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Plasma Testosterone and Sexual Function in Southeast Asian Men Receiving Methadone and Buprenorphine Maintenance Treatment

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ABSTRACT

Background: Methadone has been recognized as an effective maintenance treatment for opioid dependence. However, its use is associated with several complications, including sexual dysfunction in men.

Aim: To assess plasma testosterone and sexual function in Southeast Asian men on methadone maintenance treatment (MMT) or buprenorphine maintenance treatment (BMT).

Methods: 76 sexually active men on MMT (mean age = 43.30 ± 10.32 years) and 31 men on BMT (mean age = 41.87 ± 9.76 years) from a Southeast Asian community were evaluated using plasma total testosterone (TT) and prolactin levels, body mass index, social demographics, substance use measures, and depression severity scale.

Outcomes: Prevalence and associated factors of TT level lower than the reference range in men on MMT or BMT.

Results: More than 1 third of men (40.8%, n = 31) on MMT had TT levels lower than the reference range, whereas 1 fourth of men (22.6%, n = 7) on BMT did. At univariate analysis, MMT vs BMT ($\beta = 0.298$, adjusted $R^2 = 0.08$, $P = .02$) and body mass index ($\beta = -0.23$, adjusted $R^2 = 0.12$, $P = .02$) were associated with changes in TT after stepwise regression. There were no significant associations with age; Opiate Treatment Index Q scores for alcohol, heroin, stimulant, tobacco, or cannabis use and social functioning domain; education levels; hepatitis C status; and severity of depression. Prolactin level did not differ between the MMT and BMT groups.

Clinical Implications: The sex hormonal assay should be used regularly to check men on MMT.

Strengths and Limitations: This is the first study conducted in the Southeast Asian community. Our study was limited by the lack of a healthy group as the reference for serum levels of testosterone and prolactin.

Conclusions: The findings showed that plasma testosterone levels are lower in MMT than in BMT users. Hence, men who are receiving MMT should be screened for hypogonadism routinely in the clinical setting. **Yee A, Loh HS, Danaee M, et al. Plasma Testosterone and Sexual Function in Southeast Asian Men Receiving Methadone and Buprenorphine Maintenance Treatment. J Sex Med 2017;XX:XXX–XXX.**

Key Words: Sexual Dysfunction; Methadone; Testosterone; Buprenorphine; Sexual Desire; Methadone Maintenance Treatment

INTRODUCTION

The worldwide use of opioids is a major concern for many societies. A report by the United Nations Office on Drugs and Crime in 2014 estimated that 33 million people worldwide used opioids and 12.7 million injected drugs.[1] Opioid dependence causes a significant burden to the global community, with the 2010 Global Burden of Disease Study reporting that opioid dependence accounted for 9.2 million disability-adjusted life years. Hence, the use of medically assisted treatment, such as methadone and buprenorphine maintenance treatment (MMT and BMT), to deal with these opioid-related problems is a welcome solution to many societies. However, a new menace has

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arisen in relation to the use of these medications. One common issue faced by opioid users is sexual dysfunction.

Despite the effectiveness of MMT, previous studies have shown higher rates of sexual dysfunction in patients on MMT compared with the normal population or healthy controls.[2,3] Sexual dysfunction related to methadone use in men has been attributed to a decrease in the production of gonadotropin-releasing hormone and to a direct or indirect decrease of testicular testosterone secretion.[4] However, there are apparent contradictions in the literature relating to hormonal changes, namely prolactin and testosterone, in MMT and BMT. Previous studies have found that patients on have higher prolactin levels compared with healthy subjects, thus resulting in the decreased production of testosterone and clinical sexual dysfunction in men.[5,6] However, some recent studies have found that prolactin levels do not differ among MMT, BMT, and age-matched control groups.[7] In contrast, Bliesener et al[8] indicated that BMT was not associated with sexual dysfunction and that patients who received BMT had significantly higher mean total testosterone (TT) and free testosterone levels compared with those patients using MMT. Hallinan et al[9] also found that sexually active men who were on MMT had lower TT levels than those on BMT. In a recent quantitative meta-analysis, low testosterone was found to be significantly associated with sexual dysfunction in the MMT group compared with the BMT group.[10] However, the literature on plasma testosterone and sexual dysfunction in association with buprenorphine was limited.

The purpose of the present study was to compare serum TT levels and sexual dysfunction in men receiving MMT vs BMT. Regardless of the severity of the effects that MMT and BMT have on sexually active men, the available evidence on the relation between the use of these drugs and plasma testosterone remains scant. In addition, most studies have focused only on Western populations for various reasons. Fewer studies on the effects of MMT and BMT on the sexuality of Southeast Asian men have been done. Therefore, the present study sought to bridge that information gap by studying the effects of these 2 treatments on sexually active Southeast Asian men in a comparative way.

METHODS

Sample Size

The primary purpose of the present study was to test whether testosterone levels in men using MMT were higher than those in men using BMT. According to a previous study,[7] a sample of 76 men on MMT and 31 men on BMT would have 80% power to detect a low testosterone level between groups at the 5% significance level.[11]

Study Population

The study included 76 men who were on MMT and 31 men who were on BMT in 2 institutions, the University of Malaya Medical Centre and the University of Malaya Centre of Addiction Sciences (Kuala Lumpur, Malaysia). The data used for the study were acquired from September 2015 through September 2016. The present study fulfilled the Declaration of Helsinki and was approved by the medical ethics committee of the University of Malaya Medical Centre. Inclusion criteria were (i) age older than 18 years; (ii) married and engaging in sexual activities such as intercourse, caressing one's partner without having intercourse, foreplay, or masturbation within the past 1 month; and (iii) the ability to understand and communicate in English or Bahasa Malaysia. Exclusion criteria were (i) current treatment with antiviral medication for viral hepatitis or HIV; (ii) current use of androgen replacement therapy, phosphodiesterase type 5 inhibitors, or any traditional sexual enhancement remedies; (iii) use of psychotropic medications other than methadone or buprenorphine; (iv) an unstable medical condition such as decompensating liver disease; and (v) participation in MMT or BMT for less than 8 weeks.

After meeting the inclusion criteria, the participants were asked to complete a semistructured questionnaire, which included questions on sociodemographic and clinical factors such as age, ethnicity, and marital status. Other factors such as education level, employment status, HIV, hepatitis B, hepatitis, and other comorbid medical illness were included in the study.

The Malay version of the 15-item International Index of Erectile Function (Mal-IIEF-15) was used to assess sexual dysfunction during the past 4 weeks before the interview. The Mal-IIEF-15 is a valid and reliable measure of male sexual function with good internal consistency.[12,13] Each of the 15 items in the IIEF is rated from 0 (or 1) to 15, and scores are calculated according to each domain. Furthermore, these domains and the corresponding IIEF items explore erectile function (questions 1−5 and 15), orgasmic function (questions 9 and 10), sexual desire (questions 11 and 12), intercourse satisfaction (questions 6−8), and overall satisfaction (questions 13 and 14).[14]

The Malay version of the self-rated Montgomery-Asberg Depression Rating Scale (MADRS-BM) consists of 9 items and it is a validated instrument to assess the severity of depression. Possible scores range from 0 to 27, with higher scores indicating greater symptom severity.[15]

The Opiate Treatment Index (OTI) is a tool used to evaluate opiate treatment in an MMT or a BMT program. The OTI assesses key factors including drug use, risk-taking behavior, social performance, criminality, health status, and psychological tuning of the MMT or BMT user. In the drug-use domain, a Q score is computed by adding the quantity of the 2 most recent drug uses and dividing it by the intervals between the reported occasions during the past 4 weeks.[16]

Participants were tested for TT and prolactin levels. Blood samples from participants were obtained in the morning from 9:00 to 11:00 AM. All blood samples were sent to a single laboratory for measurement. A competitive immunoassay with a direct chemiluminescent technique (ADVIA Centaur; Siemens Healthcare,