Case report

Fixed drug eruption due to co-trimoxazole: a case report

B. C. Dwari , S. Bajracharya, S. Gupta, P. Mishra, S. Palaian, K. Alam, S. Prabhu, M. Prabhu

Department of Dermatology, Department of Pharmacology, Department of Hospital and Clinical Pharmacy, Manipal Teaching Hospital / Manipal College of Medical Sciences, Pokhara, Nepal and Department of Dermatology, Kasturba Medical College, Manipal, Karnataka, India.

Correspondence to: Dr. Binayak Chandra Dwari MD, Lecturer, Manipal Teaching Hospital / Manipal College of Medical Sciences, Pokhara, Nepal. Phone: +977 61 526416 Extn: 130/221

Background: Cotrimoxazole is a synergistic fixed dose combination of sulfamethoxazole and trimethoprim used in treatment of several infections including urinary, respiratory, gastrointestinal tract infections. Because of its wide spectrum and low cost it is one of the most preferred antimicrobial in Nepal. Fixed drug eruptions (FDEs) are drug rashes which tend to occur at the same site in the particular patient each time when an offending drug is administered. Co-trimoxazole is a drug commonly implicated for causing FDEs.

Case report: We report a case of FDE due to co-trimoxazole occurred in a patient for whom it was prescribed by a local practitioner without taking adequate medication history. We also carried out the causality, severity, preventability and predictability as well as the economic impact of the associated adverse drug reaction (ADR). The report suggests that before prescribing any drug, clinicians should take appropriate medication history and upon occurrence of any ADR the patient should be counseled and instructed to communicate with the clinicians wherever they attend for the next time.

Keywords: Causality assessment, Co-trimoxazole, Fixed drug eruption, Naranjo algorithm.

Introduction

Cotrimoxazole is a synergistic fixed dose combination of sulfamethoxazole and trimethoprim at a 5:1 ratio.[1] They have been indicated for urinary, respiratory and gastrointestinal tract infections, otitis media, gonorrhea, cholera and several other infections.[2] Antibacterial activity of cotrimoxazole is due to combined effects of inhibition of PABA into folic acid and prevention of the reduction of dihydrofolate to tetrahydrofolate which is essential for synthesis of thymidine.[3] Its major side effects are nausea, diarrhea, headache, vomiting, liver damage etc.[4] It is also known to cause fixed drug eruption commonly . We hereby report a case of Fixed Drug Eruption (FDE) caused by co-trimoxazole which can be attributed to the lack of counseling of the patient.

Case report

A 59 year female, patient, a known case of asthma on oral theophylline and prednisolone regularly, presented to the dermatology Out Patient Department (OPD) on 16-02-06 with complaints of some pruritic red colored lesions over the both legs for 2 days followed by vesiculation and pigmentation over the lesions *(Fig 1)*. She gave history of taking Tab. Cotrimoxazole for 2 days advised by the local practitioner. The patient also gave past history of two similar episodes (pruritus followed by erythematous plaque and violet plaques) over the same sites 14 and 19 month back after taking some medicines as advised by the local practitioner (details of medication not available, but based on the history it is assumed to be co-trimoxazole).

Fig. 1: Pruritic red colored lesions over the both legs followed by vesiculation and pigmentation over the lesions (The lesions are hindered with gentian violet speeded over)

On clinical examination, well-defined, erythematous, plaques over the surface of thighs along with hyperpigmentated, plaques with vesiculation over both legs, and crusted plaques over both lips were seen. Genitalia and oral cavity were normal. A provisional diagnosis of probable FDE due to co-trimoxazole was made and patient was admitted under dermatology department. All medications were stopped. Complete blood count (CBC), erythrocyte sedimentation rate (ESR), bleeding time, clotting time were sent and were found to be with in normal limits. The patient was detected to be diabetic with slight increase in the blood glucose (Fasting 112 Mg/dl and post prandial 250 Mg /dl) levels.

Patient was then started on intravenous steroids (dexamethasone), topical antibiotics, oral analgesic and antihistamines. Patient improved with no new lesions during admission and was finally discharged after seven days on tapering dose of steroids. Theophylline for asthma was also restarted. Patient was then followed up after 2 weeks in dermatology OPD. Previous lesions were healed and there were no new lesions. The patient was also educated regarding the ADR and counseled regarding the strategies to prevent similar problems in the future.

We carried out the causality, severity and preventability and predictability assessments for this Adverse Drug Reaction (ADR) as per Naranjo algorithm [5], Modified Hartwig and Siegel Scale [6] and Modified Schumock and Thornton scale [7] respectively. It was found that ADR was 'definitely' attributable due to the co-trimoxazole and was found to be 'moderately severe level 4 (b)'. The ADR was also found to be 'predictable' and 'definitely preventable'.

Discussion

Fixed drug eruptions are characterized by the fact that they tend to occur at the same site in the particular patient each time the drug administered.[8] The usual morphology is intensively pruritic bright red macules and papules, symmetric on trunk and extremities; may became confluent.[9] Common causes of fixed drug eruptions are barbiturates, phenolphthalein, tetracycline, griseofulvin, phenytoin, salicylate, sulphonamide etc.[10] The mechanism of most drug induced eruptions are unknown. However, it may be due to allergic reaction, other reaction caused by accumulation of dugs, pharmacological action of drugs or interaction with genetic factors.[11]

Many times it becomes difficult to attribute a particular ADR to a drug. This state of ambiguity can be overcome by carrying out the causality assessment. Causality assessment of ADRs is the structured and standardized assessment of individual patients/ case reports of the likelihood of a causal relationship between suspected drugs and adverse medical events. In the early 1980s, in an attempt to reduce ambiguity in the evaluation of adverse drug reactions, different standardized causality assessment scales were introduced at pharmacovigilance centers in many centers in many countries around the world.[12] A simple method to assess the causality of ADRs in a variety of clinical situations was developed by Naranjo et al in 1981. In this scale, the probability that the adverse event was related to drug therapy was classified as definite, probable, and possible or doubtful.[5] In our case the causality was found to be 'Definite' suggesting that the development of FDE is definitely attributable to co-trimoxazole.

The term severity is often used to describe the intensity of a medical event, as in grading 'mild', 'moderate' and 'severe'. Severity assessment categorizes the ADRs as mild, moderate, or severe based on the steps taken for the management of the ADRs. [14] The United States Food and Drug Administration (US FDA) classifies an ADR as serious when it results in death, life- threatening causes, or prolongs hospitalization, causes a significant persistent disability, results in a congenital anomaly, or requires intervention to prevent permanent damage.[13] Hartwig et al categorized ADRs into seven levels as per their severity. Level 1 and 2 fall under mild category, level 3 and 4 under moderate and level 5, 6 and 7 fall under category severe.[6] In our case the ADR was found to be 'moderately severe level 4 (b)' suggesting that this ADR required hospitalization for its management. It is well reported in the literature that ADRs account for 5% of all hospital admissions and causes death in 0.1% of medical and 0.01% of surgical cases.[14]

Carrying out the predictability assessment can help the clinician to predict and prevent the occurrence of similar ADRs in the future. In our case the ADR was found to be

predictable and definitely preventable. It is reported that the most common type of drug-induced disorder is dose-dependent and predictable and occurs as a result of drug-drug, drug-disease or drug-food interactions and, therefore, are preventable.[15] Some of the strategies to prevent the ADRs are educating the patients regarding the ADRs, taking appropriate history taking before prescribing any drugs and providing an alert card to the patient upon development of an ADR, which can be carried by the patient while attending any doctor in the future. In our case if the doctor had taken the history of the patient, this ADR could have been prevented.

Drug Related Complications (DRCs), are a major cause of hospitalizations, lead to huge economic burden and significant human suffering.[16] A study conducted on five major hospitals in Nepal covering 15,624 hospital admissions found that 63 (0.4%) of hospital admissions were attributed to DRCs.[17] It has been found that the total cost of drug related morbidity and mortality exceeds the cost of medications themselves.[18] It is now recognized that the cost associated with drug related morbidity and mortality is exceedingly high, between US$ 30.1 billion and US$ 136.8 billion annually in the United States (US) if direct and indirect costs are included.[19] In our case the patient got admitted in the hospital for the management of this particular ADR and thus spent a certain amount of money. Added to these cost, the impaired quality of life associated with the ADRs need to be studied. The ADRs usually affect the quality of well being on the individual to a greater extend.

Conclusion

FDE due to Co-trimoxazole is well reported in the literature. We are reporting this case to emphasize the fact that this type of ADRs can be prevented if the patient is educated thoroughly regarding the ADRs. More over, the responsibility also lies in the hands of the healthcare professional to take adequate history regarding the drugs used in the past and any sort of allergy or other ADRs experienced by the patient in the past. It is the time for us to understand the fact that " our responsibility as healthcare professionals do not end at the stage of diagnosing, prescribing and dispensing, it ends only when the patient achieve the desired out comes with out experiencing any harmful effects due to the treatment".

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