

Case Report

Another lesson from the earthquake: Transdermal fentanyl dependence in two child victims

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ABSTRACT

Thousands died in the Kahramanmaraş-centered earthquake in February 2023, and even more were injured. Some were administered transdermal fentanyl patches (TFPs) due to severe pain. Two pediatric patients, both severely injured victims of the earthquake, developed dependence on TFPs and experienced difficulties during the cessation of fentanyl treatment. The first child was discharged while still being administered fentanyl after four months. In the second case, TFPs could be ceased after four months. This study aimed to emphasize that TFPs can lead to dependence in pediatric patients as well; hence, they should be used more carefully to avoid any potential dependency.

Keywords: Fentanyl, opium dependence, pain, pediatrics, transdermal patch

Fentanyl is an opioid receptor agonist. It is 80 to 100 times more potent than morphine and is used as an analgesic in the management of severe acute and chronic pain.^[1] Fentanyl can be administered via intravenous, epidural, transdermal, and transmucosal routes. The transdermal route is safer due to its long-term effect, slow release, lower risk of euphoria, and maintenance of stable plasma levels. Misuse of transdermal fentanyl patches (TFPs), including vaporization, chewing, ingestion, and its application on buccal or rectal mucosa, causes dependence and mortality.^[2] On the other hand, there are only five case reports in the literature that demonstrate appropriate use of fentanyl transdermal patches as prescribed can lead to dependency and withdrawal symptoms,^[3-7] all of which are in adult patients. To our knowledge, this is the first pediatric case study reporting two young earthquake victims who were administered TFPs for severe pain unresponsive to other analgesics and who suffered from withdrawal symptoms during the discontinuation of the TFPs.

CASE REPORT

Case 1- A seven-year-old female patient with no known medical condition was admitted to a pediatric clinic 48 h after being rescued from an earthquake on February 6, 2023. The right arm was trapped under debris during that time. There was no fracture. Due to compartment syndrome, a fasciotomy was performed on the right arm. The patient underwent debridement twice in February 2023. The patient complained of severe pain in the right arm that did not respond to analgesics. The character of the pain was neuropathic. In February, a 25 mcg/h TFP was started in the intensive care unit (ICU), and the pain was relieved. The patch was changed every three days. The patient was transferred to the physical medicine and rehabilitation (PMR) clinic on March 22. There was a restricted and painful range of motion (ROM) in the right elbow, wrist, and finger flexion and extension. There was hypoesthesia and hyperalgesia on the right hand and forearm. Electrotherapy, mild stretching,

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ROM, and desensitization exercises were performed daily. The patient had acute epigastric discomfort whenever ibuprofen was taken to relieve the pain; however, the pain in the right arm did not improve. After five weeks, gabapentin 100 mg once daily was added to treatment on March 28, and it was planned to gradually increase the dosage to three times daily. After a few days, the patient began to scream and exhibited symptoms such as trembling, nausea, runny nose, agitation, and pain attacks. During questioning, the patient's grandmother remembered that the patch had accidentally detached when the patient was showering the day before. The grandmother did not inform the patient, doctors, or nurses as she forgot about it after the shower. After applying another patch, all the symptoms disappeared within an hour. The TFP dosage was reduced from 25 mcg/h to 12 mcg/h, and the patient tolerated it well. Even after gabapentin treatment, we could not cease fentanyl use; therefore, after several weeks of using gabapentin three times daily, a plaster was used instead of TFP as a placebo trial. However, after two days with the placebo, the patient again experienced pain and withdrawal symptoms, similar to the previous episode after the shower. When TFP was administered once more, all of these symptoms again disappeared. The patient also experienced these symptoms several times as the time for patch change approached. After four months, the patient was discharged in May 2023 with gabapentin 100 mg three times daily and a 12 mcg/h TFP. The patient was consulted with a child psychiatrist due to probable TFP dependency in the PMR clinic and followed up after discharge.

Case 2- A 13-year-old female patient without any medical condition was rescued 40 h after the earthquake in February 2023. Afterward, a right transtibial amputation and a right upper leg fasciotomy were performed. The patient was admitted to the pediatric ICU. Due to crush syndrome, plasmapheresis and dialysis were performed multiple times in February. In the ICU, a 25 mcg/h TFP was started every three days in February 2023 due to pain in the right lower extremity. Debridement procedures were performed several times. After almost two and a half months, the patient was transferred from the ICU to the PMR Clinic. There was allodynia and hyperalgesia in the right lower extremity. Electrotherapy, mild stretching, ROM, desensitization exercises, and an amputee rehabilitation program were started. A month later, similar to the first case, the TFP became unintentionally detached while taking a shower. The patient also experienced symptoms such as trembling,

yawning, nausea, runny nose, agitation, visual hallucinations (bugs crawling on her extremities, walls approaching her), and pain attacks that were controlled with supportive treatments. The dosage of TFP was lowered from 25 mcg/h to 12 mcg/h. Eventually, after nearly four months, the TFP medication was discontinued without any complications.

DISCUSSION

In this paper, we describe two pediatric cases who were affected by an earthquake and needed TFP treatment since their severe pain did not respond to nonopioid analgesics. They both experienced difficulties when attempting to cease fentanyl.

The transdermal use of fentanyl is relatively safer when used in accordance with the medical prescription, and the risk of dependency is relatively low.^[8-11] On the other hand, there are many case studies showing that misuse of TFP can cause mortality and dependency.^[2,12,13] Jobski et al.^[12] retrospectively analyzed 985 spontaneous reports on abuse, dependence, and withdrawal of fentanyl through various administration routes. Forty-three percent of these reports are related to transdermal formulations and mostly to a musculoskeletal indication. However, all their patients were adults, and they did not have information about whether those patches were misused or not. Alpcan et al.^[14] reported a child who developed respiratory arrest due to inappropriate use of two fentanyl patches at the same time.

To our knowledge, the two cases presented here are the first pediatric patients to show signs of dependence and withdrawal after discontinuation of transdermal fentanyl patches. In the literature, there were only five case reports that specifically attribute dependency and withdrawal to transdermal usage rather than misuse, all of which included adults. A 59-year-old male with a history of marijuana addiction used TFPs both by chewing and transdermally.^[3] The second case was a 78-year-old male who used TFPs for seven years for chronic low back pain.^[4] In the third case report, a 48-year-old male was diagnosed with gastric cancer, and the patient used TFPs for 18 months.^[5] The fourth case was a 63-year-old male with a history of opium gum and alcohol use disorder who used TFPs to cope with withdrawal symptoms caused by opium gum.^[6] The fifth case was an 80-year-old female in a hospice who developed withdrawal symptoms after the first TFP tapering attempt.^[7]

Noyes and Irving^[15] studied 13 children who were taking morphine to relieve cancer-related pain. They used TFPs to cease morphine and reported that only one patient had withdrawal symptoms related to discontinuation of TFPs. Similarly, Hunt et al.^[16] investigated the efficacy of the TFP in 26 children requiring opioids for pain in life-threatening disease. Among the three children who weaned off fentanyl when they became pain free, withdrawal symptoms were noted in one patient. Two cases involved in this report are seven- and 13-year-old girls, both of whom were rescued from the earthquake. The TFP was administered for severe musculoskeletal pain unresponsive to other analgesics, and the TFP discontinuation trial caused withdrawal symptoms in both patients. After four months, the first patient experienced significant difficulty during discontinuation and had to be discharged using 12 mcg/h TFPs. Maathuis and Dijkstra^[7] suggested a method that avoids withdrawal symptoms by using a tailor-made slow dosage tapering strategy. They achieved a reduction in dose as low as 3 mcg/h by reducing the surface of the patch using an insulating tape accordingly. In our case, whether tapering off TFP below 12 mcg/h with a more gradual scheme similar to that above could avoid withdrawal remains unanswered.

In conclusion, while misuse and adverse effects are more commonly reported with the transdermal route, likely due to its higher accessibility and prescription rates compared to other routes, TFPs are an effective treatment option for severe pain unresponsive to other analgesics. Dependency and withdrawal symptoms are relatively rare when the transdermal route is preferred. The two cases presented here are the first pediatric patients to show signs of dependence and withdrawal after discontinuation of TFP. To avoid dependency, TFPs should be used with caution in children with severe musculoskeletal pain, even for short periods of time.

Patient Consent for Publication: A written informed consent was obtained from the parent of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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