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Using Terazosin to Treat Methadone Associated Excessive Sweating: A Case Series Study

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Abstract

Excessive sweating is a common methadone associated adverse effect without an evidence-based treatment. In the current case series, terazosin was administered to three patients to treat excessive sweating. Patients were given three different dosages of methadone (170 mg, 95 mg and 55 mg); results showed that changing the methadone dosage had no effect on treating sweating, before prescribing terazosin. Sweating was effectively treated by terazosin while there was no remarkable adverse effect. Well-controlled clinical trial is recommended to examine the efficacy and safety of terazosin to treat methadone associated excessive sweating.

Keywords: Sweating, Methadone, Treatment, Terazosin

1. Introduction

Methadone is a long-acting synthetic opioid originally introduced to manage pain. However, it is now frequently administered to manage opioid withdrawal symptoms (1). The methadone maintenance treatment program (MMTP) provides oral methadone doses to opioid-dependent patients. This intervention potentially decreases opioid cravings (2). Moreover, methadone may reduce some opium-related behaviors such as injecting drug, risks of HIV, hepatitis, criminal and illegal behaviors. It is supposed that methadone therapy improves quality of life of these patients (3-7).

Meanwhile, sweating is one of the adverse effects of methadone. The adverse effects of methadone may negatively impact methadone maintenance therapy adherence; sometimes there are some serious consequences such as death (8-16). Some side effects of methadone including sweating, constipation, nausea, sexual dysfunction (8, 17), sleeping disorders and menstrual cycle irregularities (17, 18) are reported. The most dangerous and life threatening side effect of methadone is torsade de pointes (TdP) (9-13). Sometimes severe forms of these symptoms can interrupt patients' daily lives and even lead to poor adherence in methadone maintenance therapy.

The rate of sweating as an adverse effect in patients with methadone maintenance therapy is up to 45% (18, 19). A study reported the rate of sweating up to 70% (20). In fact, sweating and sedation are the most common adverse effects in opioid dependent patients receiving opioid maintenance therapy (21). Little is known about the exact mechanisms by which methadone influences autonomic thermoregulatory control.

There is no strong evidence based treatment to manage sweating in patients undergoing methadone therapy. Desloratidine 5 mg per day was effective for two patients on methadone maintenance regimens complaining of excessive sweating (22). In another case report, biperiden (2 - 4 mg/day) decreased methadone related sweating in addicts (23). Some physicians recommend clonidine or Botox injection to treat methadone induced diaphoresis, although there is no strong evidence for them. It is important to consider clonidine abuse in patients under methadone replacement therapy; injection of Botox is an invasive method.

Terazosin selectively blocks postsynaptic alpha 1-adrenergic receptors. It is administered to treat hypertension and benign prostatic hypertrophy. The half-life of terazosin is 12 hours (24). For the first time, it is reported that in three cases terazosin markedly reduced methadone related sweating. These cases could not tolerate biperiden due to its side effects (all cases complained of blurred vision, painful urination and dribbling), and they did not have affinity for Botox injection. Prescription clonidine abuse was a source of concern in the cases.

2. Cases Presentation

2.1. Patient 1

F was a 27-year-old male worker. He abused heroin for about five years. He had started methadone maintenance treatment from three months ago. During this period, his methadone dosage increased from 30 mg to 170 mg per day. Although he suffered from some withdrawal symptoms, his severe sweating was intolerable. Changing the dosage of methadone was ineffective to reduce his threatening sweating. His physical examination was normal. Systolic and diastolic blood pressures were 120 and 80 mmHg, respectively. No remarkable laboratory findings were reported regarding thyroid function, liver, and renal functions. Blood sugar level was in the normal range. His condition, according to clinical global impression-severity (CGI-s) questionnaire, was very sever (score = 7). Moreover, the hyperhidrosis disease severity scale (HDSS) score was 4 (this score can range from 1 to 4).

Terazosin (1 mg/day) significantly decreased sweating after two weeks. The CGI-S and HDSS scores were 3 and 2, respectively, after one month. Meanwhile, no blood pressure change was observed.

2.2. Patient 2

M was a 45-year-old female, who was an opium abuser for six years. After entering methadone (95 mg/day) maintenance treatment, she had intolerable sweating.

In physical examination, no significant pathological finding was observed. Blood pressure was 130/75 mmHg. All laboratory tests including thyroid and liver function, blood urea nitrogen (BUN), blood sugar and creatinine levels were in the normal range. The severity of sweating according to CGI-S was 5. The HDSS score was 4.

Terazosin (1 mg/day) was prescribed. After three weeks, there was a marked decrease in sweating. The CGI-S reduced to 2 and the HDSS score reduced to 1. Again, there was no marked change in blood pressure.

2.3. Patient 3

C was a 43-year-old male taking methadone (55 mg/day) for one month. He used to take opium orally before enrolling in methadone maintenance treating program. When he started the treatment, he experienced intolerable sweating. The sweating score according to CGI-S was 5. Moreover, the HDSS score was 3. There was no remarkable finding in the physical examination or laboratory analyses. Again, Terazosin (1 mg/day) was administered. The severity of sweeting decreased after one week. The severity of sweating according to CGI-S and HDSS were 1 and 1, respectively. No blood pressure change was observed.

3. Discussion

The most striking finding of the three cases indicated that terazosin was potentially effective to treat methadone related sweating in patients with opium dependency. To the best of the authors' knowledge, this effect had never been reported previously. However, there are some reports indicating that terazosin was effective to treat selective serotonin reuptake inhibitors (SSRIs) associated sweating (25). A study revealed that terazosin reduced sweating severity in patients using sertraline (26).

The exact mechanism of sweating is not known. It is supposed that both thermoregulatory and non-thermoregulatory factors are involved (27). However, the beta-adrenergic antagonist propranolol does not inhibit sweat gland function after heating (28) or sweating during exercise (29).

SSRIs induce sweating probably through the inhibition of selective 5-HT reuptake and the noradrenergic tone resulting from the interaction of noradrenergic and serotonergic neurons in various regions of the brain (30). Considering that terazosin is an alpha 1-selective adrenoceptor blocker, it is possible that sweating mechanism caused by methadone be similar to that of SSRIs.

In addition, clonidine, a post-synaptic α-adrenergic agonist, increased the sweating threshold in symptomatic postmenopausal females (31).

Terazosin might be a safe medication in such patients, because the rate of QT prolongation with terazosin is rare (0.12%) (32). Moreover, methadone causes sexual dysfunction (33). There is a report that α-adrenergic antagonists do not negatively impact sexual desire (34). Also, some physicians recommend anticholinergics, clonidine and Botox injection to treat methadone induced diaphoresis, but it is important to consider that clonidine abuse in patients under methadone replacement therapy, also anticholinergic side effects such as constipation, and injection of Botox are invasive methods.

In conclusion, if further controlled clinical trials confirm, terazosin could be administered to control excessive sweating in patients taking methadone.

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