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Case Report

Anaesthesia Section

The Incidence of Severe Diarrhea with Transdermal Fentanyl Patch: An Uncommon Event

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ABSTRACT

Cancer pain is a major problem for the health care providers. One of the most important aspects of cancer pain is palliative care management. Recently, different research finding shows the efficacy of opioid analgesics such as fentanyl transdermal patch in chronic pain management. Transdermal Fentanyl patches may cause side effects such as drowsiness, dizziness, itching, life-threatening or serious breathing difficulties and diarrhea, mainly during the first 72 h of patient's treatment initiation and any time when the drug's dose is increased. We report three case reports of severe diarrhea without most common side effects associated with Fentanyl patches during first 72 h of patient's treatment.

Keywords: Analgesics cancer, Chemotherapy, Pain

CASE REPORTS

Case 1

A 17-year-old female with bilateral breast cancer with spine metastasis was admitted on June 2014 in oncology ward of Rasool Akram medical hospital, Tehran, IRI. The patient was a known case of breast cancer from two years ago. The patient referred to our hospital because of severe pain (VAS>8) due to numerous metastases to the lungs and the spine. The patient with severe pain admitted in the Oncology Department for cancer chemotherapy and pain management. By request and consulting of the Oncology Service with pain department and after considering the other conditions, we choose the 25 micro transdermal fentanyl patch on deltoid muscle. Twelve hours after the start of treatment, the patient suffered from severe diarrhea. After the patient's visit, she mentioned over 10 times defecation without previous history of diarrhea. According to the clinical condition of the patient, we decided to remove the fentanyl patch from the deltoid area. In the 12 h after that we visited the patient frequently and saw the reducing of patient's diarrhea frequency and the return of the patient's normal defecation habitus. With respect to patient's pain continuity we used the other form of analgesic drug such as infusion of fentanyl and apotel. We routinely used fentanyl infusion in different part of our hospital (post up pain and chronic pain management) but we did not encounter any GI problem such as diarrhea.

Case 2

A 45-year-old female with right ovarian adenocarcinoma and hepatic metastasis was admitted on September 2014 in oncology ward of Rasool Akram medical hospital, Tehran, IRI. The patient was a known case of ovarian cancer from 3.5 y ago. Now the patient was referred to our hospital due to severe pain (VAS = 7) due to numerous metastases to the hepatic tissue. The patient with severe pain admitted in the Oncology Department for cancer chemotherapy and pain management. By request and consulting of the Oncology Service with pain department due to unresponsiveness to the intramuscular pethidin administration and according to the patient condition, we considered using the 50 micro transdermal fentanyl patches on deltoid muscle. Twelve hours after starting the treatment, the patient suffered from severe diarrhea. After the patient's visit, she mentioned 8 times defecation without previous history of diarrhea. According to the clinical condition of the patient, we decided to remove the fentanyl patch from the deltoid area. In the next following 12 h, we visited the patient and saw the reducing of patient's diarrhea frequency and the return of the patient's normal defecation habitus. There wasn't any other side effect other than diarrhea with fentanyl patch. With respect to patient's pain continuity we scheduled the patient for the superior hypogastric plexus block. After that and with the pain score VAS < 4 she used methadone tablets for pain treatment.

Case 3

A 55-year-old male with lung squamous cell carcinoma from two years ago and lumbar spine metastasis from 6 months ago was admitted on July 2014 in oncology ward of Rasool Akram medical hospital, Tehran, IRI. The patient admitted to our hospital in the oncology department for pain management and cancer chemotherapy. He had severe pain (VAS>8). By request and consulting of the oncology service with pain department due to unresponsiveness to the intramuscular pethidin administration and oral methadone and according to our survey, we considered the 25 micro transdermal fentanyl patch on deltoid muscle. Fourteen hours after the start of treatment, the patient suffered from severe diarrhea. After the patient's visit, he said after beginning of transdermal drug his pain diminished considerably but he had 7-8 times defecation without previous history of diarrhea. According to the clinical condition of the patient, we decided to remove the fentanyl patch from the deltoid area. In the 16 hours later, we visited the patient and saw the reducing of patient's diarrhea frequency and the return of the patient's normal defecation habitus. There wasn't any other side effect other than diarrhea with fentanyl patch. With respect to patient's pain continuity we decided to use oral opioid and intramuscular pethedine.

DISCUSSION

There was no any possibility of drug interaction because after taking a fentanyl infusion and chemotherapy, the patient was not having diarrhea problem. Other types of fentanyl patch were owned by other companies also which did not had this problem. Some reported benefits of this form of drug includes: Less frequent dosing, continuous and long term delivery of medications, lower peak plasma drug concentration and avoidance of first-pass metabolism . These benefits suggesting that this administration form may have better compliance, effectiveness and safety in compared with

oral administration [1,2]. There are four different form of fentanyl transdermal patches 25, 50, 75 and 100 mcg/hr. The fentanyl patch approximately takes 2-3 days to reach steady state, and when it is removed, the remained fentanyl absorption in the skin continues for hours. It takes approximately 17 h for 50% fentanyl blood levels dropping when the patch is removed, so interactions between fentanyl and other drugs such as sedatives, hypnotics and opioids are still possible hours after the patch has been removed. This means the removal of the fentanyl patch does not quickly eliminate the risk of interactions between these drugs.

Increased body temperature induced by fever, heating blanket, exposure to a humid and hot environment or vasodilating anesthetics increases peripheral blood flow to the skin, which subsequently increases the rate of systemic drug absorption and toxicity [3,4].

The transdermal patch released fentanyl at a constant rate for up to 72 h. Fentanyl is a synthetic opioid with short-acting analgesic activity [5]. Some of the unique property of Fentanyl compared with morphine includes: proper lipid solubility, approximately 75 times more potent than morphine, greater transdermal permeability and smaller molecular mass. Fentanyl metabolites are not pharmacologically active that means there are no side effects that are related to accumulation of metabolites. Fentanyl has more affinity and higher selectivity for μ1 receptors. Therefore, there is not side effect such as nausea, vomiting, and constipation that may be seen with morphine. These effect caused by μ2 receptors activation [5].

In all patient we use the fentanyl production by kern pharma fentanilo matrix (espanol) .The drug had expire date to the end of 2015.

Cancer pain management is one of the most important goals of palliative care [6]. Recently, different research results showed the efficacy of opioid analgesics in chronic pain management. These finding have played at least a role in inducing the standards implementation in pain treatment through the offers of government organizations worldwide [7].

Pain is a major health problem, highly prevalent (14–100%, in active phase treatment is 50– 70%) and distressing symptom in cancer patients [8]. According the literature reports survey, pain incidence in advanced stages of cancer will be seen as high as 60–90% [9].

The main reason for poor responding to optimal doses of opioid this problem is the following: adverse effects (generalized nausea, vomiting, myoclonus, delirium or severe sedation) may be developed before achieving a favorable analgesia, poor analgesic response despite rapid dose escalation [10]. Fentanyl serum concentrations increase gradually and peak serum concentrations generally reached 12 - 48 h after initial application. According to the previously done investigation we may encounter difficulties for adjusting the conversion [10].

CONCLUSION

We routinely used fentanyl infusion 4-10 micro/hour (but fentanyl patch at least released 25 micro/hour) in different part of our hospital (post up pain and chronic pain management) but we did not encounter any GI problem such as diarrhea. The problem related to fentanyl patch (specific company) but not fentanyl infusion.

The problem was not related with the type of drug or the patch dosage. There wasn't any other side effect other than diarrhea with fentanyl patch.

Thus, the case study of these patients has revealed that transdermal fentanyl patch could be causally related to the gastrointestinal event. Although, the precise mechanism of diarrhea is unclear, since other causes of diarrhea were ruled out by suitable investigations. Thus this case report high lightens the importance of close monitoring of cancer pain during use of transdermal fentanyl patch among the less common complication such as diarrhea that affect the compliance of cancerous patient before the patient's pain control achieved.

REFERENCES

[1] Ripamonti CI. Pain management. *Ann Oncol*. 2012;23(Suppl.10):294-301.
[2] Kim JH, Kim M, Sung CW, Kim HS, Jang HJ, Shin YC, et al. High-dose fentanyl patch for cancer pain of a patient with cholangiocarcinoma. *Korean J Intern Med*. 2010;25(3):337-40.
[3] Durand C, Alhammad A, Willett KC. Practical considerations for optimal transdermal drug delivery. *Am J Health Syst Pharm*. 2012;69:116–24.
[4] Wohlrab J, Kreft B, Tamke B. Skin tolerability of transdermal patches. *Expert Opin Drug Deliv*. 2011;8:939–48.
[5] Park JH, Kim JH, Yun SC, Roh SW, Rhim SC, Kim CJ, et al. Evaluation of efficacy and safety of fentanyltransdermal patch (DurogesicD-TRANS) in chronic pain. *Acta Neurochir (Wien)*. 2011;153(1):181-90.
[6] Koyyalagunta D, Bruera E, Solanki DR, Nouri KH, Burton AW, Toro MP, et al. A systematic review of randomized trials on the effectiveness of opioids for cancer pain. *Pain Physician*. 2012;15(3 Suppl):ES39-58.
[7] Christo PJ, Mazloomdoost D. Cancerpain and analgesia. *Ann N Y Acad Sci*. 2008;1138:278-98.
[8] Keefe FJ, Abernethy AP, C Campbell L. Psychological approaches to understanding andtreating disease related pain. *Annu Rev Psychol*. 2005;56:601-30.
[9] Hemati K, Zaman B, Hassani V, Imani F, Dariaie P. Efficacy of Fentanyl Transdermal Patch in the Treatment of Chronic Soft Tissue Cancer. *Anesth Pain Med*. 2015;5(1):e22900.
[10] Nomura M, Kamata M, Kojima H, Hayashi K, Kozai M, Sawada S. Six- versus12-h conversion method from intravenous to transdermal fentanyl in chronic cancer pain: a randomized study. *Support Care Cancer*. 2011;19(5):691-95.

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