

**Buprenorphine/naloxone maintenance therapy in patients with meperidine use disorder****Ahmet Bulent Yazici\*, Alime Burcin Saykan, Esra Yazici, Atilla Erol**

Department of Psychiatry,  
Sakarya University, Training  
and Research Hospital, Sakarya,  
Turkey

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Dr. Ahmet Bulent Yazici,  
Email: a.bulentyaz@gmail.com

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**ABSTRACT**

Meperidine hydrochloride is a synthetic opioid and a weak  $\mu$  receptor agonist. Meperidine use disorder is mostly iatrogenic and is common in health care workers. In addition, it is prescribed in acute and chronic pain complaints, and has a high potential for creating addiction. Treatment of meperidine use disorder is a challenging issue and there is no standardised treatment for meperidine addiction. Buprenorphine is a  $\mu$  receptor partial agonist, a long-acting synthetic opioid for the treatment of opioid dependence and has a buprenorphine/naloxone (BN) form combined with naloxone. Buprenorphine maintenance therapy is one of the treatment options performed in opiate use disorder. But there is a paucity of data about treatment of meperidine use disorder. Here, a full remission case report is presented with BN maintenance treatment for a patient with meperidine use disorder diagnosis.

**Keywords:** Addiction, Buprenorphine, Meperidine, Naloxone, Remission**INTRODUCTION**

Meperidine hydrochloride (MP) is a synthetic opioid; it is frequently used in healthcare for pre-operative preparations and post-operative pain relief. It is a relatively weak  $\mu$  opioid agonist with local anesthetic and significant anticholinergic effects. Its half-life is about 3 hours. Its withdrawal syndrome reaches its peak at 8-12 hours and ends in 4-5 days.<sup>1,2</sup>

Opiate use disorder is associated with a problematic opiate use pattern that leads to clinically significant impairments or functionality deterioration for a period of at least 12 months.<sup>3</sup> Meperidine use disorder is mostly iatrogenic and is common in health care workers.<sup>4,5</sup> Meperidine use begins to relieve sickle cell anemia crisis, urinary tract stones, pancreatitis, post-traumatic pain, and then it can turn into substance abuse.<sup>1,5</sup> Treatment of meperidine use

disorder is a challenging issue and generally it has a frustrating pattern for clinicians.<sup>6</sup> It is hard to quit and stay in remission meperidine for patients due to exacerbation of pain and harassing symptoms of withdrawal. Succeeding a full remission (staying away from the substance for 12 months) is also difficult meperidine addiction. Still there has been no standardised treatment for meperidine addiction.

In Buprenorphine/naloxone (BN) combination (Suboxone sublingual film tablet, Liba); buprenorphine is a  $\mu$  receptor partial agonist, is present in the market in a combination with naloxone to prevent abuse, which does not create an effect by sublingual administration but is antagonistic when taken intravenously.<sup>7</sup> In opiod use disorders, mostly reportedly in heroin use disorder, opioid maintenance treatments, such as BN treatment, reduce mortality, HIV transmission risk, other substance abuse rates and crime.<sup>7</sup>

Here, a case of opiate (meperidine) use disorder diagnosis and its treatment with maintenance BN is discussed. Clinical Opiate Withdrawal Scale and Substance Craving Scale were used during the evaluation of the case.

### **Assessment tools**

#### *Turkish version of Clinical Opiate Withdrawal Scale (KOYÖ-COWS)*

COWS were developed by Wesson ve Ling and validated in Turkish by Altıntoprak A.E. et al; it is a scale by which the clinician evaluates and rates all of the objective and subjective findings of the patient in a withdrawal of opiates.<sup>8,9</sup> The total score ranges from 0 to 47, with high scores indicating more severe deprivation levels. COWS ratings of 5-12 indicate mild; 13-24 indicate medium; 25-36 indicate medium-severe; and higher than 36 indicates severe withdrawal findings.

#### *Substance Craving Scale (SCS)*

Craving for substance use was evaluated using SCS. SCS is a version of the Penn Alcohol Craving Scale (PACS), which is a 5-item questionnaire developed to evaluate the desire for alcohol use during the previous week (frequency, severity, duration, resistance, and general craving).<sup>10,11</sup> Each item is scored between 0 and 6, and the maximum craving score is 30. SCS is the version of the PACS for evaluating craving in substance use disorders. Cronbach's alpha value for the SCS is 0.84. The overall item-total correlation values corrected for each item varies between 0.75 and 0.8244.

### **CASE REPORT**

The patient, aged 50, married, father of 2, graduated from high school, working as a high officer related to religion, living in a city center, applied almost every day for using meperidine out of indications. In the story of the patient; it was learned that, in his own initiative, he continued his meperidine treatment, which was first used upon the recommendation of a physician due to aches after an acute pancreatitis 15 years ago, then he showed excessive desire for meperidine use over time and withdrawal when he did not use it. It was also learned that the patient was diagnosed with trigeminal neuralgia 10 years ago, increased the amount he has been using since then, and has reached 500-900mg/day (5-9 injection) in the last 1 year. It was learned that even if the patient not have pain, he spent extra effort to access the drug, tried different ways, spent most of his time at the worksite for this, had problems in his family and job due to meperidine use, tried to quit using the drug, was administered in the psychiatry or addiction clinics of four different hospitals due to substance abuse, used antidepressants and anxiolytic and antipsychotic drugs were used in different groups but he was not relieved and could not continue his remission. As a result of the interview, he was diagnosed with severe opioid use disorder according to DSM-5 criteria and also

with moderate depressive disorders and generalized anxiety disorder.<sup>3</sup> An informed written consent was received from the patient for treatment and follow-up process of the disorders and sharing the scientific data with related literature.

When the psychiatric interview and past medical records of the patient are examined; it was seen that the patient had two clinical admissions with depression and generalized anxiety disorder diagnoses in his past psychiatric history; and had many surgeries due to stomach, gall bladder, urethral problems and trigeminal neuralgia (more than 50).

On the psychiatric examination, the time orientation of the patient, who was conscious and co-operative, was partially deteriorated. The patient, who seemed older than age, had decreased self-care. His attention and concentration was decreased. His affections were dysphoric, anxious, mildly irritable and compatible with his content of thought, his mood was depressive and anxious. Speaking speed had slowed down, the amount was normal, and his speech was suitable for its purposes. His flow of thought slowed down and his association of ideas were usual. His thought content and perception were identified as usual. His motor activities, sleep and appetite had decreased, and his abstract thinking and reasoning were maintained. In his family history, his brothers had a diagnosis of alcohol use disorder with continuous moderation. No pathologies were not detected in his routine blood and urine biochemical parameters taken during admission, except for iron and folic acid deficiency. For this reason, iron and folic acid treatment was started. Benzodiazepines and opiates were detected in his urine during substance analyses. The opiate analgesics (meperidine and tramadol HCL) used by the patient when he arrived were discontinued and BN was started after withdrawal symptoms. The Clinical Opiate Withdrawal Scale was initially measured at 12, and the patient stabilized (scale score: 4) with a dose of 6mg/day. Substance Craving Scale scores were reduced from 23 to 5 over a period of 1 month. The medications of the patient, who was using opiate and non-opiate analgesics when he arrived, were simplified, algology polyclinic was consulted for trigeminal neuralgia treatment, and his medication was set as; pregabalin 900mg/day, carbamazepine 800 mg/day. The patient displayed depressive moods and somatic complaints, his treatment began with duloxetine and amisulpride, then, mirtazapine and quetiapine treatment were added due to intense anxiety and insomnia.

The patient was discharged for ambulatory treatment and monitoring with doses of BN 6mg/day, duloxetine 90mg/day, mirtazapine 15mg/day, quetiapine 300mg/day, carbamazepine 800mg/day and pregabalin 900mg/day. The patient's BN/naloxone combination was increased to 8/2mg/day in a polyclinic control performed one month later. In his polyclinic controls, which were performed once a month in the first 6 months and every 2 months during 1 year, for a total of 18 months; it was observed that the wellness continued, and no opiate or non-opiate

substance use was found in urine drug analysis except for BN. The patient worked regularly in his job and assumed active tasks during this period. According to DSM-5 criteria, he was considered to be in the complete stage of opioid use disorder.

## DISCUSSION

Meperidine use disorder is a psychiatric disorder of mostly iatrogenic origin.<sup>5</sup> There are few case reports of meperidine abuse treatment in the literature. In one case, venlafaxine treatment was attempted in the presence of meperidine use and chronic pain, and a successful result was obtained after 1.5 months of follow-up.<sup>12</sup> In another meperidine abuse disorder case, it was reported that the patient who underwent benzodiazepine and mirtazapine maintenance treatment in the clinic continued using them after discharged and died due to overdose.<sup>13</sup> In another case report, it was reported that BN treatment was initiated and BN maintenance treatment after discharge was successful in a 5-month follow-up.<sup>14</sup> We present a successful case in literature as a case study in which BN maintenance treatment is applied to meperidine abuse in chronic pain disorders and had 12 months of remission.

This patient had a diagnosis of comorbid depression, sleep disturbance, and trigeminal neuralgia with meperidine dependence, and treatment of these diagnoses were continued (duloxetine, mirtazapine, quetiapine, carbamazepine, pregabalin). It is understood from the story that drugs used by the patient were are insufficient to relieve his opiate addiction withdrawal symptoms, tendency to seeking substances, and pains due to trigeminal neuralgia. It has been reported in previous studies that buprenorphine/naloxone may be an effective agent for in reducing opiate withdrawal symptoms of the patient and controlling substance abuse.<sup>15,16</sup> In addition, in the opinion of the panel of international experts of the World Health Organization, opioids are increasingly recommended in relieving neuropathic pain and buprenorphine is seen as a good option.<sup>17</sup>

It is known that remission periods after detoxification process in addictions are not too long even after successful treatment of withdrawal symptoms in acute remission period.<sup>18</sup> The long-term follow-up of this case is encouraging and hopeful for the treatment of other patients.

In patients with chronic pain syndrome and opiate analgesic abuse; BN maintenance therapy should be considered as an alternative treatment that may help the patient get away from opiate analgesics and side effects, and to provide the patient with functionality. More studies are required to create a better treatment algorithm.

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