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Case Report Open Access

An Adverse Drug Reaction to Atazanavir in a Client Allergic to Sulphur – A Case Report

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Abstract

Atazanavir is a protease inhibitor that is used as an antiretroviral drug. It is co-formulated with ritonavir to boost its plasma concentration and given together with two other antiretrovirals for a highly active regimen. As much as the drug literature warns of a cutaneous reaction, it has not communicated effectively on the possibility pf this occurring in patients with a sulphur allergy. No such case has been reported before. We report a case of a cutaneous adverse drug reaction in a male patient with a known allergy to sulphur in whom it was used for post-exposure prophylaxis. There is need for taking comprehensive patient history and relate it to reactions reported in literature to prevent recurrence of adverse reactions.

Keywords: Atazanavir; Sulphur allergy; Cutaneous reaction

Introduction

Atazanavir (ATV) is a highly active azapeptide inhibitor of the HIV protease being the first and the only protease inhibitor designed to be administered as a once daily dose. It is co-formulated with ritonavir(r) as a booster (Atazanavir/Ritonavir - 300 mg/100 mg). Ritonavir inhibits the CYP450 enzymes that metabolizes ATV and ensures maintenance of plasma levels above the minimum effective concentrations. The launch of ATV brought hope that it will not have the many side effects that were seen with earlier agents of this class of drugs, such as unfavorable adverse events like hyperlipidemia, diarrhea and lipodystrophy [1].

It is the most well tolerated amongst the protease inhibitors with mild and rare side effects. The most common side effects from the atazanavir monograph were jaundice; headache; fever; depression; nausea; diarrhoea and vomiting; paraesthesia; spontaneous bleeding episodes in haemophiliacs [2]. However, dolutegravir is a newer drug in the class of integrase strand transfer inhibitors that is much more effective, has a higher genetic barrier and fewer side effects. It is used in first line regimens and for pre-exposure prophylaxis [3].

In Kenya, it is recommended for use in first line regimens for people who inject drugs (PWID) and in second line regimens for clients failing on first line regimens. It is usually administered together with nucleoside reverse transcriptase inhibitors [4]. The choice of an atazanavir based regimen may be informed by; the need to simplify the regimens, minimal side effects or virologic failure. Atazanavir is also used in regimens for post-exposure prophylaxis (PEP) together with tenofovir (TDF) and lamivudine (3TC).

Case Report

On 28th January 2018 a 27-year-old, ARV naive male reported to the casualty department of a health facility with a history of potential exposure to HIV. An antibody test was done which ruled out HIV infection. He did not have other complaints and was issued with TDF/3TC/ATV/r to be taken once daily for 28 days.

He came back on the 4th of February with complaints of burning sensation around the penile area. He was reassured and given chlorpheniramine and prednisone. He came back the following day with maculopapular rashes, pruritus and peeling of the skin at the same area, now extending to the lower abdomen and inner thighs. The ARVs were stopped and the client treated with flucloxacilin, metronidazole and prednisone. He came back for review after 3 days and reported to be doing well and was advised to continue with the prescribed medicines to complete the dose.

Discussion

The case above occurred in a client with a known history of allergy to sulphur having had two previous reactions. The first reaction was due to sulphadoxine pyrimethamine which was administered to treat malaria several years before this episode. The reaction was mild, and he was treated as an outpatient and recovered well. The second reaction was due to co-trimoxazole (sulphamethoxazole trimethoprim) which was used to treat an upper respiratory infection. This was a severe reaction (most likely Steven Johnson Syndrome) that required hospitalization. The client was admitted in a health facility and managed in the burn's unit. He recovered well and was discharged after 5 days.

The client was well until he had an exposure that could have led to HIV infection necessitating the administration of PEP. The regimen issued was TDF/3TC/ATV/r. The Atazanavir (Anzavir-R ®) used in this case was formulated as a sulphate salt and this could have increased the likelihood of recurrence of the skin reaction considering the history. An independent reaction to atazanavir could also have occurred since literature reports it can cause various grades of skin reactions. Severe dermatologic reactions in the clinical trials were reported at an incidence of 1-6% [5]. Cases of SJS and erythema multiforme associated with atazanavir have been reported but the frequency has not been given [6].

The reaction in our case started after 7 days of taking atazanavir. The

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mean interval between rash onset and intake of atazanavir is reported to be 10 days [6]. Three of the cases from the literature reviewed presented with pruritis as in our case [5]. Most antiretrovirals are rapidly approved and the data from clinical trials may not sufficiently show what to expect in clinical practice. In one clinical trial, only 3 out of 323 subjects developed cutaneous adverse reactions giving an incidence rate of 0.001% and withdrawal of treatment only occurred in one case [7,8]. The incidence of severe cutaneous reactions due to ATV from other trials was 0.4%.

Conclusion

Despite having a low incidence, severe skin reactions can occur due to atazanavir. This could be made worse in cases where patients are allergic to sulphur since it is formulated as a sulphate. Clinicians need to take comprehensive medical history before initiating antiretroviral therapy with atazanavir containing regimens. The product insert clearly indicates that it is contraindicated in patients with previous demonstrated hypersensitivity such as Steven Johnson syndrome and erythema multiforme. Shorter review periods (preferably 2 weeks) should be given to allow for closer monitoring of clients starting regimens with atazanavir.

Ethical Considerations

Approval was sought from the organizations while the affected patient gave informed consent prior to collection of data.

Conflict of Interest

There is no conflict of interest to declare by all the authors.

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