

Trazodone in Methadone Induced Erectile Dysfunction

Faezeh Tatari, MD¹
Vahid Farnia, MD¹
Reza Faghieh Nasiri, MD¹
Farid Najafi, MD²

1. Behavioral Sciences Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

2. Department of Statistics and Epidemiology, Kermanshah University of Medical Sciences, Kermanshah, Iran

Corresponding author:

Vahid Farnia, MD
Behavioral Sciences Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran
Tel: +98-831-826700
Fax: +98- 831-8264163
E-mail: vahidfarnia@yahoo.com

Objective: Based on findings of previous studies, those men on Methadone Maintenance Therapy (MMT) have a high prevalence of Erectile Dysfunction(ED), related to hypogonadism and depression. We conducted this study to evaluate the efficacy of Trazodone (an antidepressant which can improve sexual function) on this sexual dysfunction.

Method: A structured interview was administered by the clinical staff. The interview contained questions about the subjects' socio-demographic characteristics, their drug use and sexual behavior.

In addition to the socio-demographic survey, erectile function was assessed using erectile dysfunction (ED) intensity scale. Of the 157 subjects, 95 suffered from ED. The subjects were informed about the study. Then, seventy five patients voluntarily received 50mg of Trazodone for four days, and the dosage was increased to 100 mg and maintained for 6 weeks. Fifty five patients who completed the treatment course were assessed by ED questionnaire again at the end of study. Statistical analysis was performed using Stata 8 software.

Results: The prevalence of ED was 60.5% in our sample. The mean erectile dysfunction (ED) intensity scale was 12.21, and 16.78 before and after the treatment course respectively. ($P < 0.05$)

ED severity had no significant relation with age and type of substance dependency ($P > 0.05$); but it had a significant relation with duration of Methadone therapy and Methadone daily dosage. ($p < 0.05$)

Conclusion: Trazodone may be effective in the treatment of methadone induced ED. Further studies with control groups and greater sample sizes are warranted.

Keywords: *Erectile dysfunction, Methadone, Trazodone,*

Iran J Psychiatry 2010; 5:164-166

Erectile dysfunction (ED) is defined as 'the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance (1). While ED is not life threatening, it may result in withdrawal from sexual intimacy and reduced quality of life (2, 3). Estimates of the prevalence of ED in methadone-maintained patients vary widely: 16% (8 cases/50 subjects) (4), 23% (21/92) (5), 30% (8/27) (6), 33% (6/18) (7).

Many patients with ED fail to mention ED to clinicians and counselors (4) and many clinicians and counselors feel uncomfortable and embarrassed about dealing with sexual problems (8). Nevertheless, the assessment of ED in these patients may be quite important.

Identification and management of ED problems can improve adherence to treatment, the effectiveness of which, as is well-known, is associated with high doses and long treatment duration (9).

There are various treatment options for ED, although

Men strongly prefer oral therapies (10). Trazodone hydrochloride is an oral antidepressant agent that also has anxiolytic and sedative/hypnotic effects. Because of reports of increased libido and sexual function associated with its use, Trazodone is also sometimes used to treat ED (11). Among oral treatments for ED, the selection of a specific agent may involve considering associated adverse effects and possible contraindications because of the patient's comorbidity or drug interactions. For these reasons among others, it is important for patients with ED to have a variety of available treatment options that are both effective and safe. Six trials (comprising 396 men) met the inclusion criteria. The trials consisted of heterogeneous populations, were small, brief and in some cases methodologically weak. Three of the six trials showed an apparently clinically meaningful benefit of Trazodone for ED compared with placebo, the differences being statistically significant in two (12).

The effect of Trazodone on erectile function may be related to its antagonism of α 2-adrenergic receptors (13). We conducted this study to evaluate the efficacy of this drug on methadone induced ED.

Materials and Method

One hundred fifty seven Patients were recruited from 3 methadone clinics of Kermanshah University of Medical Sciences. Three centers recruited patients every day, from September first 2009 to May 30th 2010. The inclusion criteria for this study were: being male; 18 years of age or older; having a history of opium dependence; and having been on methadone treatment for at least 30 days. Patients who had obvious organic illnesses (such as diabetics or patients with heart and vascular disease) and those with primary ED were excluded. Written and signed informed consent was obtained from the participants. Participation in the study was voluntary and confidential. No remuneration was provided for participation. The study was approved by the Local Ethics Committee.

A structured interview was administered by a psychiatrist for diagnosis of ED. The interview included questions on socio-demographics, drug use and sexual behavior. In addition to the socio-demographic survey, Erectile function was assessed using erectile dysfunction (ED) intensity scale [Total score: 5 to 10 (severe ED); 11 to 15 (moderate ED); 16 to 20 (mild ED); and 21 to 25 (no ED)] which was used by Tabibi A. et al in Iran previously (14). The higher the score the lower the ED. After the interview, the patients completed the erectile dysfunction (ED) intensity scale. 157 subjects met the inclusion criteria; and of them, 95 suffered from ED. After being informed about the study, 75 patients voluntarily underwent treatment with 50mg of Trazodone for four days, and the dosage was increased to 100 mg and maintained for 6 weeks. Fifty five patients who completed the treatment course were assessed by the erectile dysfunction (ED) intensity scale and by clinical interview again at the end of study.

Statistical analysis was done, using Stata 8 software. Associations between categorical risk factors and ED scores and changes in the mean erectile dysfunction (ED) intensity scale were tested by χ^2 -square.

Results

The study included 157 males; of whom, 95 suffered from ED (60.5%). The subjects were 18–51 years old (mean = 39.5). No significant relation was found between age and ED. ($P > 0.05$)

History of substance dependency indicated 40.6% dependency to opium, 37.5% to heroin, and others showed poly substance dependency. No significant association was observed between type of substance dependency and ED. ($P > 0.05$)

There was a significant association between duration of Methadone therapy and Methadone daily dosage. ($p < 0.05$)

Of the 75 patients undergoing treatment with Trazodone, 15 dropped out, and 5 discontinued treatment due to drug adverse effects (sedation).

The mean erectile dysfunction (ED) intensity scale increased from 12.21 to 16.78 in patients after the treatment course. ($P < 0.05$) No side effects were observed in our sample by using the 50-100mg dosage of Trazodone.

Discussion

In the present study, 60.5% of the patients reported ED; and the rate of reporting ED is moderately higher than the rate reported ED in previous studies (4, 6, 7).

Nevertheless, all the surveys indicate high rates of ED among methadone patients. The age of the subjects in this study ranged from 18 to 51, with a mean age of 39.5. In our study, the analysis showed no significant association between age and ED.

We found significant association between methadone daily dosage and severity of ED. Those patients who received higher methadone dosage showed a more severe ED, and this may be due to adverse effects of methadone.

The association between duration of MMT and ED severity was also significant. Those patients who were on MMT for a longer time, showed a more severe ED than others.

In this study, we found that Trazodone was effective in the treatment of ED in patients who are under Methadone maintenance therapy. Trazodone increased the mean erectile dysfunction (ED) intensity scale, and may improve this sexual dysfunction when induced by Methadone. Previous studies also showed the efficacy of Trazodone on ED in different samples but not in (11, 15). A systematic review showed that three of the six trials on Trazodone for treating ED, showed an apparently clinically meaningful benefit compared with placebo, the differences being statistically significant in two. Trazodone monotherapy appeared more likely than placebo to lead to a 'positive treatment response', although this difference was not statistically significant (37% vs. 20%; relative benefit increase, 1.6; 95% confidence interval, CI, 0.8-3.3). Subgroup analyses suggested that men with psychogenic ED might be more likely to benefit from Trazodone than those with mixed or physiological ED. The efficacy of Trazodone also appeared greater at higher doses (150-200 vs 50 mg/day) (12).

Erectile dysfunction is likely to be an important problem for many males who are under methadone treatment; and a good substance dependency treatment is also needed to address this issue. Trazodone may be effective in treating methadone induced erectile dysfunction.

It is important to note that in this study, limited data was available on ED among the subjects prior to their entry into methadone treatment, and Trazodone dosage was limited up to 100 mg. Therefore, further studies with control group, higher Trazodone dosage and greater sample sizes are warranted.

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