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# USE OF INTRAVENOUS MANNITOL PRIOR TO GLAUCOMA SURGERY (HOW LONG BEFORE THE START OF SURGERY AND HOW MUCH)

Ophthalmology

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## ABSTRACT

Intravenous Mannitol, a parenteral obligatory osmotic diuretic, reduces Intraocular pressure(IOP) by increasing the Plasma osmolality and drawing water from the eye into the circulation. The dose, concentration and administration depends on severity of condition, fluid requirement and urinary output . For reduction of IOP: In adults, a dose of 1 to 2 g/kg body weight as 15% - 25% solution and in pediatric patients, 1 to 2 g/kg body weight or 30 to 60 g/m² over 30 to 60 minutes. In debilitated patients, 500 mg/kg may be sufficient. Preoperatively, it should be given one to one and a half hours before surgery to achieve maximum IOP reduction. Onset of action in 15–30 minutes, reaches a maximum effect in 30–60 minutes with duration of action approximately 6 hours. It is administered with caution in patients with cardiac, renal, and hepatic disease. Headache, nausea, vomiting, and diuresis are common side effects.

## KEYWORDS:

Mannitol IV, IOP reduction , time of administration )

### INTRODUCTION :

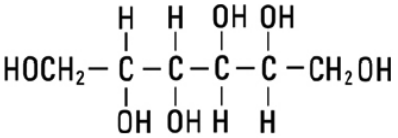
Although the effect of hyperosmotic agents on intraocular pressure (IOP) has been known for almost a century, 1–3 these agents became widely used in ophthalmology only in the past 40 years. Hyperosmotic agents are useful for the short-term management of acute glaucoma. They also may be used for lowering Iop preoperatively4. Hyperosmotic agents have reduced the risk of surgically decompressing eyes with markedly elevated IOPs. Mannitol I.V. (Mannitol Injection, USP) is a sterile, nonpyrogenic solution of mannitol in water for injection available in concentrations of 5%, 10%, 15%, 20% in flexible plastic containers and 25% in a Fliptop vial for administration by intravenous infusion only.5 The content and characteristics of the available concentrations are as follows

| CONC. (%) | G/100 ML | MOSMOL/LITER (CALC.) | PH* |
|---|---|---|---|
| 5 | 5 | 274 | 6.3 (4.5 to 7.0) |
| 10 | 10 | 549 | 6.3 (4.5 to 7.0) |
| 15 | 15 | 823 | 6.3 (4.5 to 7.0) |
| 20 | 20 | 1098 | 6.3 (4.5 to 7.0) |
| 25 | 25 | 1372 | 5.9 (4.5 to 7.0) |

*Concentrations up to 20% may contain sodium bicarbonate for pH adjustment; the 25% concentration may contain sodium bicarbonate and/or hydrochloric acid for pH adjustment.

The solutions contain no bacteriostat, antimicrobial agent or added buffer (except for pH adjustment) and each is intended only as a single-dose injection. When smaller doses are required the unused portion should be discarded.

Mannitol Injection, USP is a parenteral obligatory osmotic diuretic. Mannitol, USP is chemically designated D-mannitol (C6H14O6), a white crystalline powder or free-flowing granules freely soluble in water. It has the following structural formula:



Water for Injection, USP is chemically designated H20.

The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap, but not in amounts sufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials. Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.5

### MECHANISMS OF ACTION :

Hyperosmotic agents reduce IOP by increasing the osmolality of the plasma and drawing water from the eye into the circulation via the blood vessels of the retina and uveal tract.6 this transient effect lasts until osmotic equilibrium is re-established. Within a few hours, the hyperosmotic agent may penetrate the eye. If the agent has already cleared the plasma,7 reversal of the osmotic gradient occurs (i.e., plasma osmolality decreases to a level below that of the dehydrated tissues), with a rebound increase in IOP. For most agents in clinical use, effective IOP lowering is achieved when plasma osmolality is increased by 20–30 mOsm/l. Most of the fluid drawn from the eye comes from the vitreous; vitreous weight is reduced by 2.7–3.9% in experimental animals after administration of hyperosmotic agents in doses equivalent to those used clinically.8 Glaucomatous eyes appear to get a proportionately greater IOP lowering effect from an osmotic challenge than do normal eyes.9 Hyperosmotic agents also appear to lower IOP by a second mechanism; they decrease aqueous humor production via a central nervous system (CNS) pathway involving osmoreceptors in the hypothalamus.

| |
|---|
| 1. BY INCREASING THE OSMOLALITY OF THE PLASMA AND DRAWING WATER FROM THE EYE INTO THE CIRCULATION VIA THE BLOOD VESSELS OF THE RETINA AND UVEAL TRACT |
| 2. DECREASE AQUEOUS HUMOR PRODUCTION VIA A CENTRAL NERVOUS SYSTEM PATHWAY INVOLVING OSMORECEPTORS IN THE HYPOTHALAMUS. |

## DOSAGE AND ADMINISTRATION

For Reduction of Intraocular Pressure:

| | |
|---|---|
| ADULTS | 1 to 2 g/kg body weight as a 15% to 25% solution administered over a period of 30 to 60 minutes; |
| PAEDIATRIC | 1 to 2 g/kg body weight or 30 to 60 g/m² body surface area over a period of 30 to 60 minutes. |
| DEBILATATED | 500 mg/kg |

When used preoperatively, the dose should be given one to one and a half hours before surgery to achieve maximal reduction of intraocular pressure before operation.

The drug begins to lower IOP in 15–30 minutes, reaches a maximum effect in 30–60 minutes, and has duration of action of approximately 6 hours.[10,11,12,13]

It is not necessary to administer the full dose of the drug; when IOP falls to the desired level, the infusion can be terminated. Mannitol is excreted unchanged in the urine (i.e., it is not metabolized). Because it penetrates the eye poorly, mannitol is especially useful as a hypotensive agent in the presence of ocular inflammation.14 The 20% solution is stable and less irritating to blood vessels and subcutaneous tissue than is urea.15The major disadvantages of mannitol are the greater likelihood of cellular dehydration because of its confinement to extracellular water and the larger volume of fluid required because of its limited solubility.16 The 20% solution should be warmed to dissolve crystals, and a blood administration filter should be used in the intravenous line. An anaphylactic reaction to mannitol has been reported.[17]

## SIDE EFFECTS :

Side effects from hyperosmotic agents are relatively common. These drugs should be administered with caution in patients with cardiac, renal, and hepatic disease. Headache, nausea, vomiting, and diuresis are the most frequent side effects and are seen with all of the agents in clinical use.1[8,19]

Common side effects of mannitol are as indicated in the table below 20

| | |
|---|---|
| • Gastrointestinal<br>• Nausea<br>• Vomiting<br>• Diarrhea<br>• Abdominal cramping | • Renal/genitourinary<br>• Diuresis<br>• Loss of potassium<br>• Urinary retention<br>• Anuria |
| • Cardiovascular<br>• Angina<br>• Congestive heart failure<br>• Pulmonary edema | • Miscellaneous<br>• Skin slough<br>• Thrombophlebitis<br>• Acidosis<br>• Diabetic ketoacidosis<br>• Anaphylactic reaction<br>• Hyphema<br>• Suprachoroidal hemorrhage |
| • Central nervous system<br>• Headache<br>• Confusion<br>• Disorientation<br>• Fever<br>• Subdural hematoma | . |

### Suggestions for clinical use

With the availability of many new topical agents, the need for hyperosmotics has declined significantly. However, mannitol is useful in acute situations in which topical agents and systemic carbonic anhydrase inhibitors are unable to control IOP .

## ANGLE-CLOSURE GLAUCOMA :

Hyperosmotic agents are of great value in the management of acute angle-closure glaucoma.21, 22 The combination of a topical beta-adrenergic antagonist and an alpha- agonist will lower the pressure enough to allow a topical miotic to work. Prostaglandin agents are also useful in this context although their onset of action may be too long for an acute attack. Besides topical agents including are miotics, oral glycerol or isosorbide will terminate most attacks of angle-closure glaucoma. Intravenous mannitol should be administered as early at a dose of 1 Gm. per kg body weight, over a period of 30 to 60 min. Lower doses are frequently sufficient, and the administration should be stopped when the pressure has fallen. Once the acute attack has terminated, iridectomy becomes a much safer and often a curative procedure. Prophylactic iridectomy in the opposite eye can be performed during this interval[23.]

## SECONDARY GLAUCOMA :

Hyperosmotic agents are useful in the secondary glaucomas as a preparation for surgery or as a means of controlling IOP and preventing optic nerve damage (if topical agents fail to do so) . Hyperosmotic agents are helpful in patients with sickle cell trait or disease who develop traumatic hyphema and uncontrolled IOP and who should not receive carbonic anhydrase inhibitors.24 The acute glaucoma seen after blunt trauma often subsides spontaneously after several days but may be very difficult to control until that time. Hyperosmotic agents can be given one to four times daily in this situation, but the patient's electrolyte status should be monitored. Surgery for traumatic hyphema associated with secondary glaucoma can often be avoided or delayed when hyperosmotic agents are given. In markedly inflamed eyes and in neovascular glaucoma, glycerol and intravenous mannitol are preferable because they penetrate the eye poorly.

## MALIGNANT GLAUCOMA :

This rare form of secondary glaucoma, which follows glaucoma or cataract surgery.25In addition to lowering intraocular pressure, the action of hyperosmotic agents on the vitreous becomes vital in the therapy of malignant glaucoma. As water is transferred from the vitreous to the circulation, vitreous volume is decreased and the vitreous face moves posteriorly.

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