Skin abscess after the use of transdermal buprenorphine. Case report

Abscesso cutâneo após o uso de buprenorfina transdérmica. Relato de caso

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ABSTRACT

BACKGROUND AND OBJECTIVES: Buprenorphine is a partial agonist semi-synthetic opioid used as an option in the treatment of patients with moderate to severe pain. The only presentation of buprenorphine available in Brazil is for transdermal use. This is an important route of drug administration, especially for the treatment of chronic pain, as it has several advantages, however it is not free from complications. The objective of this study was to present a serious adverse skin reaction after the use of transdermal buprenorphine, requiring surgical intervention.
CASE REPORT: Female patient, 63 years old, hypertensive and diabetic, diagnosed with rheumatoid arthritis, fibromyalgia syndrome and lumbar disc herniation, with severe chronic pain, advised to use transdermal buprenorphine 10 mg to help control algic. After 24 hours of use, the patient developed erythema and local itching, requiring removal of the adhesive, but the lesion progressively worsened with the formation of an abscess and the need for surgical drainage.
CONCLUSION: Transdermal buprenorphine has a favorable safety and tolerability profile, as it reduces the risk of unwanted effects such as respiratory depression, constipation and suicidal ideation. However, its use in senior patients with comorbidities, such as the immunosuppression described in this case, requires greater vigilance, due to the possibility of developing more serious adverse reactions.

Keywords: Abscess, Buprenorphine, Pain.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A buprenorfina é um opioide agonista parcial semissintético utilizado como opção no tratamento de pacientes com dor de moderada a intensa. A única apresentação disponível da buprenorfina no Brasil é para uso por via transdérmica. Esta é uma via importante de administração de fármacos, principalmente para o tratamento de dor crônica, já que apresenta diversas vantagens, no entanto não é isenta de complicações. O objetivo deste estudo foi apresentar uma reação cutânea adversa grave após o uso de buprenorfina transdérmica, com necessidade de intervenção cirúrgica.
RELATO DO CASO: Paciente do sexo feminino, 63 anos, hipertensa e diabética, com diagnósticos de artrite reumatoide, síndrome fibromiálgica e hérnia de disco lombar, portadora de dor crônica intensa, com orientação de utilizar buprenorfina transdérmica 10 mg para auxiliar o controle álgico. Após 24 h de uso, a paciente evoluiu com eritema e prurido local, sendo indicada a remoção do adesivo, porém a lesão piorou progressivamente com formação de abscesso e necessidade de drenagem cirúrgica.
CONCLUSÃO: A buprenorfina transdérmica apresenta um perfil favorável de segurança e tolerabilidade, pois reduz o risco de efeitos indesejados, como depressão respiratória, constipação e ideação suicida. No entanto, seu uso em pacientes idosos portadores de comorbidades, como a imunossupressão descrita no caso, exige maior vigilância, devido à possibilidade de desenvolvimento de reações adversas mais graves.

Descritores: Abscesso, Buprenorfina, Dor.

INTRODUCTION

Buprenorphine is a partial agonist opioid drug approved by the Brazilian National Health Surveillance Agency (ANVISA - *Agência Nacional de Vigilância Sanitária*) for transdermal use in the treatment of patients with moderate to severe pain. It is a semi-synthetic opioid, partial agonist of the μ receptor and antagonist at the δ and κ receptors[1].
The characteristics of transdermal buprenorphine are its slow onset of action and prolonged duration, as well as its good use profile for patients with chronic pain, and it should not be used to treat acute

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HIGHLIGHTS
- Buprenorphine is a semi-synthetic opioid drug, partial agonist of the μ receptor and antagonist of the δ and κ receptors, indicated for the treatment of moderate to severe pain.
- The buprenorphine available in Brazil is transdermal, a drug presentation associated with reduced aggression to the gastrointestinal system, which bypasses hepatic first-pass metabolism, and greater patient adherence to treatment.
- Transdermal buprenorphine can be associated with pruritus, erythema and rash, which, in immunocompromised patients, can result in the appearance of abscess, requiring debridement and surgical drainage.

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pain, whether moderate or severe[2]. Its agonist action on the ORL-1 receptor reduces reward effects and delays the development of tolerance to analgesic effects[2]. In Brazil, buprenorphine is only available for transdermal application, a route defined for having a reservoir for drug delivery by a local or systemic mechanism of action and a specific dose formulation[2,3]. The transdermal administration of buprenorphine has become increasingly popular due to its significant advantages[3]. For instance, transdermal drugs bypass the first-pass metabolism in the liver that affects orally administered drugs, protecting it from damage[3]. In addition, transdermal drugs reduce the risk of aggression to the gastrointestinal system observed with oral drug administration, increase the likelihood of consistent patient use and allow them to be administered continuously and at stable intervals[3].

Although transdermal buprenorphine presents its own pharmacodynamics and pharmacokinetics, it is not free of adverse effects. According to the manufacturer of the Butrans brand and generic transdermal buprenorphine patches marketed in the USA, serious reactions at the application sites are rare and characterized by inflammatory processes that can lead to the appearance of burns and vesicles[4]. The onset time is also variable and can take from days to months[4]. In a 2013 pooled analysis of 16 chronic pain studies conducted in the USA, the incidence of local reactions with transdermal Butrans was considered low (23.4%). The majority of local reactions in this analysis (98.3%) were considered mild and moderate in severity, and the discontinuation rate of the transdermal device was only 4.4%[4]. To date, there is no data in the literature on the prevalence of local adverse reactions in the Brazilian population.

The present study's objective was to describe an exacerbated skin reaction with abscess formation following the use of transdermal buprenorphine, requiring debridement and surgical drainage.

CASE REPORT

A 63-year-old female patient diagnosed with systemic arterial hypertension, type 2 diabetes mellitus, rheumatoid arthritis, chronic pain secondary to fibromyalgia syndrome and lumbar disc herniation with radicular conflict in the emergent roots of L5 bilaterally. She was hospitalized with a request for an assessment by the pain clinic team at the Santa Izabel Hospital of the *Santa Casa de Misericórdia da Bahia* for pain control. She had severe pain which compromised her quality of life. The patient was regularly taking pregabalin 150 mg/day^{-1}, leflunomide 10 mg/day^{-1}, methotrexate 12.5 mg 12/12 h and folic acid 5 mg (both once a week), prednisone 15 mg/day-1, and dipyrone 1 g every 8 h.

During the anamnesis, the patient reported that she was being monitored by another health service, which indicated the use of transdermal buprenorphine 10 mg to help control the pain of associated comorbidities. However, the patient had a serious adverse skin reaction when using the drug, even though she applied the patch as recommended on the package leaflet, on intact skin, and cleaned it with soap and water.

Although the complication did not occur in this case report, it was decided to report the patient's case due to the scarcity of similar cases published in the literature and the increasingly widespread use of transdermal drugs. Some information, such as the collection of cultures and laboratory tests carried out at the time of the complication, could not be accessed.

The patient reported that she had started using the patch by applying it to her back on intact skin. After 24 hours of use, local itching and erythema began, after which the patch was removed. The patient continued to suffer from local pruritus and worsening erythema, developing the formation of pustules around 24-48 hours after the patch was removed. The condition continued to increase and 4 days after the buprenorphine patch was removed the patient reported severe pain in the back, worsening of the erythema, a sensation of heat and the presence of a large nodule in the area. She denied having fever throughout the period. The patient went to the emergency department, where she was diagnosed with a skin abscess and was hospitalized. Antibiotic therapy was started and the patient underwent surgical drainage of the large abscess on the sixth day (Figures 1, 2, 3 and 4).

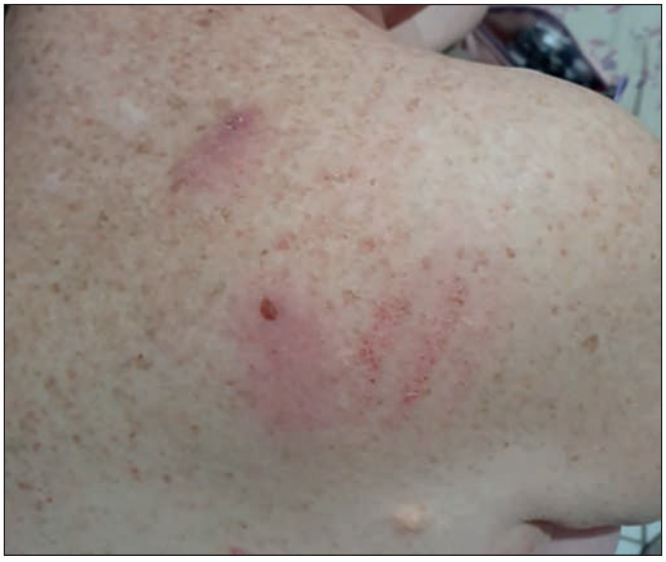

Figure 1. Skin lesion 24 hours after removing the patch

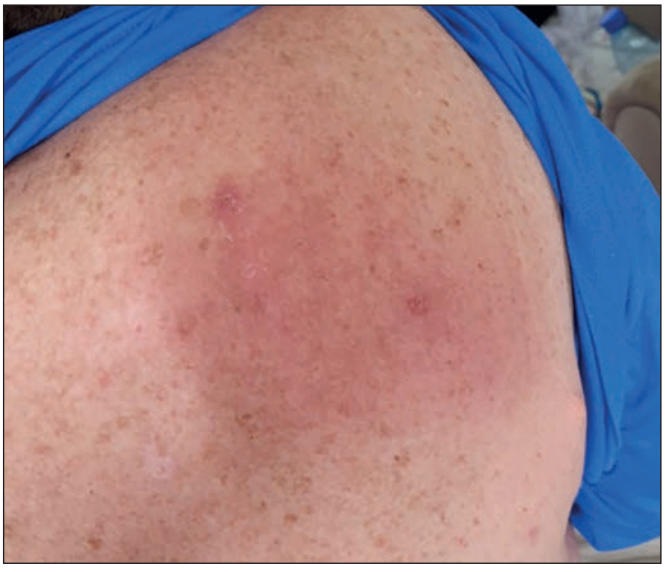

Figure 2. Skin lesion 48 hours after removing the patch

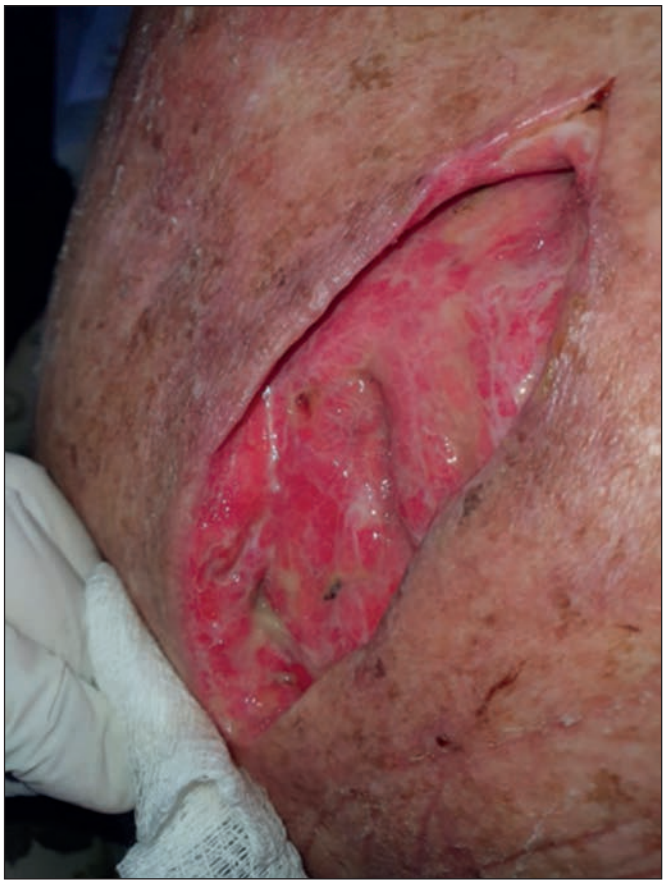

Figure 3. Skin lesion 6 days after removing the patch

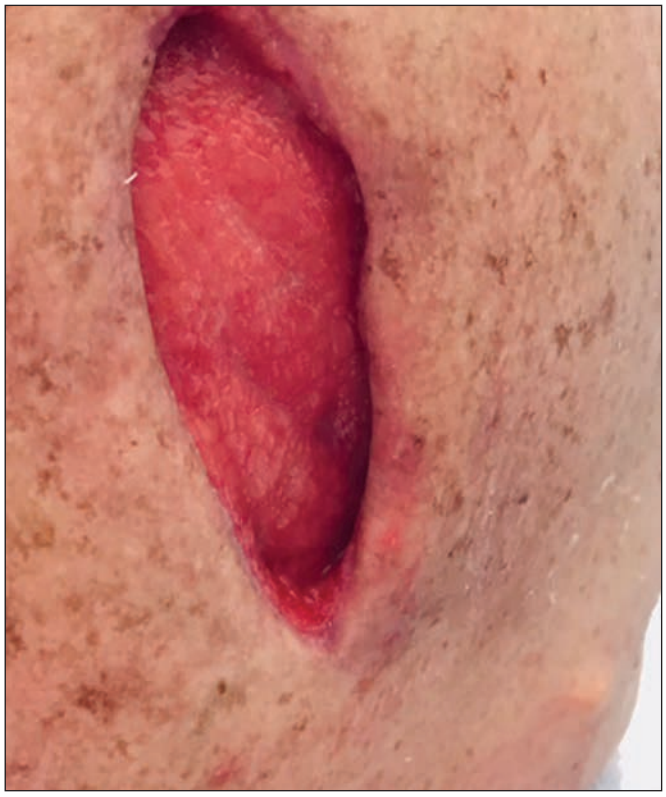

Figure 4. Skin lesion 7 days after removing the patch

During the post-operative period, the patient wore a vacuum dressing, as she had an extensive surgical incision. After that, the patient healed well.

DISCUSSION

The clinical case report presented a 63 years old patient with comorbidities, which meant she needed immunosuppressants. The patient had a contact dermatitis-type reaction after using a buprenorphine patch. She subsequently developed a secondary local infection, complicated by the formation of an abscess, which required debridement and surgical drainage.

Treatment of pain is a major challenge, especially when it becomes chronic and occurs in senior patients with comorbidities, such as in the present case, who have a potential risk of developing adverse reactions and the severity of adverse effects. It is necessary to look for new treatment strategies and drugs that make it possible to manage pain with potentially safer but equally effective therapeutic options. In this context, there is the possibility of using transdermal buprenorphine, a drug which, as it is a partial agonist at the μ opioid receptor and an antagonist at the δ and κ opioid receptors, may contribute to its favorable safety and tolerability profile, reducing the risk of adverse effects such as respiratory depression, constipation and suicidal tendencies[3,5].

The ORL-1 receptor agonist activity may also contribute to buprenorphine's analgesic efficacy, as it has been shown to promote analgesia in the dorsal horn of the spinal cord[5]. Orally administered buprenorphine is known to have only 10% bioavailability, although recent advances in drug delivery have overcome this problem[5]. The sublingual formulation provides approximately 28-51% of bioavailability, the transdermal formulation,15%,and the buccal film, 46-65%[5]. Of these, the only presentation available in Brazil is transdermal.

The buprenorphine transdermal formulation is indicated for the treatment of moderate or severe pain that justifies the use of daily, 24-hour, long-term opioid treatment and for which alternative treatment options are inadequate, such as the case mentioned above[2,3,6]. However, what the literature shows is that transdermal buprenorphine has some peculiarities, including the potential to develop other adverse effects, which go beyond the effect of the drug itself[6]. The transdermal route offers less flexibility in terms of the dose of the drug to be administered and is associated with longer delivery and elimination times. In addition, there is a risk of allergies, irritations and skin lesions, often serious, as described by the study[6], following the use of transdermal fentanyl.

A literature review[5] found that symptoms at the application site, such as pruritus, erythema and skin rash are among the most common adverse effects associated with the use of transdermal buprenorphine. A dose-response relationship between the potency of the buprenorphine patch and the appearance of local adverse reactions has already been described in other studies. In an analysis of 5 placebo-controlled studies, in which 3 different doses of the transdermal buprenorphine patch were evaluated, the 20 $\mu g.h^{-1}$ patch had

the highest incidence of local adverse reactions (17.8%), followed by the 10 $\mu g.h^{-1}$ patch (16.5%). The incidence of adverse local reactions in the placebo group was 12.7% and higher than the incidence in the group using the 5 $\mu g.h^{-1}$ patch (8.25%)[7].

For transdermal buprenorphine and other transdermal products, the size of the patch increases as its potency increases and, consequently, there is a greater area of contact with the skin[7]. The size of the patch has already been identified as a risk factor for the development of contact dermatitis with transdermal drugs[7].

Other risk factors include the type of patch (matrix-type patches are better tolerated than reservoir-type patches), duration of treatment and application site[4]. Some areas of the skin are more susceptible to developing dermatitis[4]. Contact dermatitis resulting from transdermal drug delivery systems usually occurs as a result of skin irritation by the drug itself or other components of the patch, or may even be related to the occlusive effect caused by the patch[4]. Local adverse reactions with the development of contact dermatitis can occur acutely after a single exposure or after repeated exposures and possible damage to the stratum corneum of the skin[4].

Allergies and skin irritations associated with the use of transdermal buprenorphine are generally self-limiting and have little impact on the patient's progress and quality of life, as well as being easily reversed after the device is removed[4,7]. There are no reports in the literature of patients who have developed a secondary local infection, complicated by the formation of an abscess, requiring debridement and surgical drainage. The development observed in the present case can be explained by the fact that the patient in question was immunosuppressed due to associated comorbidities[8]. In these cases, the most common dermatological manifestations are pyoderma, such as cellulitis, erysipelas and boils, although abscesses have also been described[8]. These, when extensive, should be treated with antibiotic therapy and surgical drainage[8]. After appropriate treatment, the patient progressed favorably, with complete resolution of the clinical condition.

CONCLUSION

As transdermal buprenorphine has its own pharmacodynamics and pharmacokinetics; it is considered an appropriate opioid for the treatment of chronic pain. However, its use is not without adverse effects and the possibility of complications, which must be treated appropriately. Although allergies and skin irritations are the most common adverse effects following the use of transdermal drugs, in immunocompromised patients they can develop unfavorably, and also present the formation of abscesses, requiring debridement and surgical drainage.

AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualization, Research, Writing - Preparation of the original, Writing - Review and Editing
Anita Perpetua Carvalho Rocha de Castro
Conceptualization, Writing - Preparation of the original, Writing - Review and Editing, Supervision
Waléria Rios Carneiro
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