

# Venlafaxine Pharmacotherapy In Meperidine Addiction and Chronic Pain Comorbidity: A Case Report

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## ÖZET

Meperidin bağımlılığı ve kronik ağrı birlikteliğinde venlafaksin tedavisi: Bir olgu sunumu  
Meperidin (petidin), medikal kullanımı olan, yüksek bağımlılık potansiyeli taşıyan sentetik opioid bir maddedir.  
Literatürde iyatrojenik meperidin kullanımı sonrasında gelişen meperidin kötüye kullanımı ve bağımlılığı olgu-  
ları bildirilmiştir. Venlafaksin ve diğer SNRI'ların ağrıyı ve depresif belirtileri azalttığı klinik çalışmalarda göste-  
rilmiştir. Burada, kronik ağrı sonrası iyatrojenik meperidin bağımlılığı gelişen, Alkol Madde Bağımlılığı Araştırma  
Tedavi ve Eğitim Merkezi'nde (AMATEM) bağımlılık tedavisiyle birlikte kronik ağrı ve depresif yakınmalara  
yönelik venlafaksin kullanılarak etkin bir şekilde tedavi edilen bir olgu sunulmuştur.

**Anahtar kelimeler:** Meperidin bağımlılığı, kronik ağrı, venlafaksin

## ABSTRACT

Venlafaxine pharmacotherapy in meperidine addiction and chronic pain comorbidity:  
a case report

Meperidine (pethidine) is a synthetic opioid substance with high addiction potential with medical use. Cases  
of meperidine abuse and addiction developed after iatrogenic meperidine use have been presented in  
the literature. Venlafaxine and other SNRIs were shown in clinical trials to alleviate pain and depressive  
symptoms. In this report, we present a case of iatrogenic meperidine addiction that started after the use of  
the drug for chronic pain treatment. The treatment for addiction was completed in Research, Treatment  
and Training Center for Alcohol and Substance Dependence (AMATEM) along with the successful  
treatment of chronic pain and depression with venlafaxine pharmacotherapy.

**Key words:** Meperidine addiction, chronic pain, venlafaxine

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## INTRODUCTION

Meperidine (pethidine) is a synthetic opioid  
substance with medical uses and a high addiction  
potential. It is a relatively weak  $\mu$  opioid agonist with  
marked anticholinergic and local anesthetic effects. The  
half-life of meperidine is approximately 3 hours (1,2).  
Withdrawal symptoms begin rapidly, reach a peak level  
between 8-12 hours and end in 4-5 days. Meperidine  
is frequently used during the preoperative preparation  
period and to relieve postoperative pains. It is useful in  
relieving acute pain caused by trauma, kidney or biliary  
colic. Reports have indicated that it should not be used  
for treating chronic pain, malignancy, head injuries,  
heart failure, unidentified acute abdominal pain and in  
cases where opioid addiction is suspected (2). Cases of  
meperidine abuse and addiction that developed after  
iatrogenic meperidine use have been presented in the  
literature (3-5).

Antidepressants remain a central tool for coping with  
chronic pain (6). In clinical studies, serotonin and  
noradrenalin reuptake inhibitors (SNRI) have been  
shown to alleviate pain and depressive symptoms (7,8).  
SNRIs have been reported effective for treating various  
chronic pain conditions independent from comorbid  
depression (8). Venlafaxine is also an SNRI that has  
been reported to be effective in pain relief (9).

In this report, we present a case of iatrogenic  
meperidine addiction, arising after the use of the drug  
for chronic pancreatitis and followed up in our inpatient  
clinic. Our patient used venlafaxine during addiction  
treatment and showed a marked improvement in pain  
symptoms, as well as an alleviation of withdrawal  
symptoms, with this treatment.

## CASE

F.A. is male, born in 1955, a high-school graduate,

married with two children and currently retired. He reported to an algology (pain treatment) center with a complaint of "very severe abdominal pain" and was then referred to our clinic with a suspected meperidine hydrochloride addiction. The patient was admitted to our clinic with a pre-diagnosis of meperidine hydrochloride addiction on December 1, 2009.

During his interview, we learned that patient has been drinking alcohol since 1982, including 20-30 cl of rakı (Turkish alcoholic beverage) 2-3 times per week. At that time, he did not increase his alcohol intake. The patient had not had an alcoholic drink in the last 3 years; he did not experience withdrawal symptoms during that period as a result of terminating alcohol use.

Both the interview and the patient's medical records confirmed that the patient was treated once per 2-3 months for abdominal pain of 3-4 day periods, in both outpatient and inpatient clinics in his district's state hospital, since 2001. The patient had been diagnosed with acute pancreatitis in 2003, following tests conducted in the university hospital of the province where he lived. He had been tested due to a two-year period of intermittent pain. He was prescribed medication and abstained from alcohol for one year and stopped experiencing pain during this time. In 2004, the patient resumed intermittent alcohol use and his pain symptoms returned. At this point, a course of meperidine hydrochloride was introduced to treat the pain symptoms. The medication was injected intramuscularly (1/2 ampoule twice per day) during the period that he was treated; he was diagnosed with chronic pancreatitis in an inpatient clinic in the district state hospital and in the university hospital of a nearby province in 2006. He was referred to a special pain center by the state hospital where he was treated on an inpatient basis, as he continued to be in pain. In this center, transdermal fentanyl and other various analgesics were prescribed. The patient did experience a decrease in the severity and frequency of his pain symptoms but continued use meperidine hydrochloride in addition to the other medications whenever he experienced pain. The patient's pain episodes increased in severity and frequency over time

and he was hospitalized and treated in the university hospital of the province where he lived in 2008. During this period, he had a stent implanted into his pancreatic canal and celiac blockade was conducted twice. Meperidine hydrochloride was administered almost every day throughout his hospitalization as pain persisted despite these procedures. His pain persisted, also, after he was discharged the hospital and so his meperidine hydrochloride dose was increased to 1/2 ampoule (or 1 ampoule 3-4 times per day); the severity of the pain had greatly increased and it had become chronic approximately 3 months earlier. His pain persisted despite these measures and so the patient had the following procedure - pancreaticojejunostomy and cholecystectomy, i.e. Puestow operation - in the general surgery department of the university hospital. His pain symptoms persisted after the operation, and so he was referred to an institution also housing an algology center and an alcohol/substance addiction treatment center. The algology center evaluated the patient and managed his pain treatment; at this point he was referred to our clinic with a diagnosis of intense meperidine hydrochloride addiction.

The patient's pain severity was evaluated using a 10 cm Visual Analog Scale (VAS) (10). The patient was asked to assess the level of pain, at that moment, between 0 ("no pain") and 10 ("the most severe pain imaginable"). When the patient presented to our clinic, he had not used meperidine hydrochloride for approximately 4 days. His abdominal pain was a 10 in severity on the VAS and other issues emerged within the next 2-3 months, i.e. appetite loss, inability to eat, fatigue, inability to get out of bed, desperation, inability to perform daily activities and insomnia, all due to pain.

At the psychiatric examination, the patient was cognizant, cooperative and oriented. His speech was normal in both speed and volume. His mood was slightly depressive and consistent with this, he was distressed and restless. The patient's Clang associations were appropriate and focused and he did not describe hallucinations. There was not any delusion and patient's cognitive functions were normal.

This was the first presentation of the patient

for psychiatric reasons and he had no psychiatric disease history except the aforementioned alcohol and meperidine hydrochloride use in his medical history. There was no familial history of mental illness, alcohol or psychoactive substance use.

At the physical examination, the patient had a cachectic appearance, a surgical scar in his epigastric region, pain and tenderness during palpations of the epigastric region. No symptoms were determined to be withdrawal symptoms, except minimal sweating. The patient's functioning score was assessed at 40-50.

Routine biochemistry, hemogram, sedimentation, thyroid function tests, hepatitis and HIV marker tests and urine tests were given and a posteroanterior lung graph and ECG were taken after hospitalization. No pathological finding consistent with that of the clinic was determined. The patient's urine tested positive for opioid metabolite. In addition to metamisole sodium, paracetamol and codeine treatments recommended by the algology center, hydroxyzin hydrochloride (37.5 mg/day), mirtazepine (15 mg/day), lansoprazole (30 mg/day) and diazepam (15 mg/day) courses were initiated. Diazepam and codeine were discontinued by gradually decreasing the dose; the other analgesic treatments were maintained. After discontinuing codeine, a course of venlafaxine (75 mg/day) was started on the fourteenth day of the treatment. The patient's complaints of pain decreased gradually after he started taking the venlafaxine, and we gradually decreased his analgesic treatment. During clinical follow-up, the patient's appetite and sleep patterns improved, his depressive complaints reduced and he began to engage in routine daily activities. The dose of venlafaxine was increased to 150 mg/day on the twenty-third day of treatment. The grounds for increasing the dose were that both serotonin and noradrenalin needed to be addressed for maximum efficacy. While serotonin reuptake inhibition is stronger at with a venlafaxine dose of 75 mg/day, higher doses are required for noradrenalin reuptake inhibition (11). The patient continued to experience improvement in his condition on a maintenance dose of venlafaxine (150 mg/day) and lansoprazole (30 mg/day). On the 45th day of treatment, the patient was discharged from the hospital with a pain severity of

2 on the VAS scale, a functioning score of 80-90 and a normal psychiatric examination by the attending polyclinic control.

The patient did not return for polyclinic control until the 45th day after his discharge because he lived far from the clinic, in another district. He reported that he felt excellent; he used no meperidine after the discharge but regularly used the medical treatment arranged by us during the discharge and his pain severity was less than 1 on the VAS scale.

## DISCUSSION

Opioid analgesic abuse and addiction occur rather frequently. According to findings in literature, meperidine abuse is usually iatrogenic (2). In a study conducted in AMATEM on 6 patients, meperidine abuse was reported in patients diagnosed with chronic gastritis, pancreatitis, malignancy and surgical procedures to address complaints of abdominal, head and back pains (3). In another study, the most frequent diagnosis reported for patients with meperidine addiction was chronic pancreatitis (4).

The factors that could contribute to a patient developing an addiction include chronic pain and non-diminishing pain, inefficient relationship between the treatment team and the patient, low pain threshold, low tolerance pain due to anxiety or depression, history of substance abuse/tendency to substance abuse, placebo and inappropriate analgesic use (4). The case presented here was followed up with diagnoses first, of acute pancreatitis, then of chronic pancreatitis and addiction developed due to iatrogenic meperidine use for abdominal pain. In some studies, the predictors of opioid abuse were investigated in patients with chronic pain. In one study, findings indicated that a past history of opioid or alcohol abuse was not determinative for opioid abuse; another study noted that patients with a history of alcohol or cocaine abuse should be carefully observed if prescribed opioid derivative drugs (5,12). In this case, a several-year duration of alcohol consumption that did not meet the criteria for abuse or addiction is striking.

Persistent pain is frequently accompanied by depression. The use of various antidepressant drugs correlates with pain alleviation, irrespective of the mood improving effects of these drugs. Alleviation of pain is a consequence of the various effects of antidepressants on neuroregulator mechanisms, related to perception and transmission of pain (6). Clinical studies have shown that venlafaxine, a SNRI, alleviated pain and depressive symptoms (7,9). The patient in this report also complained of depression, in addition to persistent pain, and remained slightly depressed during the period he presented. His symptoms did not meet major depression diagnostic criteria at the interview conducted with SCID-I and we learned that these complaints emerged after years of chronic pain. The patient showed a marked improvement with venlafaxine treatment; this is consistent with the findings in the literature. The failure of many treatments, including meperidine, to alleviate pain suggest that the patient's pain may be psychological. Again, with chronic pain like fibromyalgia is considered psychological.

Venlafaxine treatment has been reported to be effective in treating anxiety, depression or pain symptoms (13). The most probable mechanism of the pain experienced by patients suffering from fibromyalgia is dysfunction in the descending pain inhibition pathway mediated by serotonin and noradrenalin (14). The most likely cause of the benefit provided for the pain, for our patient, is the dual effect of venlafaxine.

## CONCLUSION

Patients presenting with complaints of chronic pain should be addressed with the following: a detailed psychiatric evaluation, an investigation of comorbid depression or another psychiatric diagnoses, a determination of the risk factors and, if necessary, simultaneous follow-up the attending psychiatrist. When potentially addictive medication like meperidine is used for treatment purposes, it is advisable to follow the patient closely, and review other options that could be as effective in treating chronic pain.

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