatment in opioid-addicted patients on sexual function.

A qualitative research showed a number of patients on MMT who faced sexual impairment had pulled back from intercourse with their partners leading to dissensions. Outcome of these dissensions were undesirable influences on the rehabilitation, early treatment termination, methadone dose cutting, and using under counter drugs for sexual power. Sexual impairments are not potentially fatal but can reduce the quality of life due to withdrawal from sexual relations.

Given that sexual impairment is a serious problem, the present study aimed to assess the sexual impairment in patients undergoing MMT, BMT, or OMT.

Methods

This randomized, open trial was conducted from November 2017 to February 2018 in an addiction quitting clinic, affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran. This research was accepted by the Research and Ethics group of the School of Medicine at Shahid Beheshti University of Medical Sciences. All patients were enrolled in the study after obtaining written informed consent.

The study sample consisted of opium-addicted men candidates for maintenance treatment. After obtaining written informed consents, the subjects (n = 84) were randomly assigned to three groups (of the equal number), receiving either methadone, buprenorphine tablet, or opium tincture for 12 weeks. Regular follow-up was conducted every two weeks by a psychiatrist asking patients about the status of their sexual problems.

Patients permitted were those who had the following criteria: 1. receiving maintenance...
treatment for the first time; 2. having no comorbidity that could affect sexual performance; 3. no alcohol consumption; 4. recent cessation of benzodiazepines; and 5. not using drugs or stimulants.

The criteria for exclusion were as follows: 1. leaving the MMT program; 2. the psychiatrist’s conclusion for ending the bupropion or opium tincture treatment for any rational; and 3. seizures.

The average score of sexual performance was evaluated using the Arizona Sexual Experiences Scale (ASEX) score. Methadone, bupropion, or opium tincture was administered by a nurse who was not involved in the rating of patients. The sample size was calculated as 28 subjects per group to detect 20% difference in ASEX score between groups.

The ASEX is a brief 5-item questionnaire designed to measure sexual functioning in the domains of sexual drive, arousal, penile erection/vaginal lubrication, satisfaction, and ability of orgasm. A 6-point scale from 1 (hyperfunction) to 6 (hypo-function) was used, total score was between 5 and 30. Higher score was in favor of higher sexual dysfunction. The subjects were assessed for the past three months. The ASEX had a Cronbach’s alpha of 90%, a good reliability, and a correlation coefficient of 0.80.21

Before and after intervention, data were collected from all participants, using ASEX. Organization, supervision, data collection, data evaluation, and conclusion were performed by a psychiatric resident. For data analysis, $t$, chi-square, and ANCOVA tests were performed, using SPSS software (version 18, SPSS Inc., Chicago, IL, USA). P-value of less than 0.05 was statistically significant.

### Results

Eighty-four men candidates for maintenance treatment participated in this study (each group had 28 patients). There was no remarkable difference between mean age of participants in MMT (37.05 ± 10.40 years), BMT (38.78 ± 9.40) and OMT (42.21 ± 9.60 years) group ($p > 0.05$).

Table 1 shows demographic features of patients including employment status, level of education, and marital status in three groups at baseline. There was no significant differences between the groups.

#### Table 1. Demographic and treatment characteristics of participants at the baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>MMT</th>
<th>BMT</th>
<th>OMT</th>
<th>P’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>10</td>
<td>15</td>
<td>9</td>
<td></td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Unemployed</td>
<td>18</td>
<td>13</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>&lt; 12</td>
<td>13</td>
<td>15</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-16</td>
<td>11</td>
<td>13</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 16</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Single</td>
<td>10</td>
<td>11</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>18</td>
<td>17</td>
<td>15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment; OMT: Opium tincture maintenance treatment

*Based on the chi-square test.

The results represented in table 2 show the mean scores of sexual dysfunction in the MMT, BMT, and OMT groups at the start. No remarkable difference was seen in baseline sexual function mean scores, based on ASEX questionnaire, between three groups at the start of the study.

#### Table 2. Comparison of the mean Arizona sexual experiences scale (ASEX) domain scores in study groups at the baseline

<table>
<thead>
<tr>
<th>Domain</th>
<th>Group</th>
<th>MMT</th>
<th>BMT</th>
<th>OMT</th>
<th>P’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desire/drive</td>
<td></td>
<td>2.3 ± 1.1</td>
<td>2.5 ± 1.0</td>
<td>2.1 ± 1.0</td>
<td>0.42</td>
</tr>
<tr>
<td>Arousal</td>
<td></td>
<td>2.5 ± 1.3</td>
<td>2.5 ± 1.3</td>
<td>2.4 ± 1.1</td>
<td>0.61</td>
</tr>
<tr>
<td>Erection</td>
<td></td>
<td>2.4 ± 1.3</td>
<td>2.6 ± 1.3</td>
<td>2.2 ± 1.2</td>
<td>0.47</td>
</tr>
<tr>
<td>Ability to reach orgasm</td>
<td></td>
<td>2.9 ± 1.7</td>
<td>2.7 ± 1.4</td>
<td>2.1 ± 1.0</td>
<td>0.22</td>
</tr>
<tr>
<td>Satisfaction with orgasm</td>
<td></td>
<td>2.8 ± 1.3</td>
<td>2.7 ± 1.3</td>
<td>2.2 ± 1.1</td>
<td>0.12</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>13.1 ± 5.6</td>
<td>13.2 ± 5.3</td>
<td>11.0 ± 1.4</td>
<td>0.27</td>
</tr>
</tbody>
</table>

The amounts are presented as mean ± standard deviation (SD). ASEX: Arizona sexual experiences scale; MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment; OMT: Opium tincture maintenance treatment

*Based on the one-way ANOVA test.
Table 3. Comparison of the mean Arizona sexual experiences scale (ASEX) domain scores in study groups after 3 months of therapy

<table>
<thead>
<tr>
<th>Domain</th>
<th>Group</th>
<th>MMT</th>
<th>BMT</th>
<th>OMT</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desire/drive</td>
<td>3.3 ± 1.1</td>
<td>3.6 ± 0.7</td>
<td>3.4 ± 1.1</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Arousal</td>
<td>4.3 ± 1.1</td>
<td>4.2 ± 1.1</td>
<td>4.1 ± 1.0</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Erection</td>
<td>3.3 ± 1.3</td>
<td>3.5 ± 1.2</td>
<td>3.6 ± 0.8</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>Ability to reach orgasm</td>
<td>4.0 ± 1.1</td>
<td>4.2 ± 1.1</td>
<td>4.1 ± 0.9</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td>Satisfaction with orgasm</td>
<td>3.9 ± 1.5</td>
<td>3.3 ± 0.9</td>
<td>3.3 ± 1.2</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>19.0 ± 5.1</td>
<td>18.6 ± 4.1</td>
<td>18.8 ± 4.0</td>
<td>0.92</td>
<td></td>
</tr>
</tbody>
</table>

The amounts are presented as mean ± standard deviation (SD).
ASEX: Arizona sexual experiences scale; MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment; OMT: Opium tincture maintenance treatment
*Based on the one-way ANOVA test.

The follow-up of sexual function assessment in patients on MMT, BMT, and OMT at week 12 of the study did not show any significant difference between groups (Table 3).

Although there was no significant different in ASEX scores at the beginning and end of the study between groups, but this difference was significant in each group in comparing by themselves (Table 4).

Table 4. Comparison of the mean Arizona sexual experiences scale (ASEX) total scores in the study groups after 3 months of therapy

<table>
<thead>
<tr>
<th>Group</th>
<th>ASEX score Before</th>
<th>ASEX score After</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMT</td>
<td>13.1 ± 5.6</td>
<td>19.0 ± 5.1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>BMT</td>
<td>13.2 ± 5.3</td>
<td>18.6 ± 4.1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>OMT</td>
<td>11.0 ± 1.4</td>
<td>18.8 ± 4.0</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

The amounts are presented as mean ± standard deviation (SD).
ASEX: Arizona sexual experiences scale; MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment; OMT: Opium tincture maintenance treatment
*Based on the paired-samples t test.

An analysis of marital status showed that there were no important differences in ASEX scores between married (Table 5) and single (Table 6) patients in all groups (P > 0.05).

Table 5. Comparison of the mean Arizona sexual experiences scale (ASEX) scores of married patients in study groups after 3 months of therapy

<table>
<thead>
<tr>
<th>Domain</th>
<th>Group</th>
<th>MMT</th>
<th>BMT</th>
<th>OMT</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desire/drive</td>
<td>3.3 ± 1.1</td>
<td>3.4 ± 0.7</td>
<td>3.5 ± 1.1</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>Arousal</td>
<td>4.0 ± 1.1</td>
<td>4.0 ± 1.1</td>
<td>4.2 ± 1.0</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Erection</td>
<td>3.3 ± 1.3</td>
<td>3.3 ± 1.2</td>
<td>3.5 ± 0.8</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>Ability to reach orgasm</td>
<td>3.7 ± 1.1</td>
<td>3.9 ± 1.1</td>
<td>4.3 ± 0.9</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Satisfaction with orgasm</td>
<td>3.2 ± 1.5</td>
<td>3.3 ± 0.9</td>
<td>3.3 ± 1.2</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17.9 ± 5.1</td>
<td>18.2 ± 4.1</td>
<td>18.3 ± 4.0</td>
<td>0.92</td>
<td></td>
</tr>
</tbody>
</table>

The amounts are presented as mean ± standard deviation (SD).
ASEX: Arizona sexual experiences scale; MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment; OMT: Opium tincture maintenance treatment
*Based on the one-way ANOVA test.

Discussion

Our purpose was to evaluate the outcomes of methadone, bupropion, and opium tincture on sexual activity in maintenance treatment. Our results revealed that there was a remarkable increase in sexual impairments after 3-month therapy with no notable difference between groups in final total and subtest scores.

In our study, the total score of ASEX in BMT group was higher than other groups but it was not statically significant. Our findings were consistent with other research suggesting that MMT and BMT are related with sexual impairment with no remarkable differences.22 Tafreshian et al. showed that methadone treatment caused more frequent sexual impairment than buprenorphine treatment.23
In a meta-analysis by Yee et al., sexual dysfunction was significantly higher in MMT group in comparison with BMT group. Our justification for the differences is the differences in characteristics of study population. Moreover, the difference in results may be due to socio-economic differences across the communities.

Some research shows the interference of methadone with the production of hormones of hypothalamus and pituitary regulatory which enhances serum prolactin, and reduces gonadotropin releasing hormone leading to reduced testosterone production. Reduction in testosterone levels cause tiredness, weakness, disturbances of the mood, reduction of libido, and sexual performance. The effect of methadone and anti-androgen drugs on sexual performance are similar. On the other side, buprenorphine, a partial opioid agonist of the μ receptor and an antagonist for the κ opioid receptor, causes the release of dopamine and does not inhibit the sex hormones to the same degree that the methadone does.

As our knowledge, our study is the first that investigated sexual adverse effects of opium tincture in patients undergoing maintenance treatment. Our results showed that sexual dysfunction in OMT group increased significantly during 3 months of study and the final total score of ASEX was higher than BMT group and lower than MMT group.

Morphine is the main substance of opium tincture that may be the important reason for sexual dysfunction in OMT group. Animal studies show that the misuse of morphine remarkably lessens testosterone levels. Long-term use of morphine affects luteinizing hormone (LH), testosterone, and body weight in rats, with no notable changes in follicle-stimulating hormone (FSH) and testicular weight. Cicero et al. stated a decrease in testicular and seminal vesicle weight. Morphine effects on the measures of hypothalamic monoamines has been shown in rats. Gabriel et al. showed the suppression of GnRH by morphine and testosterone.

Ahmadnia et al. showed the reduction of sex hormonal features and spermatogenesis, LH levels, and mature sperms of the target group. In human studies also evidence showed that long-term use of morphine is associated with sexual dysfunction. Ajo et al. showed that sexual dysfunction is higher in men who received a significantly higher mean of opioid.

In subtest analysis, there was no remarkable difference in sexual dysfunction between three groups. Not only biological issues determine sexual desire but interpersonal (existence of partner) and social issues influence psychological part of the sexual desire. Orgasm means a quick release of sexual excitement during a sexual cycle starting with the rhythmic contractions of the pelvic muscles which is known as sexual pleasure. To determine orgasm, medical doctors point out physiological changes but psychologists and psychiatrists point out spiritual and cognitive changes. In the current study, we excluded all patients who had a history of psychiatric illness, and treated with medication during the study to exclude psychological effects on sexual function. Marital status has a remarkable role in the sexual functioning of patients during maintenance treatment. Some patients continued single without a sexual partner because of orgasmic complications in the study of Chekuri et al. Yee et al. found that men with no sexual partner on MMT had greater orgasmic complications than men.
with no sexual partner on BMT. In a study by Ramdurg et al. sexual partner had a significant effect on orgasm problems in men underwent BMT.

Low serum testosterone, due to opioid effects on the hypothalamic-pituitary-gonadal axis, may explain libidinal depression. However, as psychological factors are common causes of depression of sex drive, and because psychiatric comorbidity is so prevalent in the substance-dependent population, mental and emotional health should be investigated in addition to hormonal assays. Conditions of potential importance include mood disorders, psychosis, situational stressors, gender identity issues, and age-related psychological issues. Medications other than opioid substitution treatment should also be reviewed, as these are also common causes of a depressed sex drive. Common offenders include anti-hypertensive and psychotropic agents.

Other etiologies should be ruled out; given the associations in the literature for the dose of methadone and serum testosterone, reasonable therapeutic approaches may include replacement (parenteral or transdermal) of irregular low testosterone or a reduction in daily methadone dose. In an open-label study, methadone-maintained men with depressed testosterone levels responded to transdermal testosterone in terms of serum testosterone levels, sexual function, and measures of well-being. Bromocriptine may be a therapeutic alternative, as well. Bromocriptine may act via reestablishment of central nervous system (CNS) levels of dopamine and normalization of dopaminergic regulation of prolactin production.

ED usually has an organic or iatrogenic origin. Non communicative diseases such as diabetes mellitus, chronic liver disease, renal failure, chronic pulmonary disease, cardiovascular disease, or malignancy can cause ED. Surgery, trauma, and congenital and anatomic anomalies in genitourinary can also lead to ED. Medications commonly associated with ED include antihypertensive, psychotropic agents, and anticholinergic drugs. Smoking has a strong correlation with ED. Every 10 pack-year of smoking enhances the relative danger for ED by 1.31,12,23 Mental and spiritual health problems may have a remarkable role. Symptoms of depression have strongly been correlated with ED; as 90% of men with severe depression showed ED in one research. Anxiety disorders has also been reported to have a correlation with ED.

In our study, there was no significant difference in subtest scores between groups. This finding can have two reasons. First, no remarkable difference was found between the number of single and married individuals in the investigated groups. Second, patients in the group of single patients may not have the reality of having a sexual partner due to social and religious issues.

Two main restrictions of our study was first, response bias related to sex privacy among patients, and the difficult feeling to talk about them with the researcher.

Second, LH and FSH were not studied in this research due to financial limitations. Previous studies show patients on MMT and OMT have reduced testosterone measures in comparison with patients on BMT; this is why sexual dysfunction is more in patients on MMT.

In brief, for rehabilitation of sexual performance is important to enhance the quality of life. Although a few studies exist assessing safety and efficacy of OMT in treating opioid use disorder with promising results, especially for detoxification, results of this study showed that use of opium tincture is associated with acceptable sexual dysfunction in compare with buprenorphine and methadone in opioid-dependent patients. Thus, future clinical trials are required to provide adequate evidence about the risks and success of OMT in opioid reliance treatment, particularly in long-term maintenance therapy.

### Conclusion

These results showed that sexual dysfunction became better after opioid substitution therapies, and no differences had been observed on sexual dysfunction between three groups.

### Conflict of Interests

The Authors have no conflict of interest.

### Acknowledgements

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References


25. Galea S, Vlahov D. Social determinants and the


مقایسه تأثیرات درمان‌های نگهدارنده با متادون، بوپرنورفین و تنتور اپیوم بر عملکرد جنسی

علی خردمند، احد فاضلی، آزاده مظاهری میبدی

چکیده

مقدمه: درمان‌های نگهدارنده با متادون و بوپرنورفین، از جمله روش‌های رایج در درمان نگهدارنده مصرف مواد مخدر می‌باشند. هدف از انجام پژوهش حاضر، بررسی تأثیرات درمان نگهدارنده با متادون، بوپرنورفین و تنتور اپیوم بر عملکرد جنسی و مقایسه تأثیرات این سه درمان با هم در عملکرد جنسی بود.

روش‌ها: 84 بیمار مرد که به صورت تصادفی از مرکز درمان مواد مخدر شهر تهران در سال 1396 انتخاب شده بودند. به سه گروه (هر گروه 28 نفر) تقسیم شدند. جهت یک گروه درمان نگهدارنده با متادون، گروه دیگر بوپرنورفین و گروه سوم تنتور اپیوم شروع گردید. برای این بیماران، پرسشنامه تجربیات جنسی (Arizona Sexual Experiences Scale) در ابتدای درمان و سه ماه بعد برای تمام بیماران تکمیل شد. نمرات به دست آمده در هر گروه قبل و بعد از درمان مشاهده شد.

یافته‌ها: تفاوت معنی‌داری بین سه گروه در نمرات مقیاس ASEX وجود نداشت، اما تفاوت معنی‌داری دوباره در نمرات سه ماه بعد از درمان با ابتدای درمان مشاهده شد.

نتیجه‌گیری: درمان نگهدارنده در بیماران مصرف‌کننده مواد مخدر، همگی عملکرد جنسی را بهبود می‌بخشد ولی نوع روش درمانی تأثیری در عملکرد جنسی بیماران ندارد.

واژگان کلیدی: مصرف مواد مخدر، بوپرنورفین، تنتور اپیوم، اختلال عملکرد جنسی

ارجاع: خردمند علی، فاضلی احد، مظاهری میبدی آزاده. مقایسه تأثیرات درمان‌های نگهدارنده با متادون، بوپرنورفین و تنتور اپیوم بر عملکرد جنسی. مجله اعتیاد و سلامت 1398؛ 11 (2)؛ 128–132.

تاریخ دریافت: 1397/9/9

ارجاع 1: وادی توسوم و تحصیلات اولیی به شناخت تاریخ و گروه سیاست‌گذاری‌های، دوره انجمن علوم پزشکی شهر تهران، ایران.

ارجاع 2: گروه روانپزشکی دانشگاه، علوم پزشکی شهر تهران، ایران.

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