Ifosfamide – induced encephalopathy

Overview
Ifosfamide – induced encephalopathy is an acute neurological disturbance occurring during or shortly after ifosfamide infusion. Although it is usually reversible, it is a serious and potentially fatal complication and should always be discussed with the Consultant on call.

Presentation
- Agitation/drowsiness/coma
- Aphasialataxia
- Urinary incontinence
- Convulsions

Risk factors include:
- Impaired renal function
- Low albumin
- Pelvic tumours.

Remember that CNS infection, vascular events, metabolic disturbance and metastatic disease may all occur in these patients and cause similar symptoms.

Treatment
- Stop ifosfamide!
- Supportive – correct any electrolyte disturbance etc.
- Lorazepam/diazepam – repetitive discharges are usually present on EEG even if no overt fitting. Watch for respiratory depression
  - Lorazepam 50 – 100 microgram/kg IV max. dose 4mg over 30 – 60 secs
  - Diazepam 300 – 400 microgram/kg IV max. dose 10mg over 30 – 60 secs
- Methylene blue (methylthioninium chloride) : if symptoms persist after benzodiazeplpine, then give 1 – 2 mg/kg/dose (max. 50mg) in 50ml glucose 5% for Proveblue® brand (check fluid compatibility in package insert or monograph for other brands) over 5 to 10 minutes. Repeat 1 – 2mg/kg/dose (max. 50mg) q8hourly until symptoms resolve. Watch BP as can cause hypertension. Methylene blue (methylthioninium chloride) is stocked in the drug cupboard on the ward, if not, obtain through on call pharmacist.
- Subsequent ifosfamide doses:
  - Next dose of ifosfamide to then be given over 8 hours, continuing with methylene blue (methylthioninium chloride) 1 – 2mg/kg/dose (max. 50mg) q8hourly
In subsequent courses, commence methylene blue (methylene thioninium chloride) 1 – 2mg/kg/dose (max. 50mg) q8hourly 24 hours prior to ifosfamide, then q8hourly during course of chemotherapy.

Change to cyclophosphamide if repeated encephalopathy.

References


Review

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Sheila Lane, Paed Oncology consultant</td>
<td>New doc</td>
<td>Jun 2011</td>
<td>1.0</td>
<td>Jun 2013</td>
</tr>
<tr>
<td>Dr Sheila Lane, Paed Oncology consultant</td>
<td>Not recorded</td>
<td>Jun 2013</td>
<td>2.0</td>
<td>Jun 2015</td>
</tr>
<tr>
<td>Dr Shaun Wilson, Paed Oncology consultant</td>
<td>Format change Process update</td>
<td>Dec 2015</td>
<td>3.0</td>
<td>Dec 2017</td>
</tr>
</tbody>
</table>