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Case Report / Olgu Sunumu

Fentanyl Dependence Associated with the Use of Transdermal Fentanyl in a Cancer Patient: A Case Report

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ABSTRACT

Fentanyl dependence associated with the use of transdermal fentanyl in a cancer patient: a case report

Fentanyl is a syntetic narcotic analgesic that is available for the management of chronic cancer and noncancer pain. Its analgesic potency is 75-100 times greater than that of morphine. Apart from the lipofilic nature and the high potency, fentanyl is characterized by low molecular weight and thus, is suitable for transdermal use. The transdermal fentanyl patches are designed to deliver fentanyl at a constant rate for periods of 72 hours. Patches with a delivery rate of 25, 50, 75 and 100 μ/h are avaiable. Transdermal fentanyl is effective and safe in many cancer patients. Abuse/misuse of fentanyl patches has been increasingly reported along with different routes of administration such as intravenous, oral, rectal, inhalational use. However, there are two reports associated with transdermal fentanyl dependency in literature. Here, we report a case of fentanyl dependence associated with the use of transdermal fentanyl in a cancer patient.

Key words: Cancer, dependence, fentanyl, transdermal patch

ÖZET

Bir kanser hastasında deri bandı kullanımıyla oluşan fentanil bağımlılığı: Olgu sunumu

Fentanil, kronik kanser ve kanser dışı ağrıların tedavisinde kullanılan bir sentetik narkotik analjeziktir. Ağrı kesici gücü morfininkinin 75-100 katıdır. Yağda çözünebilirliği, yüksek ağrı kesici gücü, düşük moleküler ağırlığı deri bandı olarak kullanılabilmesini sağlar. Fentanil deri bandı plazmaya 72 saat süreyle fentanil geçişini sağlar. Saatte 25, 50, 75, 100 mcg salınabilen formları mevcuttur. Fentanil deri bandı birçok kanser hastasında, etkili ve güvenilir bir preparattır. Ancak son zamanlarda, literatürde, fentanil deri bandı içeriğinin damar içi, oral, rektal ve inhalasyon gibi farklı yollarla alınmasına bağlı kötüye ya da uygunsuz kullanıma dair olgular yer almaktadır. Uygunsuz/kötüye kullanımın aksine, literatürde fentanil deri bandıyla oluşan fentanil bağımlılığına dair yalnızca iki olgu vardır. Biz bu yazımızda, bir kanser hastasında fentanil deri bandı kullanımına bağlı gelişen fentanil bağımlılığı olgusunu sunduk.

Anahtar kelimeler: Kanser, bağımlılık, fentanil, deri bandı

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INTRODUCTION

Fentanyl is a synthetic and selective opioid agonist with a high affinity for μ-receptors. Due to its high solubility in fat, it passes quickly through the blood-brain barrier. This characteristic means that its analgesic potency is 75-100 times greater than that of morphine (1). The main routes of use are oral, intravenous, epidural, transdermal, intranasal and transmucosal. The fentanyl skin patch entered the market in America in 1991. The skin patch is an alternative to oral morphine in treating cancer pain. Its pain-killing property in cancer patients is at least as great as that of oral opioids, while its side-effects are much less. It has therefore become more popular in cancer patients in recent years. It is available in 25, 50, 75 and 100 mcg/hour forms and is generally applied to the skin over the scapula. It is effective over 72 hour. Its effect is at the maximum level in the blood on the first day. That effect persists but decreases on the second and third days (2).

The transdermal fentanyl patch can frequently be misused/abused. The literature contains case reports concerning intravenous (3), oral (4), rectal (5) and inhalation (6) abuse/misuse. There are two case reports in the literature of dependence developing due to transdermal fentanyl patch use. The first case is a 59-year-old man who became dependent to transdermal fentanyl patches belonging to his wife (7). The second case concerns dependence in a 78-year-old patient using transdermal fentanyl patches for 7 years due to chronic back pain (8).

Our case report concerns dependence in a gastric cancer patient who continues to use transdermal fentanyl patches after the cancer remission and cessation of the pain. Our case is important in terms of drawing attention to the need to avoid long-term misuse in the treatment of cancer pain.

CASE

Our patient was a 48-year-old male. He was married, a high school graduate, worked as a laborer and had three children. He presented to our clinic on 09.03.2011 complaining of long-term transdermal fentanyl patch use, failed attempts to give them up and depressive symptoms. The patient's history revealed that he had undergone surgery for bladder cancer in 2007, and had admitted to the doctor with severe abdominal pain again in 2008 and had been diagnosedwith gastric cancer. The patient underwent surgery for the stomach cancer, received 6-month chemotherapy and radiotherapy and entered remission. Throughout that time the radiation oncologist prescribed transdermal fentanyl patches at 50 mcg/hour due to abdominal pain. At the end of the 6 months, although the disease was now in remission, he told the doctor that the abdominal pain persisted and that he wished to continue using fentanyl. Although the doctor told him the disease was in remission and that pain was not expected, he/she continued to prescribe fentanyl. The patient had been in remission for 18 months, receiving no cancer treatment and experiencing no cancer pain, however, he continued to use fentanyl transdermal patches applied to the scapular region at a dose of 50 mcg/hour three times daily. Throughout that 18-month period, he had tried to quit using fentanyl for several times on his own. However, on each occasion he experienced pain in the entire body, restlessness, contractions in the feet and legs, nausea, lacrimation, nasal discharge, sweating and trembling, and had the drug prescribed again by his doctor. He was only able to withstand the symptoms that appeared after trying to give the patches up for one day at most. During that time, he insisted on the prescription of the drug, and often waited outside his/her door. For that reason he was sometimes unable to go to work, resulting in problems at work. During this time, the doctor (radiation oncologist) attempted to assist him to quit the drug by twice reducing the dosage (from 50 mcg/hour to 25 mcg/hour). However, the doctor then had to prescribe 50 mcg/hour once more when the patient again experienced the above withdrawal symptoms. He applied to his own doctor when he experienced withdrawal symptoms several times, before finally attending our hospital, despite using a dose of 50 mcg/hour. The doctor raised the dosage to 75 mcg/hour, but warned the patient that he might be dependent and advised him to consult a psychiatrist. This new dose suited the patient, but he did not feel as well as in the earlier periods when he was using 50 mcg/hour. The psychiatrist he consulted planned to reduce and stop the fentanyl, and in the first stage the dose was lowered to 50 mcg/hour. He was started on diazepam at 15 mg/day for symptomatic treatment and duloxetine at 30 mg/day for depressive symptoms. At his own request the patient was referred to our institution for hospitalization. Epicrisis written by the psychiatrist responsible from his treatment revealed that the patient experienced pronounced withdrawal symptoms when fentanyl was reduced from 75 to 50 mcg/hour. No pathology was determined at laboratory tests. The patch on his back was removed. Diazepam was increased to 20 mg/day due to symptoms of restlessness, tiredness, unhappiness, sleeplessness, pain and contractions in the legs and feet, lacrimation, nasal discharge, feelings of cold and shivering. Duloxetine was raised to 60 mg/day due to increasing symptoms of depression. Diclofenac sodium for pain was started at 150 mg/day dose. On the second day, the patient reported that muscle pains had spread throughout his

body and complained of nausea. On the seventh day, the patient's feelings of cold, shivering and tirednessincreased, and therefore he wore a coat on the ward, but his nasal discharge and lacrimation had decreased. At this time the patient reported that the situation was intolerable, that he had 25, 50 and 75 mcg fentanyl patches at home and that he wanted to go home and stick them all on his back at once. On the 15th day the patient's withdrawal symptoms decreased. By the 26th day the patient was allowed to visit home. He reported that he felt the desire to use fentanyl, but did not use it. He gave the fentanyl patches from home to the ward nurse. Diazepam was reduced to 10 mg/day. On the 32nd day, the patient still had mild muscle pain, but the other withdrawal symptoms and urge to use fentanyl had disappeared. The patient was discharged with duloxetine 60 mg/day and diazepam 10 mg/day. At check-up one month later, he reported no symptoms apart from mild muscle pains, and no urge to use fentanyl. The patient's depressive symptoms had also resolved at this check-up. Early period full remission of dependence was assessed. He was advised to continue with duloxetine and polyclinic check-ups.

DISCUSSION

The desire to increase the dosage, inability to achieve the desired effect despite the dose being raised, unsuccessful attempts to quit (both the patient's own attempts to suddenly stop using the drug and the doctor's efforts to gradually reduce it), the withdrawal symptoms experienced, frequent visits to the doctor to obtain more of the substance and the persistent attitude, time-wasting, work problems and the picture of clinical depression that emerged in this case all meet the diagnostic criteria for opioid (fentanyl) dependence in DSM-IV.

Fentanyl is used via the oral, intravenous, epidural, spinal, transdermal, intranasal, rectal, sublingual, subcutaneous and transmucosal routes (2,10). Compared with other forms of fentanyl, the fentanyl skin patch is slow-release and has a long-term effect, thus producing a settled but not elevated opioid level in plasma. It rarely leads to the euphoria and withdrawal symptoms seen between doses in other forms. Due to these properties, the fentanyl skin patch is regarded as having a low risk of leading to tolerance development or physiological dependence (11). One study of 532 patients with non-cancer chronic pain determined no misuse or physiological dependence in any patient (12). The risk of dependence in patients using it for the treatment of cancer pain is suggested as being very low (10). One study assessing efficacy and reliability in cancer pain reported no dependence (13).

The literature contains a large number of case reports of misuse/abuse of transdermal fentanyl patch content by the intravenous, oral, rectal and inhalation routes. These were cases leading to intoxication or death and published in medicolegal or emergency medicine journals. It is not known that whether dependence was present in these cases or not (3-6).

In contrast to misuse/abuse, there are only two case reports in the literature of the fentanyl skin patch causing dependence. The first was published in 2010 and the second in 2011 (7). A 59-year-old man developed dependence by attaching fentanyl skin patches belonging to his wife, who was receiving lung cancer-related pain treatment, to his own scapula and also by chewing them. He first began using fentanyl at a dose of 25 mcg/hour, but this gradually rose to 50, 75 and 100 mcg/hour. The patient had a 20-year history of marijuana use. The second case (8) involves dependence in a 78-year-old patient using transdermal fentanyl patches for 7 years for chronic back ache. In our case, dependence was due to the continuation of the use of transdermal patch after cancer remission. In the first case, the patch was used both transdermally and orally. Given that the risk of dependence will be higher if the fentanyl is used orally, it is unclear whether dependence would have emerged in that individual through transdermal use alone. However, in the light of the 20-year marijuana use and oral misuse of fentanyl, that individual was clearly predisposed to dependence. Dependence in the second case and our own case was resulted from constant use of fentanyl patches by the transdermal route only.

Loss of volume in the amygdala, white matter anisotropy in the afferent and efferent pathways of the amygdala and a decrease in functional connections in the amygdala have been determined in individuals prescribed long-term opioid for therapeutic reasons (14). These findings are clinically important in terms of showing functional changes in regions of the brain associated with motivation and reward functions, impulse control and affect regulation in individuals prescribed long-term opioid.

Although the risk of dependence is reported to be low in the literature, increasing use in chronic pain patients in recent years suggests that more cases of dependence will be encountered. Grattan et al. (15) suggested that since an improvement associated with opioid use is seen in depressive symptoms in patients using opioid for pain treatment, patients have a tendency to use more opioid than necessary, and that this can establish a risk for opioid misuse and dependence. Clinicians must therefore bear in mind that depression, frequently masked in cancer patients, may pose a risk for opioid dependence. When depression is determined in such patients, treatment with antidepressants is essential. In our case, depressive symptoms were brought under control using duloxetine 60 mg/day.

In conclusion, in our case, the transdermal fentanyl patch continued to be prescribed in the absence of cancer pain. The reason may be the inaccurate belief about the safety of this treatment or the difficulties in diagnosis of patients exhibiting dependence behavior, among professionals engaged in the treatment of cancer pain. Training of the professions involved in these issues may prevent potential cases of dependence in the future.

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