Hypersensitivity to Intravenous Mannitol: A Case Report

Introduction - Mannitol is an osmotic diuretic, mostly used to reduce intracranial tension, for treatment of intraocular pressure. It is associated with various adverse effects. In this paper, we describe a hypersensitivity reaction to a single intravenous dose of Mannitol.

Case report: A 43 yrs old women presented to our institute with history of severe vaginal bleeding. She had a diagnosis of CA-Cervix stage–IIIB and had on treatment with intravenous ondansetron 16mg, dexamethasone 16mg, esmoprazol 40mg and finally Mannitol 200ml. There was no reaction with ondansetron and dexamethasone and esmoprazole but after starting Mannitol 200ml i.v within 10 min. she developed urticaria and swelling all over the body specially puffiness of face which was treated with inj.hydrocortisone100mg and inj. Avil 2ml(44mg). The reaction abated within few minutes and she was discharged within hour. She was asymptomatic at 72 hours of follow up.

Discussion: Mannitol is an osmotic diuretic (Tripathi KD, 2013) occurs naturally in many plant foods. Symptoms of anaphylaxis included generalized urticaria, angioedema, difficulty in breathing and loss of consciousness. The proposed mechanism for sensitization involves the reaction of D-mannose with exposed amino groups of proteins in vivo to form Schiff base intermediates bearing a D- mannitol moiety, which closely resembles D- mannitol. Once an individual is sensitized with the formation of mannitol-specific IgE, mannitol can cause anaphylactic reactions by acting either as a univalent anaphylactogen or a bivalent hapten. (Yedulkar P . et.al 2003)

Preservatives, excipients and dyes in drug formulations represent a true puzzle for allergies and dermatologists. At a first sight, the active pharmaceutical molecule is usually considered the responsible agent for a hypersensitivity reaction following the drug assumption. According to the literature reports, alimentary route seems the most likely pathway able to induce mannitol sensitization. So, beyond a food allergen, a drug allergen and an excipient allergen, mannitol might even be a respiratory allergen. (G.F.calogiuri et.al. 2015).

Adverse drug event was ‘6’ indicating a Probable reaction to mannitol. (Narango CA et.al.1981)

According to Findlay SR.et.al. patient experiencing anaphylactic reactions may be identified by use of in vitro basophil histamine release. D- Mannitol is known to cause immediate – type hypersensitivity reactions when given intravenously. Such manifestations are usually attributed mannitol hyperosmolar properties, able to trigger a non-specific mast-cells or basophils degranulation. (Findlay SR. et.al 1984).

Allergy to a small molecule depends on its reactivity with proteins to form an effective hapten-carrier complex to induce an immune reaction. Mannitol is used in a variety of clinical situations(chemotherapy, cerebral oedema) for its osmotic diuretic qualities. Daniel Vervloet stated that hyperosmolar solutes are capable of inducing non-cytotoxic basophil histamine release.
Also, IgE-mediated mannitol hypersensitivity has been identified by in vitro histamine release assay. (Daniel V, 2009)

Hedge VL studied anaphylaxis to excipient mannitol to identify allergenic component and its mechanism in the pharmaceutical preparation and he found that testing by Skin Prick test (SPTs) and HPLC analysis of various pharmaceuticals indicated that excipient mannitol in the causative allergen with develop rare adverse effects like urticaria and angioedema. (Hegde VL et al. 2004).

**Conclusion:**

It appears that mannitol causes anaphylactic reactions in sensitized individuals by acting either as a univalent anaphylactogen or as a bivalent hapten. Based on the description of cases of mannitol hypersensitivity in the literature, it is evident that none had sensitivity to D-mannose, erythritol or any other related compounds. Hence, it is likely that mannitol specific IgE antibodies may be very specific, without any cross-reactivity.

In the wake of the above evidence, and the increasingly availability, we need to be more cautious while using this drug and also aware of various unusual side effects.

Our case report underscores the importance of physician judiciously using the drug so as to reduce incidence of similar avoidable adverse drug reaction.

**References**