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Letter to the Editor

DRUG ERUPTION AFTER SUSTAINED-RELEASE NALTREXONE PELLET IMPLANTATION

Dear Editor,

It is known that the frequency of heroin use and addiction are increasing rapidly in our country as is in the rest of the world (TUBIM 2018). Heroin use disorder presents various difficulties in diagnosis and treatment. Selection of the treatment type appropriate for the patient characteristics, as well as the application of the treatment-specific procedures, requires expertise, experience and a well-established system in this field. Treatment compliance problems seen in the majority of patients, difficulties experienced in the family and in accessing and maintaining treatment have rendered the approach to heroin addiction a specific application area.

In the world and in our country, two types of pharmacological treatment approaches are prominent in heroin use disorder. The first is treatment with agonist drugs defined by the term "substitution". In this approach, drugs such as buprenorphine and methadone are used. The second approach is the antagonist treatment which will be discussed in this letter. In this approach, drugs with naltrexone as the active component have been in use for a long time (Schwartz et al. 2018). Trials on the use of naltrexone in heroin use disorder began in the 1970s and approval was given by the American Food and Drug Administration (FDA) in 1984 for its use in opiate and alcohol use disorders. Although the idea of using naltrexone as a subcutaneous implant instead of taking it orally was put forward in the 1970s, this was first approved in Russia in 2005 (Strang et al. 2019, Krupitsky et al. 2019). While oral buprenorphine / naloxone as agonists and oral naltrexone tablet as an antagonist were being prescribed in Turkey, the Ministry of Health approved the use of naltrexone subcutaneous long-acting implants for heroin use disorders in our country in the last months of 2016. After this approval, long-acting naltrexone subcutaneous implant treatment was started in our clinic in January 2017 in patients diagnosed with alcohol and opiate use disorder. Up to the date of this letter, approximately 280 implantations have been performed in our clinic. The aim of this paper is to report an adverse side effect of naltrexone subcutaneous implantation. The frequency of this side effect and other follow-up data related to this treatment will be reported in another research paper.

Naltrexone implant is placed in the subcutaneous adipose tissue by a minor surgical procedure by psychiatrists who are the authors of this article. Allergic reactions have been observed in some of our patients in the 4 weeks following the implantation. The maculopapular type of rashes that were first observed around the implant area, often mid-lateral to the anterior abdominal wall, tended to merge and spread on the whole body with severe itching (Figure 1). Because of this side effect, the implants of two patients were removed with the recommendation of the dermatology department and five other patients were followed up with the dermatology department of our hospital without removing the implants. Skin biopsy from a patient was reported by the dermatology department as "drug caused skin eruption". The rash and the itch symptoms of the patients whose implants were not removed were controlled by oral antihistaminic drugs and

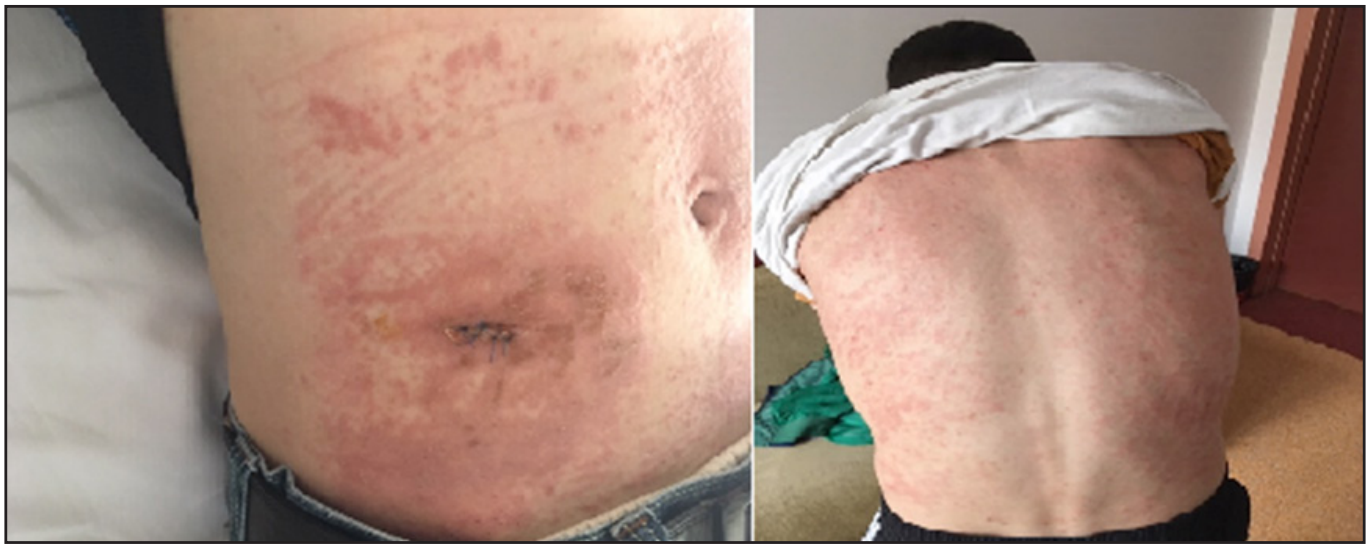

Figure 1. Local and general rash that develops after naltrexone application (same patient)

steroids without any additional side effects following the discontinuation of drugs in approximately eight weeks. While heroin use disorder treatments could be continued with in situ naltrexone implants.

A subcutaneous naltrexone implant is a drug in pellet formulation. In addition to the active ingredient naltrexone, this pellet contains triamnisonolone, a steroid derivative, to prevent naltrexone from causing such reactions. In the 2 patients whose drug eruption necessitated the removal of the implants by the recommendation of the dermatology department, the side effects started early after pellet implantation. In the period following the diagnosis of drug eruption, starting these patients on antihistaminic agents and steroids enabled the continuation of naltrexone implant therapy. According to the verbal information received from other centers using naltrexone subcutaneous implants, each patient was given antihistaminic and steroid-containing drugs concurrently with implant application. We believe that routine administration of antihistaminic drugs and steroids to patients may not be appropriate considering that the adverse side effect has been observed in only 7 of the 280 patients with naltrexone pellet implants.

Sincerely.

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