Recurrent severe symptomatic hyponatraemia induced by low-dose oral cyclophosphamide in a patient with ANA-related vasculitis.

Dineen R¹, Pazderska A¹, Mullan R², Gibney J¹, Sherlock M¹

¹Department of Endocrinology, ²Department of Rheumatology, Adelaide and Meath Hospital incorporating the National Children’s Hospital, Tallaght, Dublin, Ireland

Introduction

- Cyclophosphamide is an alkylating agent used in the treatment of malignant and autoimmune diseases.
- Severe hyponatraemia is a serious electrolyte disorder with life-threatening neurological sequelae.
- It has been reported in association with a variety of cytotoxic agents such as vincain alkaloids, platinum compounds and alkylating agents.¹
- Severe hyponatraemia after administration of low-dose cyclophosphamide therapy (<15 mg/kg) is extremely rare.

Clinical Presentation

- 61 year old lady commenced on intravenous cyclophosphamide for mononeuritis multiplex

Medical History:

- ANA positive systemic vasculitis
- Sjogrens syndrome
- Osteoarthritis
- Multinodular Goitre

First Cycle - May 2014

- Low dose cyclophosphamide, 620mg (12.5mg/kg).
- Oral mesna pre & post infusion.
- Oral Ondansetron 8mg pre & post infusion.
- Prehydration ; 1L 0.9% saline
- 3L of H₂O₂ to prevent haemorrhagic cystitis.

Second Cycle - June 2014

- Low dose cyclophosphamide,
- Reduced Prehydration; NO IV saline, Consumed 2L of H₂O₂

Trend in Serum Sodium Post Cycle 2 : Cyclophosphamide infusion

- 12hrs post infusion, her serum sodium fell to 121mmol/l without neurological symptoms
- Placed on fluid restriction of 1.5L with gradual rise in serum sodium

Third Cycle - July 2014

- Low dose cyclophosphamide
- NO prehydration
- 1.5L fluid restriction
- Fall in serum sodium from 135mmol/L to 129mmol/L
- No neurological symptoms
- Spontaneous correction

Conclusion

- Patients receiving cyclophosphamide are at high risk of developing symptomatic hyponatraemia due to SIADH even at low doses of therapy.
- Cyclophosphamide may induce SIADH, by potentiating the renal actions of AVP.
- The combination of both increased ADH effect and excess water intake to prevent haemorrhagic cystitis can induce potentially life-threatening hyponatraemia.
- Clinicians need to be aware of this threat when encouraging large volume prehydration and diuresis with cyclophosphamide therapy.
- It is possible that pre-hydration with isotonic saline rather than oral water may minimise the incidence of this complication

Investigations

<table>
<thead>
<tr>
<th>Serum Osmolality</th>
<th>240mOsm/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Osmolality</td>
<td>347 mOsm/kg</td>
</tr>
<tr>
<td>Urinary Sodium</td>
<td>121mmol/L</td>
</tr>
<tr>
<td>Sam Cortisol</td>
<td>800nmol/l</td>
</tr>
<tr>
<td>FT4</td>
<td>15.4pmol/l</td>
</tr>
<tr>
<td>TSH</td>
<td>1.04mIU/L</td>
</tr>
</tbody>
</table>

References