



## Hypersensitivity to Intravenous Mannitol: A Case Report

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### ABSTRACT

**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, esmaprazole 40mg and finally Mannitol 200ml. There was no reaction with ondansetron and dexamethasone and esmaprazole 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.hydrocortisone 100mg 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.

**Conclusion:** Mannitol is commonly used after surgical process. Urticaria and angioedema are rare adverse effects so drug is commonly used in clinical practices. In our case, reaction could be either anaphylaxis or anaphylactoid.

### KEYWORDS

CA cervix stage IIIb, Mannitol, urticaria, angioedema.

### Introduction-

Mannitol, a non- toxic and non- metabolizable osmotically active compound, mostly used in many clinical situations, such as drug oliguric renal failure, glaucoma and increased intracranial pressure and to promote prompt removal of renal toxins. (Yedulkar p 2003, Karzung 2009). It is widely used as a food additive in processed foods and as an excipient in pharmaceutical preparations. It is commonly used after cardiac catheterization, cardiovascular surgery and exposure to intravenous contrast dyes. (Priya Viswesaran et.al 1997).

As it is a white crystalline sugar also named mannite or manna sugar. Manna is one of most ancient sweeteners in Europe before the introduction of the sugar cane. Mannitol is an acyclic hexitol sugar derived from the reduction of D- mannose (an Aldohexose), which is not metabolized and therefore is excreted unchanged in the urine. (G.F.Calogiuri et.al. 2015).

### Case Presentation:

A 43 year old female patient visited our institute with history of severe vaginal bleeding since 5 months. She had been diagnosed as CA-Cervix stage-IIIb and had been planned to give chemotherapy(Cisplatin) and radiotherapy. In first week when she had been on treatment with inj. Ondansetron 16mg stat i.v followed by 8 mg BD, Inj. dexamethasone 16mg i.v and Inj. Esmoprazole to avoid Cisplatin side effects. There was no reaction with these drugs, so mannitol 200ml was started i.v., before starting Cisplatin. Patient developed redness and itching all over the body. Swelling and Puffiness of face within 10 minute of Mannitol infusion. There was no history of bronchospasm and hypotension. She was immediately treated with inj. hydrocortisone 100 mg, inj. Avil 2ml(44mg) i.v. The reaction abated within few minutes. The patient did not complain of any other symptoms and was discharge after an hour of observation. She was asymptomatic at 72 hours of follow-up. On further history taking, the patient gave no previous history of use of mannitol or other drug exposure and no drug or food allergy. There was no history of a similar episode in the past. She gave no personal or family history of atopy, asthma or bronchitis. On the Naranjo's causality assessment, the

adverse drug event was '6' indicating a Probable reaction to mannitol. (Narango CA et.al.1981)

### 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- mannitoyl 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).

According to Findlay SR.et.al. patient experiencing anaphylactoid 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.(Hedge 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.

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