Reducing the risk of hyponatraemia when administering intravenous infusions to children

The National Patient Safety Agency (NPSA) is issuing advice to healthcare organisations on how to minimise the risks associated with administering infusions to children.

The development of fluid-induced hyponatraemia in the previously well child undergoing elective surgery or with mild illness may not be well recognised by clinicians. To date, the NPSA’s National Reporting and Learning System (NRLS) has received only one incident report (that resulted in no harm), but it is likely that incidents have gone unreported in the UK.

Since 2000, there have been four child deaths (and one near miss) following neurological injury from hospital-acquired hyponatraemia (see definition on page 7) reported in the UK.\(^1\)\(^2\)\(^3\) International literature cites more than 50 cases of serious injury or child death from the same cause, and associated with the administration of hypotonic infusions.\(^4\)

**Action for the NHS and the independent sector**

The NPSA recommends that NHS and independent sector organisations in England and Wales take the following actions by 30 September 2007 to minimise the risk of hyponatraemia in children:

1. Remove sodium chloride 0.18% with glucose 4% intravenous infusions from stock and general use in areas that treat children. Suitable alternatives must be available. Restrict availability of these intravenous infusions to critical care and specialist wards such as renal, liver and cardiac units.

2. Produce and disseminate clinical guidelines for the fluid management of paediatric patients. These should give clear recommendations for fluid selection, and clinical and laboratory monitoring.

3. Provide adequate training and supervision for all staff involved in the prescribing, administering and monitoring of intravenous infusions for children.

4. Reinforce safer practice by reviewing and improving the design of existing intravenous fluid prescriptions and fluid balance charts for children.

5. Promote the reporting of hospital-acquired hyponatraemia incidents via local risk management reporting systems. Implement an audit programme to ensure NPSA recommendations and local procedures are being adhered to.
The recommendations made in this patient safety alert relate to paediatric patients from one month to 16 years old. They are not intended for paediatric and neonatal intensive care units or specialist areas such as renal, liver and cardiac units where hypotonic solutions have specialist indications.

Further information on the action points

1. Remove sodium chloride 0.18% with glucose 4% intravenous infusions from stock and general use in areas that treat children. Suitable alternatives must be available. Restrict availability of these intravenous infusions to critical care and specialist wards such as renal, liver and cardiac units.

There is evidence that there is a greater level of risk of hyponatraemia associated with the use of hypotonic solutions in comparison to other types of solution. Within the range of hypotonic solutions available, the use of sodium chloride 0.18% with glucose 4% presents an even greater risk. All children are potentially at risk. Since 2000, UK literature has cited four deaths and one near miss following neurological injury associated with the use of sodium chloride 0.18% with glucose 4%. In two of the institutions where these incidents took place, the solution was removed from ward stock, and no further cases of iatrogenic hyponatraemia have been reported.¹,³

In 2003, the Royal College of Anaesthetists issued a statement advising against the use of sodium chloride 0.18% with glucose 4% due to the possibility of water overload with severe hyponatraemia, and recommended suitable alternatives.⁵ This statement was supported by the Royal College of Paediatrics and Child Health (RCPCH). A subsequent survey of consultant anaesthetists showed that less than half of the respondents were aware that the statement had been issued, and this suggests that action has not been taken in some organisations.⁶
2 Produce and disseminate clinical guidelines for the fluid management of paediatric patients. These should give clear recommendations for fluid selection, and clinical and laboratory monitoring.

The NPSA has developed a template that can assist the development of local guidelines for prescribing and monitoring infusions for children outside of critical care areas. This is available at www.npsa.nhs.uk/health/alerts

Much of the international and UK literature on appropriate paediatric fluid management reinforces the need for rigorous clinical and laboratory monitoring, and raises concerns about the frequent absence of baseline parameters before infusions are started.7-11

While there is much debate about the management of paediatric fluid therapy in the literature, there are some common principles which should be applied. These are:

• when fluids are prescribed, they must be given the same consideration as other medicines with reference to indications, contraindications, dose, monitoring and, particularly, volume;11

• prescribed fluids must be individualised;12

• whichever fluid is used, the optimal way of avoiding dangerous hypo- or hypernatraemia is to calculate fluid balance and monitor the plasma sodium concentration regularly.

Carefully managed oral fluids are preferable to intravenous infusions. However, when intravenous infusions are prescribed, local guidelines should be based on the following clinical recommendations:

Resuscitation: intravascular volume depletion should be managed using bolus doses of sodium chloride 0.9% (isotonic solution).

Deficit: estimate any fluid deficit and replace as sodium chloride 0.9% with glucose 5% (isotonic solution) or sodium chloride 0.9% over a minimum of 24 hours.

Maintenance: do not use sodium chloride 0.18% with glucose 4%.

The low sodium content of sodium chloride 0.18% with glucose 4% infusion increases the risk of the patient developing hyponatraemia, particularly in the absence of individualised prescribing and robust on-going monitoring.

The majority of children may be safely administered sodium chloride 0.45% with glucose 5% (hypotonic solution), or sodium chloride 0.45% with glucose 2.5% (hypotonic solution). There is currently little evidence to recommend a particular strength of glucose.

Some children at high risk of hyponatraemia should only receive isotonic solutions (see Table 1). These include children who are peri- and post-operative, require the replacement of ongoing losses or have:

• plasma sodium at the lower normal reference range and definitely if less than 135mmol/L;

• intravascular volume depletion;
• hypotension;
• central nervous system (CNS) infection;
• head injury;
• bronchiolitis;
• sepsis;
• excessive gastric or diarrhoeal losses;
• salt-wasting syndromes;
• chronic conditions such as diabetes, cystic fibrosis and pituitary deficits.

Some examples of isotonic solutions include sodium chloride 0.9% with glucose 5%, sodium chloride 0.9% and compound sodium lactate solution (Hartmann’s solution/ Ringer-Lactate solution). The choice should be determined by the individual patient’s circumstances.

Sodium chloride 0.18% with glucose 4% should be restricted to specialist areas to replace ongoing losses of hypotonic fluids. These areas include high dependency, renal, liver and intensive care units.

Children requiring both maintenance fluids and the replacement of ongoing losses should receive a single isotonic fluid such as sodium chloride 0.9% with glucose 5% or sodium chloride 0.9%.

While most children will tolerate standard fluid requirements, some acutely ill children with increased anti-diuretic hormone (ADH) secretion may benefit from their maintenance fluid requirement being restricted to two-thirds of the normal recommended volume. Such children include post-operative patients and those with intracranial infections or head injuries.

Children found to have significant hypernatraemia with a plasma sodium greater than 160mmol/L should receive only isotonic solutions to reduce the risk of neurological injury associated with a rapid fall in plasma sodium concentration. Where hypernatraemia exists, plasma sodium should be reduced at a maximum rate of 0.5mmol/L/hour, or more slowly if it has prevailed for more than five days.13

Children in the peri-operative period should receive isotonic intravenous fluids. These should contain glucose to avoid the risk of hypoglycaemia. If glucose-free solutions are used during anaesthesia and surgery then plasma glucose levels should be monitored.

Consider adding potassium chloride up to 40mmol/L to maintenance fluids once plasma potassium levels are known.
Losses
Ongoing losses should be assessed every four hours. Fluids used to replace ongoing losses should reflect the electrolyte composition of the fluid being lost. In most circumstances an isotonic solution is the safest choice, for example, sodium chloride 0.9%, or compound sodium lactate solution (Hartmann’s solution/Ringer-Lactate solution) with or without the addition of potassium. In this way, for example, gastro-intestinal losses should be replaced with sodium chloride 0.9%.

Monitoring
Hyponatraemia can develop within a short timescale and a robust monitoring regime is essential. Weight should be measured, if possible, prior to commencing fluid therapy, and daily thereafter. Fluid balance including oral intake should be recorded using a fluid balance chart.

Plasma sodium, potassium, urea and/or creatinine should be measured at baseline and at least once a day. Consider measuring every four to six hours if an abnormal reading is found. This should definitely be done if the plasma sodium is below 130 mmol/L. Check plasma electrolytes immediately if clinical features suggest hyponatraemia is developing. Symptoms include increased headaches, vomiting, nausea, irritability, altered levels of consciousness, seizures and apnoea.

Ideally, use the same sample technique, either capillary or venous blood sampling, and analytical method on each occasion. This can avoid potentially misleading changes in serial sodium measurements.¹⁴

Urine chemistry may be useful in a small number of high-risk cases.¹⁵

Acute hyponatraemic encephalopathy
This medical emergency should be treated under senior medical supervision with hypertonic sodium chloride and should never be managed with fluid restriction alone.¹,⁴

3 Provide adequate training and supervision for all staff involved in the prescribing, administering and monitoring of intravenous infusions for children.

The NPSA has developed a proposed work competence statement for the prescribing and monitoring of intravenous infusions in the format developed by Skills for Health (www.skillsforhealth.org.uk). It is available at www.npsa.nhs.uk/health/alerts
The NPSA will work with Skills for Health to develop these proposed competences as national workforce competences in the future.

The NPSA has developed an e-learning module to enable practitioners to assess their current level of competence and knowledge. The module also provides training materials to improve knowledge and understanding of the safe prescribing and use of infusion fluids in children. The e-learning module is available at www.npsa.nhs.uk/health/alerts

Doctors in training are responsible for prescribing 80 to 90 per cent of intravenous fluids on general wards.⁹,¹⁶ A research study tested pre-registration and senior house officers’ knowledge of fluid prescribing practices. This study showed significant gaps in knowledge. Conclusions from the survey included the need to review the fluid and electrolyte prescribing of doctors-in-training and also supervision arrangements. It recommended that under- and post-graduate medical training puts an emphasis on practical application.¹⁶
The 1999 report of the National Confidential Enquiry into Perioperative Deaths recorded 20 per cent of patients sampled had either poor documentation of fluid balance or unrecognised/untreated fluid imbalance. The report recommended that prescribing fluids be accorded the same status as other medicines. It also recommended that medical and nursing staff should receive training to raise their awareness of risks with infusion therapy and spread good practice of prescribing, monitoring and completion of healthcare documentation.\textsuperscript{17}

4 **Reinforce safer practice by reviewing and improving the design of existing intravenous fluid prescriptions and fluid balance charts for children.**

A suggested template for an infusion fluid prescription chart that can be adapted for local use is available at [www.npsa.nhs.uk/health/alerts](http://www.npsa.nhs.uk/health/alerts)

The design of the intravenous fluid prescription and fluid balance chart can reinforce safer practice by including guidelines for infusion fluid selection; methods for calculating infusion fluid requirements; and a record of essential monitoring data such as a patient’s weight and blood electrolyte levels.

5 **Promote the reporting of hospital-acquired hyponatraemia incidents via local risk management reporting systems. Implement an audit programme to ensure NPSA recommendations and local procedures are being adhered to.**

The incidence of moderate and severe hyponatraemia and associated harm resulting from hospital fluid treatment regimes is difficult to quantify because prospective studies have not been done and, it is suggested, incidents are not recognised or reported.\textsuperscript{4}

All NHS staff should report incidents via their local risk management reporting system. This will enable both local and national monitoring of the incidents of hospital-acquired hyponatraemia, and can inform future understanding of the issues.

The NPSA recommends that healthcare organisations should audit infusion therapy in children as part of their annual medicines management audit. This will help to ensure that NPSA recommendations and local procedures are being adhered to. Audit results should be reviewed alongside local patient safety incident data concerning infusion therapy in children. The NPSA has developed a template audit form and this is available at [www.npsa.nhs.uk/health/alerts](http://www.npsa.nhs.uk/health/alerts)
Background information

Further information about the content of this patient safety alert can be found at www.npsa.nhs.uk/health/alerts

Table 1: features of commonly used intravenous fluids in the UK

<table>
<thead>
<tr>
<th>Solution</th>
<th>Osmolarity (mOsmol/L)</th>
<th>Sodium content (mequiv/L)</th>
<th>Osmolality (compared to plasma)</th>
<th>Tonicity (with reference to cell membrane)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride 0.9%</td>
<td>308</td>
<td>154</td>
<td>Isosmolar</td>
<td>Isotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.45%</td>
<td>154</td>
<td>77</td>
<td>Hyposmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.45%               with glucose 5%</td>
<td>432</td>
<td>75</td>
<td>Hyperosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Glucose 5%</td>
<td>278</td>
<td>–</td>
<td>Isosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Glucose 10%</td>
<td>555</td>
<td>–</td>
<td>Hyperosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.9%               with glucose 5%</td>
<td>586</td>
<td>150</td>
<td>Hyperosmolar</td>
<td>Isotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.45%               with glucose 2.5%</td>
<td>293</td>
<td>75</td>
<td>Isosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.18%               with glucose 4%</td>
<td>284</td>
<td>31</td>
<td>Isosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Hartmann's solution</td>
<td>278</td>
<td>131</td>
<td>Isosmolar</td>
<td>Isotonic</td>
</tr>
<tr>
<td>4.5% human albumin solution</td>
<td>275</td>
<td>100-160</td>
<td>Isosmolar</td>
<td>Isotonic</td>
</tr>
</tbody>
</table>

Definition of hyponatraemia

The normal range for plasma sodium varies between different laboratories but is often quoted as 135-145mmol/L. Hyponatraemia is defined as a plasma sodium of less than 135mmol/L. Severe hyponatraemia is defined as a plasma sodium of less than 130mmol/L. Severe acute hyponatraemia is defined as a decrease in plasma sodium from normal to less than 130mmol/L in less than 48 hours.
Mechanism of hyponatraemia

Hyponatraemia has been documented in otherwise healthy children on intravenous fluids and can be due to too much water or too little sodium in extracellular fluid. Most commonly, it indicates an expanded extracellular fluid volume and is rarely caused by sodium (or salt) depletion. The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Non-osmotic secretion of ADH can be induced in a variety of clinical situations, including pain, anxiety, the post-operative state, nausea, vomiting, certain drugs, pyrexia, sepsis, reduced circulating volume, respiratory disorders, CNS infections, and metabolic and endocrine disorders.\textsuperscript{18}

Mechanism of hyponatraemic encephalopathy

A major consequence of hyponatraemia is an influx of water into the intracellular space resulting in cellular swelling, which can cause cerebral oedema, seizures and brain stem herniation. Hyponatraemic encephalopathy is a serious complication and children are a group of patients particularly susceptible to developing neurological complications.

This is due to the reduced space for brain swelling in the skull and impaired ability of the paediatric brain to adapt to hyponatraemia compared to adults. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

Hospital-acquired hyponatraemic encephalopathy is most often seen in patients with excess ADH secretion, frequently in the post-operative period. Mortality directly attributed to encephalopathy in children with post-operative hyponatraemia is estimated as eight per cent. The most important contributing factors are the failure to recognise that the patient’s ability to manage free water may be compromised, and the administration of hypotonic solutions in such situations.\textsuperscript{19-22}
Prevention of hyponatraemia

The practice of prescribing hypotonic solutions dates back to the work of Holliday and Segar in the 1950s and hypotonic solutions are still in common use today. Their approach recommended a simple methodology for calculating fluid and energy requirements and the use of an ‘ideal’ hypotonic solution, glucose 5% and sodium chloride 0.2% (sodium chloride 0.18% and glucose 4% in the UK). These recommendations do not take into account deficits, losses, unusual metabolic demands or the secretion of excess ADH during illness and particularly in the peri-operative period. A number of investigators, including Holliday, have since concurred that the administration of hypotonic parenteral fluids can result in dangerous hyponatraemia.\textsuperscript{1,2,23-28}

There is much debate in recent literature about the preferred approach to paediatric fluid management and the prevention of hyponatraemia. However, there are no reports of clinical trials. The literature emphasises that, where possible, oral administration remains the preferred route of choice but it must be remembered that injudicious use of oral fluids can also be life-threatening.\textsuperscript{4} In relation to parenteral fluid choice, the differing clinical opinions for prevention include: continued use of hypotonic solutions with fluid restriction,\textsuperscript{29} isotonic solutions with fluid restriction,\textsuperscript{30} the use of only isotonic solutions\textsuperscript{22} or the use of isotonic and hypotonic solutions in specific clinical situations.\textsuperscript{1,12}

Whilst there is evidence of harm associated with the use of hypotonic solutions, there is an absence of definitive evidence for clinicians that can help them when choosing a solution. It is against this backdrop that the NPSA is making the recommendations outlined in this patient safety alert.

Acknowledgements

The NPSA gratefully acknowledges the contributions of members of the multi-disciplinary working group and the individuals, teams and organisations who contributed to the consultation process. Further information about contributors can be found at www.npsa.nhs.uk/health/alerts

Further details

For further information about this patient safety alert, please contact:

Linda Matthew, Senior Pharmacist, Safe Medication Practice
National Patient Safety Agency
4-8 Maple Street
London W1T 5HD
Tel: 020 7927 9500
Email: paediatric-infusions@npsa.nhs.uk

For more information on the NPSA, visit www.npsa.nhs.uk
Patient safety alert 22
Reducing the risk of hyponatraemia when administering intravenous infusions to children

Page 10 of 12

References

5. Royal College of Anaesthetists. News: Possibility of water overload with severe hyponatraemia developing after the use of glucose 4% and sodium chloride 0.18%. (November 2003).

A patient safety alert requires prompt action to address high risk safety problems.

This patient safety alert was written in the following context:

It represents the view of the National Patient Safety Agency, which was arrived at after consideration of the evidence available. It is anticipated that healthcare staff will take it into account when designing services and delivering patient care. This does not, however, override the individual responsibility of healthcare staff to make decisions appropriate to local circumstances and the needs of patients and to take appropriate professional advice where necessary.

© National Patient Safety Agency 2007. Copyright and other intellectual property rights in this material belong to the NPSA and all rights are reserved. The NPSA authorises healthcare organisations to reproduce this material for educational and non-commercial use.
Suggested template for local development of intravenous fluid guidelines

For previously well children aged one month to 16 years (excluding renal, cardiac, diabetic ketoacidosis and acute burns patients)

**Maintenance fluids**

**Type of intravenous fluid**

The majority of children may be safely administered sodium chloride 0.45% with glucose 5% or sodium chloride 0.45% with glucose 2.5% – although there is little evidence to support the choice of a particular strength of glucose.

In some circumstances, children should only ever be administered isotonic fluids such as sodium chloride 0.9% with glucose 5%, sodium chloride 0.9%, Hartmann’s solution/Ringer-Lactate solution. Solution choice should be tailored to the patient’s needs.

These circumstances include:

- serum sodium at the lower normal reference range and definitely if less than 135mmol/L;
- intravascular volume depletion;
- peri- and post-operative patients;
- hypotension;
- CNS infection;
- head injury;
- bronchiolitis;
- sepsis;
- excessive gastric or diarrhoeal losses;
- salt-wasting syndromes and chronic conditions such as diabetes, cystic fibrosis and pituitary deficits, and those requiring replacement of ongoing losses.

Children with a plasma sodium in excess of 160mmol/L should receive isotonic solutions to reduce the risk of neurological injury associated with a rapid fall in plasma sodium.

**Volume of intravenous fluid**

- Less than 10kg: 100ml/kg/day or 4ml/kg/hour;
- 10-20kg: 1000ml plus 50ml/kg/day for each kg over 10kg or 40ml/hour plus 2ml/kg/hr for each kg over 10kg;
- Over 20kg: 1500ml plus 20ml/kg/day for each kg over 20kg or 60ml/hour plus 1ml/kg/hour for each kg over 20kg;

Up to a maximum of 2500ml/day in males and 2000ml/day in females.

Consider adding potassium chloride, up to 40mmol/L, to maintenance fluids once plasma potassium concentration is known.

Some acutely ill children with increased ADH secretion may benefit from restriction of maintenance fluids to two-thirds of normal recommended volume.

---

**Fluid deficit**

Estimate any fluid deficit and replace as sodium chloride 0.9% or sodium chloride 0.9% over a minimum of 24 hours.

Those requiring maintenance fluids and replacement of ongoing losses should receive a single isotonic fluid such as sodium chloride 0.9% or sodium chloride 0.9% with glucose 5%.

**Ongoing fluid losses**

Reassess ongoing fluid losses every four hours. Fluids used to replace ongoing fluid losses should ideally reflect the electrolyte composition of the fluid being lost. Sodium chloride 0.9% is appropriate in most cases (with or without the addition of potassium chloride).

**Hyponatraemia** may develop as a complication of any fluid regime.

If shock is present administer 20ml/kg sodium chloride 0.9% (10ml/kg in the setting of trauma). Repeat if necessary and call for senior help immediately.

Symptomatic hyponatraemia is a medical emergency.

Check plasma electrolytes.

**Monitoring**

Check plasma electrolytes before commencing the infusion, except prior to the majority of elective surgery. Monitor plasma glucose if glucose-free solutions are used during surgery.

Check plasma electrolytes every 24 hours whilst intravenous fluids are being administered. If plasma electrolytes are abnormal, consider rechecking every four to six hours, but definitely if plasma sodium concentration is below 130mmol/L.

Check plasma electrolytes if clinical features suggestive of hyponatraemia develop; these features include nausea, vomiting, headache, irritability, altered level of consciousness, seizure and apnoea.

Where possible, all children on intravenous fluids should be weighed prior to the commencement of therapy and be weighed again each day.

Document accurate fluid balance daily. Assess urine output – oliguria may be due to inadequate fluid, renal failure, obstruction or the effect of ADH.