Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(8D):3228-3231 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2017.v05i08.049

Case Report

Successful Slow Induction of Tolerance to Co-Trimoxazole in HIV Positive Patient Cross Reactive to Co-Trimoxazole and Dapsone

Sukalyan Saha Roy[1], Nikhil Era[1], Shatavisa Mukherjee[1*], Santanu Kumar Tripathi[1]
Department of Clinical & Experimental Pharmacology, Calcutta School of Tropical Medicine, Kolkata

***Corresponding author**
Ms. Shatavisa Mukherjee
Email: shatavisa100@gmail.com

Abstract: Co-trimoxazole and alternatively Dapsone is used for chemoprophylaxis for opportunistic infection in HIV positive patients. Desensitization to Co-trimoxazole is attempted when there is no other alternative. Different desensitization protocols are studied abroad but Indian data are much scarce. The present case reports a 28 year old newly diagnosed treatment naïve HIV positive patient who was intolerant to NACO recommended protocol but induction of tolerance was successful when dose was up-titrated at a slower rate.
Keywords: co-trimoxazole, cross-reactivity, dapsone, immunological desensitization, sulfa allergy

INTRODUCTION

Co-trimoxazole (TMP-SMX) is regularly used for chemoprophylaxis against opportunistic infections in HIV positive patients having low CD4 count (CD4<250/cmm) [1]. TMP-SMX is quite inexpensive, which is quite a rarity in the field of HIV treatment. Adverse reactions to TMP-SMX in HIV infected patients occur in above 25% of the population. Statistics from published studies states that the rate of adverse reactions leading to discontinuation of cotrimoxazole varied from 9.4% to 54%. Reports suggest that incidence of allergy to Co-trimoxazole [1] is presumed to vary from 2.2% in males to 3.4% in females. Dapsone is recommended as an alternative in such cases. Cross reactivity with Co-trimoxazole and Dapsone is known though rare. There is a dearth of evidence from Indian context in this regard. However studies abroad [2] concluded that Dapsone might be considered to patients allergic to TMP-SMX where 21% of patients were cross reactive. Induction of tolerance is usually attempted when there is no other alternative drug. Several methods of sulfa desensitization have been tried and a success rate of more than 80% especially in patients with CD4 counts of less than 200 /cmm has been achieved. Published literature from India is however much scarce in this regard. In India, National Aids Control Organisation (NACO) follows the WHO desensitization guideline as described in Table 2.

The present report discusses a case where a patient could not tolerate NACO recommended sulfa desensitization protocol but a slower approach of tolerance induction was found successful.

CASE REPORT

On January 2016, a 28 year old male reporting with prolonged fever and weight loss was diagnosed to be HIV positive. This treatment naïve patient having CD4 count 186/cmm was started on co-trimoxazole prophylaxis. Antiretroviral therapy (ART) as per NACO recommendations was scheduled for initiation after at least two weeks. Fifteen days after the initiation of Co-trimoxazole, patient reported back with rash. On examination, erythematous rash was noted in front of chest and neck which gradually progressed to the condition of maculo-papular rash in trunk and upper limbs. The drug was stopped and he recovered within 5-7 days. On February 27, Tab Dapsone 100 mg per day was prescribed as an alternative. 10-11 days after starting Dapsone therapy rash appeared. Patient immediately stopped the medication and attended OPD after 1-2 days. On March 20, Patient was admitted in a tertiary healthcare facility with erythematous maculo-papular rash all over the trunk and upper limbs which

was diagnosed to be drug induced erythema multiforme (Fig 1 & 2). He was managed conservatively and discharged after the subsidence of rash. About 2 weeks after recovery on readmission, sulfa desensitization was attempted according to NACO recommendation after obtaining consent. He received 2 ml of syrup TMP-SMX (40 mg Trimethoprim/5 ml) on day 1; and 4 ml on day 2. Itching and erythema started from night at day 2 and progressed. Next doses were further withheld and the patient recovered gradually. After 7 days following recovery, a slower desensitization protocol was attempted starting with 1 ml TMP-SMX syrup and continuing that dose daily for 3 days before uptitration (Table 1). The patient tolerated the drug, and was discharged after completion of the protocol. Patient was successfully desensitized. Patient continued CPT and was initiated on TLE regimen from May 29. As on Dec 2016, his last CD4 count was noted 234/cmm.

The patient thus intolerant to NACO recommended protocol demonstrated successful slow induction of tolerance on slower up-titration of dose.

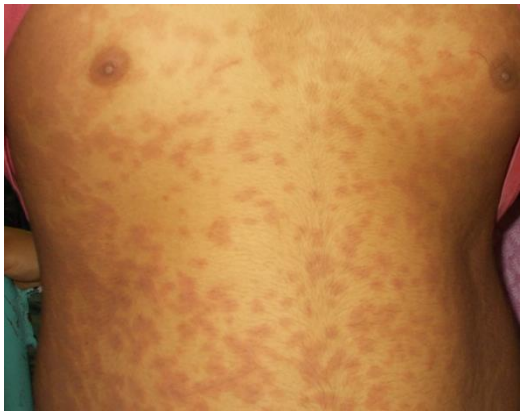
ILLUSTRATIONS

Table–1: Slower desensitization protocol applied successfully in the mentioned case

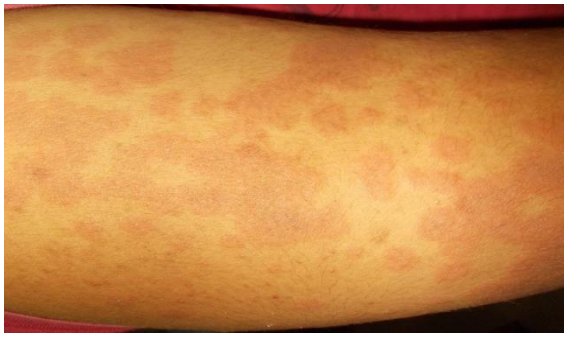
Day of therapy	Dosage (syr/tab)	Dose (SMX/TMP)
April 27, 28, 29	1 ml	40/8 mg
April 30, May 1, 2	2 ml	80/16 mg
May 3, 4, 5	4 ml	160/32 mg
May 6, 7, 8	6 ml	240/48 mg
May 9, 10, 11	8 ml	320/64 mg
May 12, 13,14	1 single strength tab	400/80 mg
May 15 onwards	1 double strength tab	800/160 mg

Table–2: NACO recommended protocol for sulfa desensitization

Steps of therapy	Dosage (syr/tab)	Dose (mg) (SMX/TMP)
Day 1	2 ml syr	80/16
Day 2	4 ml syr	160/32
Day 3	6 ml syr	240/48
Day 4	8 ml syr	320/64
Day 5	1 SS tab	400/80
Day 6	1 DS tab	800/160



Fig–1: EM after Dapsone therapy (trunk)



Fig–2: Erythema Multiforme (upper limb)

DISCUSSION

Trimethoprim-sulfamethoxazole (TMP-SMX) is a key antibiotic for prophylaxis and treatment of several HIV-related illnesses. Apart from being the most effective prophylaxis and the first-line treatment for Pneumocystis jiroveci pneumonia (PCP), it is also used as a preventive alternative in toxoplasmosis encephalitis in severely immunocompromised patients who have evidence of previous exposure and is also effective against certain bacterial infections. TMP-SMX is quite inexpensive, which is a rarity in the field of HIV treatment. Because of its effectiveness, availability and lesser cost, which is a rarity in the field of HIV treatment, it is used widely throughout the world. However, adverse reactions to TMP-SMX and other sulfa drugs occur in a high proportion of HIV-infected patients (roughly 25%), and such reactions may limit to fewer treatment alternatives like Dapsone. However certain studies abroad [2] have found 21% of such patients being cross reactive to co-trimoxazole and dapsone. In such cases, induction of tolerance is usually attempted. Desensitization to TMP-SMX should be considered when there are no reasonable or available alternatives and the patient has not experienced severe reactions (e.g., Stevens-Johnson syndrome or toxic epidermal necrolysis) to sulfa drugs. Several methods of desensitizing patients with previous reactions to TMP-SMX have been tried. These methods vary in starting dosage and length of dosage escalation, but success rates are around 80% in most cases and may be higher in patients with CD4 counts of <200 cells/µL**.**

Published literature on cross reactivity with Co-trimoxazole and Dapsone from India is scarce. Documentation and publication of Indian data on prevalence, severity and risk factors of cross reactivity between Co-trimoxazole and Dapsone is thus a mandate. Data on incidence of sulfa allergy in India is much underreported. However a review suggests about 13.4% of all cutaneous ADRs were implicated to sulfa drugs. Different slow sulfa desensitization protocol in HIV positive patients have been explored abroad.

Indian data on studies exploring different desensitization protocol is also lacking. Absar *et al* tried a 10 days regimen to desensitize and 23 out of 27 patients showed positive results [4]; Rich *et al* succeeded in 18 out of 22 cases [3]. NACO still recommends the WHO desensitization guideline but its short duration seems to be one of its limitations (Table 2). Our report however supports a slower regimen for sulfa desensitization in Indian population as compared to the NACO protocol. AIDS education and training centers National Coordinating Resource Centre (AETC NCRC) promotes a much slower regimen [6] where regimen starts with 1 ml of syrup TMP-SMX (each ml contains 8 mg TMP and 40 mg SMX) for consecutive 3 days and on the next 3 days patient gets 2 ml per day. If tolerated, 5 ml syrup is administered daily for next 3 days and then patient is given 1 single strength tablet daily for 3 days. By this protocol, patient can start double strength tablet on day 13. The present report suggests extensive exploration of various desensitization protocols from Indian perspective, its development and subsequent assessments.

Informed consent: Duly obtained

Source of funding: Nil

Conflict of Interest: None Declared.

REFERENCES

1. Macy E, KY TP. Self-reported antibiotic allergy incidence and prevalence: age and sex effects. The American journal of medicine. 2009 Aug 31; 122(8):778-e1.
2. Holtzer CD, Flaherty JF, Coleman RL. Cross-Reactivity in HIV-infected Patients Switched from Trimethoprim-Sulfamethoxazole to Dapsone.

Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 1998 Jul 8; 18(4):831-5.

3. Rich JD, Sullivan T, Greineder D, Kazanjian PH. Trimethoprim/sulfamethoxazole incremental dose regimen in human immunodeficiency virus-infected persons. Annals of Allergy, Asthma & Immunology. 1997 Nov 1; 79(5):409-14.
4. Absar N, Daneshvar H, Beall G. Desensitization to trimethoprim/sulfamethoxazole in HIV-infected patients. Journal of allergy and clinical immunology. 1994 Jun 30; 93(6):1001-5.
5. Patel TK, Thakkar SH, Sharma DC. Cutaneous adverse drug reactions in Indian population: A systematic review. Indian dermatology online journal. 2014 Dec; 5(Suppl 2):S76.
6. Riddler SA, Haubrich R, DiRienzo AG, Peeples L, Powderly WG, Klingman KL, Garren KW, George T, Rooney JF, Brizz B, Lalloo UG. Class-sparing regimens for initial treatment of HIV-1 infection. New England Journal of Medicine. 2008 May 15; 358(20):2095-106.