Prevention of multiple drug allergy by histaglobulin

Cutaneous drug allergy is a common manifestation of adverse drug reaction and poses problem to the treating physician. The reaction rate varies from 0% to 8% and is highest for antibiotics. Histaglobulin, a product of the Serum Institute of India, contains histamine with human immunoglobulin. When administered subcutaneously, it forms antibodies against histamine, which increases the histamine-binding capacity of the serum. It is indicated for the treatment of atopic dermatitis, allergic rhinitis, and other chronic allergic states. In both allergic rhinitis and urticaria, histamine is the primary mediator and it plays a major role in Type-I allergic skin reaction induced by various drugs.

The prevention of drug-induced skin reactions using histaglobulin was tried in some patients in the Clinical Pharmacology Unit of the Department of Pharmacology, S. C. B. Medical College and Hospital, Cuttack, with approval of the Institutional Ethics Committee. One such case is reported here.

In April 1999, a 40-yr-old male police employee, posted in a tribal area of Orissa, was referred from the Dermatology OPD to our department for complaints of repeated attacks of cutaneous allergy to multiple drugs for the past 4–5 years. The diagnosis of multiple drug allergy was made by the dermatologist after excluding skin diseases such as eczema, atopic dermatitis, psoriasis, and other coincidental etiological factors in the patient, before referring him to our department. The skin allergy was manifested, within 2–36 h of consumption of drugs, such as urticarial eruptions, erythema, and pruritus. He had a history of allergic skin reaction after using almost all commonly used drugs, such as sulphonamide, penicillin, ampicillin, cloxacillin, chloroquine, tinidazole, ibuprofen, nimesulide, and paracetamol, over the past 4–5 years. For this reason he was unable to take these medicines. Causality assessment was done in our department, based on the medical records of the patient, taking into consideration the timing of appearance of cutaneous skin reactions, their remission on drug withdrawal, their reappearance on subsequent therapeutic reintroduction and absence of other etiological factors. Laboratory tests were done to exclude presence of diabetes, worm infestation, eosinophilia, and leucocytosis.

These evidences confirmed the diagnosis of multiple drug allergy as of “certain” category. This time he presented with urticarial skin rash all over the body with pruritus, 8 h after consumption of metronidazole orally, which was not relieved by chlorpheniramine maleate or cetirizine. On examination, urticarial rashes and scratch marks were observed on his back, chest, and arms. There was associated erythema and swelling of mucocutaneous junctions. His blood, stool, and urine reports revealed no abnormality.

After obtaining informed consent, in May 1999, the patient was administered with 2 ml histaglobulin subcutaneously, after skin testing, at weekly intervals for 3 weeks, followed by booster doses after 1, 3, and 6 months. Inj. adrenaline, inj. hydrocortisone, inj. chlorpheniramine maleate, and oxygen were kept handy each time to tackle any hypersensitivity to histaglobulin. Since histaglobulin has a short-lived activity, he was advised to attend our OPD for receiving booster doses of histaglobulin every 6 months and for taking any prescribed medicine under our supervision.

In January 2000, he attended our OPD, with a prescription of 500 mg paracetamol s.o.s. for his fever and myalgia. He was reintroduced with a low dose of 250 mg paracetamol with all precautionary measures at hand. As the peak blood concentration after oral paracetamol is usually reached in 30–60 min, he was kept under observation for 6 h. He did not develop any cutaneous rash. On the next two days he took 500 mg tablets of paracetamol for his body ache and fever, which he tolerated without any allergic reactions. In September 2000, he suffered from amebic dysentery and was again prescribed metronidazole tablet of 400 mg, 8 hourly. He came to our department for administration of metronidazole under supervision. He was reintroduced with a low dose of metronidazole (200 mg), under observation for 6 h. There were no allergic reactions and he was allowed to take the full course of metronidazole. On the second day he complained of mild itching, which subsided with 1 tablet of cetirizine, and did not require drug withdrawal. He continued to take booster doses of histaglobulin every 6 months.

In April 2001, he visited our department with a prescription of chloroquine for suffering from an acute attack of malaria. He was administered with 1 tablet of 250 mg chloroquine phosphate, under observation for 6 h. Then, he was allowed to take the full course of chloroquine under strict supervision with all precautionary measures at hand. There were no signs of drug allergy throughout the period of observation. In February 2002, he consumed nimesulide and roxithromycin on prescription from the local dispensary for upper respiratory tract infection without any sign of allergy. In May 2003, he was administered with 500 mg tablet of tinidazole, prescribed by a local practitioner at his place of posting for amebic dysentery. He tolerated the drug without any side effect. In October 2004, he was successfully treated with 400 mg ibuprofen tablet for pain in his legs. The last three drug administrations were not supervised by our department, but was reported by the patient retrospectively during his visit to take booster doses of histaglobulin.

Many drugs, such as ACE inhibitors, antiepileptics, sulphonylureas, sulphonamides, and NSAIDs have cutaneous drug allergy as their side effect. Mild-to-moderate degree of
drug-induced urticarial reactions not only limits the use of certain first-line drugs but also increases the morbidity of the patient. In case of specific indications, these drugs can be used under the coverage of histaglobulin. Histaglobulin administered subcutaneously induces production of antibody against the histamine–immunoglobulin complex, which binds and inactivates histamine released during allergy. Repeated doses of histaglobulin increase this antibody titer, for which booster doses of histaglobulin were administered every 6 months to maintain an optimal titer of antibody in the serum, which might have prevented the occurrence of cutaneous drug allergy in the patient. Histamine-added human gammaglobulin (histaglobulin) has been clinically used as an antiallergic drug for asthma, allergic rhinitis, and atopic dermatitis. Clinical trials have indicated that subcutaneous administration of histaglobulin not only improves clinical symptoms in allergic patients but also inhibits allergen-induced eosinophil accumulation, which is comparable with cyclosporine. It has also been successfully tried to treat chronic recurrent urticaria. Thus, the use of histaglobulin for the prevention of multiple drug allergy is a new dimension that needs to be evaluated in various other centers.

References