Anaesth Intensive Care 2014; **42: 258-262**

Intravenous infusion of sterile water for the treatment of hypernatraemia

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SUMMARY

Little research has been carried out into the infusion of intravenous sterile water for the treatment of hypernatraemia, and it remains a contentious issue. We conducted a review of the literature and extract results following an extensive search of Medline 1946, Embase 1974, ProQuest, evidence-based practice resources, national and international guideline sites and the publications of various professional bodies. The review is presented on the infusion of sterile water (hypotonic fluid) to lower serum sodium level in those circumstances when enteral supplementation of water is not possible, such as in postoperative patients or when other isotonic fluids (such as 5% dextrose in water infusion) are less than ideal—for example, hyperglycaemic patients on an insulin infusion. Absence of guidelines has limited the use of sterile water, even as an off-label drug when it can be administered relatively safely via a central line.

Key Words: sterile water, intravenous infusion of sterile water, water for injections, hypotonic fluids, intensive care, hypernatraemia, haemolysis, off-label drug

We investigated the role and available evidence around the intravenous infusion of sterile water for treating patients with hypernatraemia in an intensive care unit (ICU). We instigated this investigation following the novel (for our unit) requirement to infuse intravenous water to lower a postoperatively elevated serum sodium in a morbidly obese, type 2 diabetic individual who required a high dose of insulin. This patient underwent emergency surgery for a massive strangulated hernia. The abdomen was left open for further washouts with instructions to keep the patient nil by mouth. The patient was successfully discharged home without any complications following the use of sterile water intravenously via a central line.

This paper focuses on the role of intravenous infusion of sterile water and its prescription where appropriate in the management of hypernatraemia. It does not attempt to discuss in detail the aetiology or pathophysiology of hypernatraemia and its effects and management strategies[1–8].

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Accepted for publication on November 18, 2013

METHODS

A thorough review of the literature on the infusion of sterile water was conducted, including Medline 1946, Embase 1974 and ProQuest; evidence-based practice resources; guideline sites; and professional bodies such as the Agency for Healthcare Research and Quality, the National Institute for Health and Care Excellence, the Scottish Intercollegiate Guidelines Network, the Australian and New Zealand Intensive Care Society, the Australasian College for Emergency Medicine, the Society of Critical Care Medicine, the Emergency Care Institute, UpToDate, McMaster PLUS, British Medical Journal Best Practice, the Cochrane Library and the Joanna Briggs Institute. A review of the dose, rate of infusion, route of administration and the duration and safety profile was undertaken with a combination of search items such as intensive care, critical care, infusion of sterile water, sterile water, water, hypotonic fluids and hypernatraemia. Extract results from the search were not limited to the English language. Full-text case reports of both human and animal data did not reveal any review articles or any national or international guidelines for the safe administration of intravenous sterile water for hypernatraemia in ICUs. Only a few anecdotal case reports were found. References of the retrieved articles considered relevant were reviewed and representative information included.

DISCUSSION

Hypernatraemia is defined as a serum sodium of more than 145 mmol/l and is a common electrolyte abnormality seen in hospitalised and intensive care patients[9–11]. The causes are multifactorial, including vomiting, diarrhoea, nasogastric suctioning, hyperalimentation (enteral or parenteral), burns, fever, open wounds, drugs (diuretics, antibiotics such as penicillins (especially ticarcillin/clavulanic acid), lactulose, lithium, 8.4% sodium bicarbonate, hypertonic saline), central or nephrogenic diabetes insipidus and others[12,13]. The incidence is 5.7 to 9%, and mortality in this patient group is over 40%, reaching 75% if the serum sodium is above 160 mmol/l[1,9–11,13,14].

The management of hypernatraemia is based on the history, examination and assessment of the volume status of the patient and identifying its cause and whether it is acute or chronic hypernatraemia, treating as appropriate[12,15].

Assessing the volume status is critical as it is the free movement of water that helps to keep the different compartments in osmotic equilibrium. If the total body water level changes (volume), the concentration of sodium changes, as they are interdependent. The clinical assessment of hydration is difficult at the best of times and more so in critically ill patients, young or old, obese or otherwise, with associated comorbid conditions.

The various clinical and biochemical indicators to suggest hydration status include temperature; heart rate; blood pressure; urine output; skin turgor; elevation of haematocrit, urea and electrolytes; plasma and urine osmolality; and arterial blood gas analysis[16–21]. Furthermore, volume loss and dehydration are to be differentiated prior to resuscitation, as volume loss or depletion can be replenished rapidly (where early and rapid resuscitation is essential to restore stable haemodynamics[22–24]) while dehydration is corrected slowly, although both can be present concomitantly and there is no general consensus about the calculation of the required volume, the rate of fluid administration or the selection of the ideal type of fluid prescription in hospitalised patients[4–8,22,25–28].

The goal of treating hypernatraemia after assessing the volume status and calculating the water deficit is to lower the serum sodium by 0.5 to 1.0 mmol/l/hour by using the following formulae[1,2,29]: change in serum Na (Δ Na)=(Na content in intravenous fluid+K content in intravenous fluid)–serum Na/(total body water+1). Total body water=weight in kilograms ×correction factor. The correction factor for elderly men and women is 0.5 and 0.45 and for non-elderly men and women it is 0.6 and 0.5 respectively.

In asymptomatic chronic hypernatraemia, the water deficit should be corrected slowly (over 48 hours)[29] to avoid adverse outcomes associated with rapid correction or over-correction of the elevated serum sodium, such as cerebral oedema, seizures, permanent brain injury and death[20,30–32].

Osmolality and the sodium content of the intravenous fluid determine the type of fluid prescription required while correcting hypernatraemia. Sterile water is a hypotonic fluid with an osmolality of zero. Nine grams of salt (as in 0.9% saline) or 50 grams of dextrose in a litre of sterile water (as in 5% dextrose) is required for the solution to become iso-osmotic[33].

Outside the hospital setting, thirst generally ensures enough free water is taken to avoid hypernatraemia[34–36]. However, in the ICU setting many patients are intubated and/or have impaired mental function[11,21].

Although the preferred route of administration of water is oral or via a nasogastric tube, when neither of these routes is available to clinicians, sterile water can only be administered intravenously via a central

Table 1
Sodium content and osmolality of some intravenous fluids

Type of fluid	Sodium content (mmol/l)	Osmolality mOsmol/kg
0.9% sodium chloride	154	300
0.45% sodium chloride	77	150
0.2% sodium chloride	34	69
3% sodium chloride	513	1000
Hartmann's	129	273
Plasma-Lyte 148 Replacement	140	294
4% albumin	140	250
Gelofusine	154	274
5% dextrose in water	0	253
Sterile water	0	0

line, which may be preferable to the use of 5% glucose in the setting of difficult-to-control hyperglycaemia.

To assess current practice around the prescription of intravenous water to correct hypernatraemia, a query was posted on 'ICU Connect' (Intensive Care and Coordination Monitoring Unit), an online internet forum, to elicit views from colleagues and to source relevant information for guidance and protocols[37], and a literature search was commenced.

The Institute for Safe Medication Practices, a registered, non-profit organisation in North America that collects and analyses medication error reports, published a series of articles in their fortnightly newsletters on the inadvertent administration/use of sterile water intravenously for hypernatraemia and resultant adverse effects, such as pain at the injection site (if incorrectly administered via a peripheral intravenous cannula), haemolysis, acute renal failure and death. The reasons for inadvertent administration of sterile water were attributed to the misconception of the free water concept while treating patients with hypernatraemia and also to errors of prescribing (i.e. prescribing intravenous water instead of normal saline) and mistaking labelling (package insert on look-alike bags of normal saline and sterile water)[38–48]. Haemolysis as a complication was recorded following administration of intravenous distilled water as early as 1914 by Krumbhaar[49], following the use of 25% concentrated albumin diluted with sterile water during therapeutic plasma exchange in a case series[50] and also in patients who were inadvertently dialysed against distilled water[44,51].

An alternative to the use of intravenous sterile water to lower elevated serum sodium is to use dextrose-containing fluids. Sterns and Silver[33] suggested considering that salt (or saline) and water are drugs that have indications, contraindications and appropriate doses and modes of delivery. They consider that prescribing salt-containing water when the sodium is high and rising is the moral equivalent of giving warfarin to a patient with a high International Normalized Ratio. Because water cannot be infused directly into a small vein without causing haemolysis, intravenous water is usually mixed with glucose[34]. However, using fluids containing glucose would also increase the blood glucose level in euglycaemic or diabetic patients due to the stress mechanism[52,53]. Blood glucose management is itself a contentious issue in critically ill patients and is discussed elsewhere[54–57]. Furthermore, hyperglycaemia might also lead to osmotic diuresis limiting the reduction of elevated serum sodium[53].

Worthley[58] demonstrated in 1986 that sterile water of 500 ml per hour administered in each of three different patients via central line did not result in any evidence of haemolysis, with hourly analysis of the markers of haemolysis. He used sterile water over a 6 to 12 hour period. Hilton et al[59] have opined that the administration of intravenous fluids has been primarily based on physiological concepts rather than on evidence, advocating that sterile water may safely be administered via central line without haemolysis in the presence of hypernatraemia and hyperglycaemia.

Considering the high blood-flow in major vessels and with an effective cardiac output of 5 l/minute, infusion of intravenous sterile water, even at a rate of 500 ml/hour (less than 10 ml/minute), via a central line should not result in haemolysis. This is probably a reasonable inference from the successful outcome and reduction of high serum sodium in Worthley's case series[58] and also from the 'ICU Connect' forum[37] discussion on the safe administration of sterile water if appropriate in the ICU.

We believe, therefore, that the infusion of sterile water may be safe if administered cautiously via a central line, as in our patient and as in the research cited[58,59]. We acknowledge that if the route of administration or dosage (volume) is incorrect the result may be fatal[38,50,51]. Overzealous administration or rapid correction of hypernatraemia could result in rapid shifts of water into brain cells causing cellular swelling and cerebral oedema[30–32].

We suggest, furthermore, that infusion of sterile water be considered an 'off-label drug' with the caveats that accompany such use. The practice of prescribing registered drugs outside of the approved indications is not regulated or controlled by the Therapeutic Goods Administration, as it is at the discretion of the prescribing physician. In these circumstances, the Therapeutic Goods Administration is unable to vouch for the quality, safety or efficacy of this unapproved product and its use is therefore regarded as experimental. It should also be realised that the Australian Government, the Secretary of the Therapeutic Goods Administration or a delegate of the Secretary cannot be rendered liable to a person in respect of loss, damage or injury of any kind suffered by the person as a result of, or arising out of the use of, a therapeutic good for a non-approved indication (communication with the pharmacist).

Off-label drug use may be case-by-case, based on the individual practitioner's expertise, which may have been acquired in their previous experience or by their colleagues in different locations, for other

indications, or for use in age ranges, doses or routes that are not approved by the regulatory authorities[60].

CONCLUSION

Limited evidence suggests that sterile water for injection can be safely administered as an off-label drug for treating patients with hypernatraemia if indicated and appropriate in intensive care settings, only via central line when other routes are unavailable and administering dextrose-containing fluids is less than ideal. Such off-label use is accompanied by implications for the prescriber. Further research is needed in this area.

ACKNOWLEDGEMENT

We would like to acknowledge personnel at Hunter New England Health Libraries, Newcastle, New South Wales, for doing research for us, dating back to c1830, on the use of intravenous water and also checking with other national and international evidence-based resources.

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