PHARMACY PEARLS: OSMOTHERAPY

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OBJECTIVES

• UNDERSTAND THE TREATMENT GOALS AND TARGETS IN MANAGEMENT OF ELEVATED INTRACRANIAL PRESSURE

• COMPARE HYPERTONIC SALINE AND MANNITOL IN REGARDS TO DOSING, ADMINISTRATION AND ADVERSE EFFECTS
CRANIAL VAULT

- RIGID COMPARTMENT THAT CONTAINS BLOOD, BRAIN AND CSF
- IN NORMAL CRANIAL PHYSIOLOGY, THESE THREE COMPONENTS EXIST IN EQUILIBRIUM
- IF THE VOLUME OF ONE COMPONENT INCREASES, THE VOLUME OF ANOTHER MUST DECREASE

MONRO-KELLIE HYPOTHESIS

• PATHOGENESIS OF ELEVATED INTRACRANIAL PRESSURE (ICP) VARIES DEPENDING ON THE INITIAL INSULT

• GOALS OF ICP MANAGEMENT:
  • MAINTAIN ADEQUATE BRAIN OXYGEN DELIVERY
  • AVOID FURTHER INJURY
  • PREVENT HERNIATION

• TARGETS:
  • ICP < 22 MMHG
  • CEREBRAL PERFUSION PRESSURE (CPP): 60 – 70 MMHG

ICP TREATMENT OPTIONS

Osmotic therapy uses agents to create an osmotic gradient across the blood-brain barrier that draws water from the brain into the vascular space.

Agents:
- Mannitol
- Hypertonic saline (HTS)

Regardless of the cause of elevated ICP, osmotherapy is considered a mainstay of medical therapy, and should be administered as soon as possible.

OSMOTHERAPY

MANNITOL
- DOSE: 0.25 – 1 G/KG
- ADMINISTRATION: CENTRAL OR PERIPHERAL
  - 0.22-MICRON INLINE FILTER REQUIRED
- ADVERSE EFFECTS:
  - ACUTE KIDNEY INJURY
  - ELECTROLYTE ABNORMALITIES
  - HYPOTENSION

HYPERTONIC SALINE (HTS)
- DOSE/ADMINISTRATION: DEPENDS ON SODIUM COMPOSITION
- ADVERSE EFFECTS:
  - ACUTE KIDNEY INJURY
  - OSMOTIC DEMYELINATION SYNDROME
  - ELECTROLYTE ABNORMALITIES

<table>
<thead>
<tr>
<th></th>
<th>20% Mannitol</th>
<th>3% HTS</th>
<th>23.4% HTS</th>
<th>8.4% Sodium Bicarbonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equiosmolar Dose</td>
<td>0.5 g/kg</td>
<td>2.5 mL/kg</td>
<td>30 mL</td>
<td>1 mL/kg</td>
</tr>
<tr>
<td>Osmolality (mOsm/L)</td>
<td>1098</td>
<td>1027</td>
<td>8008</td>
<td>2000</td>
</tr>
<tr>
<td>Infusion Site</td>
<td>Central or PIV</td>
<td>Central, PIV or IO</td>
<td>Central</td>
<td>Central or PIV</td>
</tr>
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MANNITOL DOSING

- 20% MANNITOL
- 20 GRAMS/100 ML
- 100 KG PATIENT:
- DOSE: 1 GRAM/KG
- 100 GRAMS = 500 ML
MANNITOL ADMINISTRATION

- CRYSTALLIZATION CAN OCCUR AT LOW TEMPERATURES
  - SHOULD NOT BE ADMINISTERED IF CRYSTALS PRESENT
  - 0.22-MICRON INLINE FILTER REQUIRED
- ADMINISTERED OVER 10 – 20 MINUTES TO AVOID TRANSIENT HYPOTENSION
MANNITOL ADVERSE EFFECTS

- ACUTE KIDNEY INJURY
  - INCIDENCE: 6 – 12%
  - USUALLY TRANSIENT AND REVERSIBLE WITH CESSATION OF ADMINISTRATION
- ELECTROLYTE ABNORMALITIES
  - HYPER/HYPONATREMIA
- HYPOTENSION
  - AVOID IN HYPOTENSIVE (SBP < 90 MMHG) PATIENTS
**HYPERTONIC SALINE**

- DOSING OF HTS DEPENDS ON CLINICAL SCENARIO AND WHAT IS AVAILABLE
  - BOLUS VS CONTINUOUS INFUSION

- ADMINISTRATION RATE CAN VARY
  - 3% - CAN BOLUS 250 ML OVER 15 – 30 MINUTES
    - CAN ADMINISTER 30 ML/HR VIA PERIPHERAL LINE X 48 HOURS
  - 23.4% - CAN BOLUS 30 ML OVER 15 – 30 MINS OR IVP OVER 2 – 5 MINS BY PROVIDER
    - REQUIRES CENTRAL LINE

- RAPID ADMINISTRATION CAN LEAD TO TRANSIENT HYPOTENSION
HYPERTONIC SALINE ADVERSE EFFECTS

• ACUTE KIDNEY INJURY
  • INCREASED RISK WHEN SODIUM LEVELS GREATER THAN 160 MEQ

• OSMOTIC DEMYELINATION SYNDROME
  • CAUSED BY RAPID INCREASES IN SODIUM (GREATER THAN 8-12 MEQ/L WITHIN 24 HOURS)
  • INCREASED RISK IN PATIENTS WITH CHRONIC HYPONATREMIA

• ELECTROLYTE ABNORMALITIES
  • HYPERNATREMIA
  • HYPERCHLOREMIA
  • HYPOKALEMIA
## PHARMACOKINETIC EFFECTS

<table>
<thead>
<tr>
<th></th>
<th>20% MANNITOL</th>
<th>HYPERTONIC SALINE</th>
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</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>5 – 10 mins</td>
<td>Rapid</td>
</tr>
<tr>
<td><strong>Peak effect</strong></td>
<td>15 mins</td>
<td>10 – 15 mins</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>2 – 5 hours</td>
<td>2 – 6 hours</td>
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</tbody>
</table>

MANNITOL VS. HYPERTONIC SALINE

• BRAIN TRAUMA FOUNDATION TBI GUIDELINES, 4TH EDITION:
  • “ALTHOUGH HYPEROSMOLAR THERAPY MAY LOWER INTRACRANIAL PRESSURE, THERE IS INSUFFICIENT EVIDENCE ABOUT EFFECTS ON CLINICAL OUTCOMES TO SUPPORT A SPECIFIC RECOMMENDATION, OR TO SUPPORT USE OF ANY SPECIFIC HYPEROSMOLAR AGENT, FOR PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY”

• NEUROCRITICAL CARE SOCIETY GUIDELINES FOR ACUTE TREATMENT OF CEREBRAL EDEMA:
  • “WE SUGGEST USING HYPERTONIC SALINE SOLUTIONS OVER MANNITOL FOR THE INITIAL MANAGEMENT OF ELEVATED ICP OR CEREBRAL EDEMA IN PATIENTS WITH TBI.”

OSMOTHERAPY TAKE AWAY POINTS

• THERE ARE RISKS & BENEFITS ASSOCIATED WITH BOTH MANNITOL AND HYPERTONIC SALINE, SO USE PATIENT SPECIFIC FACTORS TO GUIDE THERAPY

• TIME IS BRAIN: UTILIZE WHICHEVER AGENT THAT CAN BE QUICKLY ADMINISTERED

• HTS ADMIN: 30 ML 23.4% = 250 ML 3%
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