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Fixed drug eruption due to flupirtine: A case report with review of literature

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Abstract

Fixed drug eruptions (FDE) are common cutaneous adverse drug reactions, commonly caused by antibiotics and analgesics. Flupirtine, a selective potassium channel opener is non-opoid, non- NSAID analgesic used for the treatment for musculoskeletal pain. Of all the mentioned side effects of flupirtine in literature, fixed drug eruption is absent. Here, we report a case of 55-year-old female of FDE due to flupirtine.

Keywords: Flupirtine, Fixed drug eruption, FDE

Introduction

Flupirtine is a non-opioid, non-NSAIDS analgesic without antipyretic or anti-phlogistic properties. This selective neuronal potassium channel opener, evolved rapidly into one of the most preferred analgesics for the treatment of musculoskeletal pain.[1,2] Although it is not approved by United State Food and Drug Administration (USFDA), still it is being used over various countries including India. Flupirtine induced cutaneous side effects are not commonly reported.[1,2] We are hereby reporting a case of fixed drug eruption (FDE) induced by flupirtine. Current literature search did not show any FDE with flupirtine.

Case Report

A 55-year-old female presented with multiple painful, slightly itchy, hyperpigmented patches over trunk and lower extremities of one day duration. Patient gave history of taking tablet flupirtine 100 mg twice daily for past three days for backache. There was no history of similar lesions in the past. There was no history of fever or any other drug intake prior to the onset of skin lesions. Three well defined, erythematous plaques with violaceous border of varied sizes from 3x2 cm to 5x6 cm present over trunk and lower extremity. (Fig. 1) There was no involvement of any mucosa or genitalia. Routine investigations were within normal limits. The causality assessment was carried out using Naranjo ADR probability scale and the score was of 6, which signifies flupirtine as a probable cause for FDE. Patient was asked to stop the offending agent and was started on topical corticosteroid and oral anti-histaminics with complete recovery within a week. Patient was not ready for rechallenge for the offending drug.

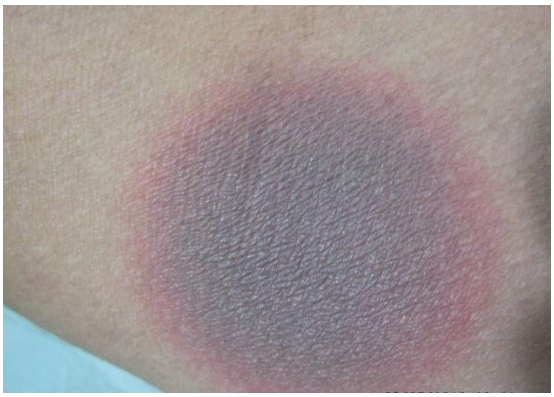

Fig. 1: Violaceous plaque with erythematous disorder over trunk

Discussion

Fixed drug eruption (FDE) represents the most common form of adverse drug reactions amongst Indians.[3] It characteristically recurs at the same site or sites, every time the drug is administered.[4] With each exposure, however, the number of involved sites may increase. FDE presents as round to oval, sharply marginated, edematous patch with violaceous or dusky erythema associated with itching and burning.[4] The eruptions usually occur within hours of administration of the offending drug and resolves spontaneously within days to weeks with residual pigmentation.[2] Most common sites involved are oral mucosa, genitalia, although any skin or mucosal sites can be involved. FDE appeared after consumption of flupirtine. In index case, our assessment of this adverse drug event on Naranjo scale, the score was 6, which make flupirtine as the probable cause of this adverse drug event.[5]

Flupirtine is a non-opioid, non-NSAIDS analgesic without antipyretic or anti-phlogistic properties.[1,2] It constitutes a unique class within the group of WHO-I analgesics and was first approved in Germany at the national level in 1989.[6] This selective neuronal potassium channel opener, evolved rapidly into one of the most preferred analgesics for the treatment of

musculoskeletal pain.[1,2] Although it is not approved by United State Food and Drug Administration (USFDA), still it is being used over various countries including India.

It is a triaminopyridine having a chemical structure -2-amino-3- ethoxy-carbonylamino-6-4 fluoro-benzylamino-pyridine.[7] Flupirtine is used primarily as analgesic with muscle relaxation, and neuro-protection are additional benefits.[1,2,7] It acts indirectly as N-methyl-D-aspartate (NMDA) receptor antagonist by activation of potassium channel. It binds and activate G protein coupled inwardly rectifying potassium channel. This leads to hyper-polarization of neuronal membrane causing its stabilization. The drugs activating these channels are called as selective neuronal potassium channel opener (SNPCO) and flupirtine is the prototype drug.[1] It is a hydrophilic compound and is completely absorbed from the gastrointestinal tract. Metabolism of flupirtine occurs in liver and excreted by urine and feces. Safety of flupirtine in pregnant, lactating mother and children below 6 years of age is not established. Dose of flupirtine should be reduced to 50% in patients with hepatic and renal impairment.[7,8] Flupirtine is contraindicated in patients with history of hypersensitivity to flupirtine, cholestasis, chronic alcoholism, hepatic encephalopathy, myasthenia gravis and liver disease.[1] Studies have shown effectiveness of flupirtine in acute pain state like post operative pain, traumatic injury, headache, migraine, as well as in chronic pain such as musculoskeletal pain, cancer pain.[1,2,7,8]

Dizziness, drowsiness, pruritus, dry mouth and gastric fullness, nausea and muscle tremor are common side effects. Other side effects are vomiting, disturbed sleep, heartburn, sedation, headache and fatigue. Rare and serious side effects includes increase in transaminase levels, drug induced hepatitis, ataxia and nervousness.[1,2,6,7,8]

Gold standard for diagnosis for FDE is drug rechallange, which leads to reappearance of the lesions at the same sites.[4] Going through the literature, we could not found any case report or study regarding FDE caused by flupirtine. We hereby reporting first case of FDE induced by flupirtine.

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