# Inadvertent sodium loading in critically ill patients

Shailesh Bihari, Judy Ou, Andrew W Holt and Andrew D Bersten


## ABSTRACT

**Background:** Recommended daily intake of sodium is 1–2 mmol/kg. Sodium administration is rarely separated from fluid administration in critically ill patients.

**Objective:** To estimate the amount of sodium administered to patients who were invasively ventilated, and to investigate whether sodium administration affected oxygenation, length of stay in ICU and serum sodium level.

**Design, participants and setting:** Retrospective audit of adult patients who received invasive mechanical ventilation for ⩾ 5 days in a tertiary-level intensive care unit.

**Main outcome measures:** Total sodium administered from resuscitation and maintenance fluids, infusions, flushes, medicines, transfusions, enteral feeds and total parenteral nutrition; oxygenation, length of ICU stay and serum sodium level.

**Results:** 13 men and 7 women were included. Their median age was 71.9 years (range, 19.8–89.2 years). Median duration of mechanical ventilation was 9 days (range, 6–20 days) and median ICU stay 11.6 days (range, 6–21 days). Median APACHE II score was 29 (range, 18–41). Daily sodium administration was 225.5 mmol (151–355 mmol). The median daily net fluid balance was 351 mL (range, – 759 to + 1125 mL) and median daily fluid intake was 2352 mL (range, 1437–3798 mL). Daily sodium administered correlated with net fluid balance ($P < 0.001$; $r = 0.35$). Of total sodium administered, infusions contributed 22.2% (1.2%–39.9%); drugs 21.6% (0.0–35.5%); flushes 17.4% (9.3%–24.5%); enteral feeds 17% (0.0–39.5%); resuscitation 16.0% (2.5%–36.9%); maintenance fluids 5.8% (0.0–24.0%); transfusions 3.9% (0.0–9.5%) and parenteral nutrition 0.1% (0.0–2.6%).

**Conclusion:** Sodium administration to this cohort of critically ill patients requiring prolonged mechanical ventilation was high. Further studies should examine ways of limiting the amount of sodium administered to such patients and to examine if this influences patient outcomes.


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Inadvertent positive fluid balance has been shown to be associated with poorer outcomes in critically ill patients,[1] probably due to extracellular fluid expansion. Therefore, both water and sodium may be important, because water distributes to both intra- and extracellular spaces, and sodium distributes into the extracellular spaces and can exacerbate interstitial oedema in the lungs and systemic circulation.

This effect might be more relevant in mechanically ventilated patients. Positive pressure ventilation and positive end-expiratory pressure (PEEP) both raise intrathoracic pressure. This results in reduced venous return, and consequent complex neurohumoral responses in turn lead to sodium and water retention.[2]

As potential sources of sodium in critically ill patients include resuscitation fluids, maintenance fluids, enteral and parenteral feeds, venous and arterial line flushes, transfusions, replacement fluids and many medications, we hypothesised that critically ill patients are inadvertently given excess amounts of sodium during their stay in intensive care units.

To examine this, we performed a retrospective sodium administration audit on consecutive patients receiving prolonged mechanical ventilation during their ICU stay. Our primary objective was to estimate the amount of sodium administered to patients who were invasively ventilated for 5 days or more in the ICU; secondary objectives were to investigate whether sodium administration had any effect on oxygenation, length of stay in ICU or serum sodium level.

## Methods

A retrospective analysis of the amount of sodium administered per day from all sources was performed on 20 consecutive patients who required mechanical ventilation for 5 days or more (120 hours) at the Flinders Medical Centre ICU, Adelaide, South Australia, between January and May 2009. This is a 32-bed, tertiary-level adult general ICU. Ethics approval was granted by the Flinders Clinical Research Ethics Committee (application no. 217/09).

Patients were excluded if they were younger than 18 years, were pregnant, required chronic haemodialysis, had an admission diagnosis of traumatic brain injury, or had diabetic ketoacidosis or were in a hyperosmolar hyperglycaemic state.

Patient case notes, data sheets, operation notes and total parenteral nutrition data sheets were retrieved and reviewed. The following patient baseline data were recorded: demographics, diagnosis, Acute Physiology and Chronic Health Evaluation (APACHE) II score at admission, duration of invasive mechanical ventilation, length of stay in ICU, ICU outcome, requirement for diuretics, requirement for dialysis, daily administered fluid and fluid balance (taking account of all recorded sources, including urine, drains and gastrointestinal).

Total daily administered sodium (from all sources) was recorded in the following categories:

- Resuscitation — total sodium administered as fluid boluses during initial management or ongoing care.

- Maintenance — sodium administered (including given as a replacement for renal and/or gastrointestinal loss) as a constant infusion.
- Infusion — sodium used as a vehicle for medicines, such as sedatives, vasopressor agents, antimicrobials and insulin.
- Flushes — sodium given as flushes with each central venous and arterial access. The flush used in this study was heparinised (2 U/mL) 0.9% saline, administered at a rate of 4 mL/h for every flush-based catheter present.
- Medicines — sodium present in administered medicines.
- Transfusions — sodium from packed red blood cells, platelets, fresh frozen plasma and cryoprecipate administration.
- Enteral feeds.
- Total parenteral nutrition.

A master table was constructed with the sodium content of all drugs and fluids administered to these patients (Appendix 1). The sodium content of blood products was estimated by taking the average of sodium contained in 10 samples of each type of blood product.

Also recorded from each patient's daily data between 08:00 and 09:00 each day were: daily renal function, serum sodium concentration, daily $PaO_2/FiO_2$ ratio, $PaCO_2$, minute ventilation, PEEP and central venous pressure. Hypernatraemia was defined as a sodium concentration $\geqslant$ 150 mmol/L.

Data were recorded from 24 hours before intubation, or from the time of admission to hospital (if less than 24 hours) until 24 hours after extubation or death (if the patient remained intubated and ventilated at time of death).

### Statistical analyses

Data were analysed using SPSS, version 19.0 (IBM, Armonk, NY, USA). Most data were not normally distributed and are reported as median (range). The Pearson correlation was used to correlate the daily administered sodium with: APACHE II score, total ICU stay, $PaO_2/FiO_2$ ratio (on the following morning), net fluid balance and serum sodium concentration. For all analyses, $P < 0.05$ was considered statistically significant.

## Results

### Patient characteristics

Twenty patients were included in the study (13 men, seven women). Their median age was 71.9 years (range, 19.8–89.2 years). The median duration of mechanical ventilation was 9 days (range, 6–20 days), and median ICU stay was 11.6 days (range, 6–21 days). Of the 20 patients studied, 12 died, five were discharged home, two were readmitted to ICU and one was transferred to another hospital. The median APACHE II score at admission was 29 (range, 18–41). Seven patients required dialysis. Twelve patients were administered diuretics at some stage during the course of their ICU stay.

**Figure 1. Median daily sodium intake (interquartile range)**

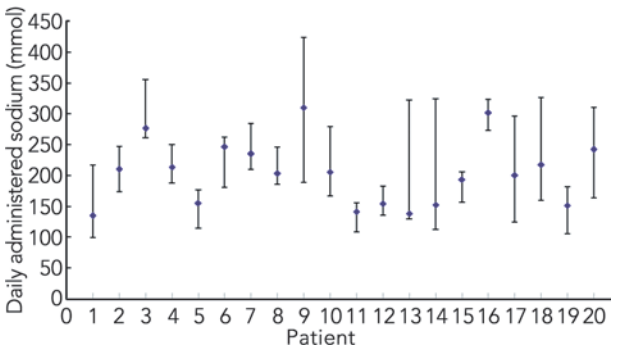



**Table 1. Contributions of each source to the total sodium administered**

| Sodium source | Median % (range) |
|---|---|
| Resuscitation | 16% (2.5%–36.9%) |
| Maintenance fluids | 5.8% (0–24.0%) |
| Infusions | 22.2% (1.2%–39.9%) |
| Flushes | 17.4% (9.3%–24.5%) |
| Medicines | 21.6% (0–35.5%) |
| Transfusions | 3.9% (0–9.5%) |
| Enteral feeds | 17.0% (0–39.5%) |
| Total parenteral nutrition | 0.1% (0–2.6%) |

### Sodium and fluid

The median average daily sodium administration was 225.5 mmol (range, 151–355 mmol) (Figure 1). The median daily net fluid balance was 351 mL (range, – 759 to + 1125 mL) and median daily fluid intake was 2352 mL (range, 1437–3798 mL). The contributions to the total sodium administered from each source are shown in Table 1.

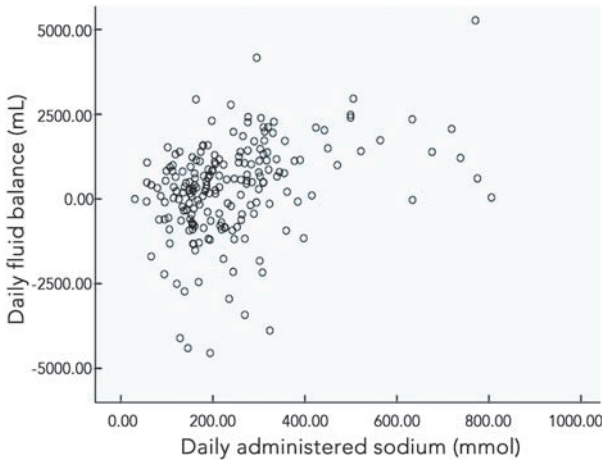
The mean daily serum sodium level was 141 mmol/L (SD, 5 mmol/L). Fourteen of the 20 patients had serum sodium concentrations greater than 145 mmol/L and three patients developed hypernatraemia at some stage during their stay in ICU.

Daily sodium administered was correlated with net daily fluid balance ($P < 0.001$; $r = 0.35$; Figure 2). However, there was no correlation between daily administered sodium and APACHE II score ($P = 0.10$); total ICU stay ($P = 0.48$); $PaO_2/FiO_2$ ratio the next morning ($P = 0.62$); or daily plasma sodium concentration ($P = 0.67$).

## Discussion

In our study, ICU patients receiving prolonged mechanical ventilation were administered over 220 mmol of sodium daily. The average daily net fluid balance here was comparable to the conservative group of the Fluid and Catheter Treatment

**Figure 2. Correlation of daily administered sodium and daily fluid balance ($P < 0.001$; $r = 0.35$)**




Trial (FACTT),[3] and the average daily fluid intake was less than the conservative group in the FACTT, suggesting that we achieved good fluid balance in our cohort of patients. However, their average daily sodium intake indicates that critically ill mechanically ventilated patients inadvertently receive a high load of sodium, despite achieving neutral fluid balance. A high level of non-dietary sodium administration has also been recently reported in cardiac patients.[4]

This high level of sodium administration, surprisingly, was not due to resuscitation as generally expected; but was from infusions, flushes and medicines. The amount of sodium administered in infusions is most surprising. Similarly, the amount of sodium administered in flushes is very high and may still be underrecorded. Some medications (especially antibiotics) contain large amounts of sodium. It is noteworthy that the usual maintenance fluid in our ICU is 4% dextrose and 0.18% saline, which has a relatively low sodium content. Many ICUs around the world administer 0.9% saline as the usual maintenance fluid, which can lead to a large increase in sodium intake.

Fourteen patients had a serum sodium level ⩾ 145 mmol/L, and three patients developed hypernatraemia at some stage during their stay. Hypernatraemia is a common and important electrolyte disorder among critically ill patients and has been shown to be an independent predictor for mortality.[5] Most cases of hypernatraemia in the ICU developed after admission, suggesting an iatrogenic component. The strategy of aiming to achieve a negative fluid balance evidenced by use of diuretics in our study, combined with a high sodium load and balance, predisposes to hypernatraemia, as has been previously described.[6,7]

High levels of daily sodium administered to mechanically ventilated patients were correlated with net positive fluid balance. This has been associated with poorer lung function,[3] poorer kidney function,[8] delayed return of gastrointestinal function after surgery[9] and an increased risk of mortality.[1] This association with worse outcomes is probably due to extracellular fluid expansion, which in turn can affect other organ systems.

This is a small retrospective observational study with all the inherent limitations of this study design. This audit was not powered to study the correlation of daily administered sodium and APACHE II score, total ICU stay and oxygenation, and a larger study is required to examine these variables. Although our data are consistent with inadvertent sodium loading in critically ill patients, they were gathered in a single centre and sodium balance was not estimated. It remains to be seen whether our observations are applicable to other ICUs.

Sodium administration to critically ill patients requiring prolonged mechanical ventilation is high. Further studies, strategies and guidelines are needed to find ways of limiting the amount of sodium administered to such patients and to examine whether this influences patient outcomes.

## Competing interests

None declared.

## Author details

**Shailesh Bihari,** Registrar
**Judy Ou,** Resident Medical Officer
**Andrew W Holt Senior,** Intensivist
**Andrew D Bersten,** Director
Intensive Care Unit, Flinders Medical Centre, Adelaide, SA, Australia.
***Correspondence:*** biharishailesh@gmail.com

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## Appendix 1. Sodium content in medicines and fluids

| Medicine | Sodium content | Medicine | Sodium content |
|---|---|---|---|
| Acetazolamide 500 mg | 2.0 mmol/500 mg[1] | Hydrocortisone 100 mg/2 mL | 0.3 mmol/100 mg[1] |
| Acetylcysteine (NAC) 2 g | 0 mmol[1] | Imipenem–cilastatin 500 mg | 1.6 mmol/500 mg[1,3] |
| Aciclovir 250 mg | 4.2 mmol/g[2] | Ketamine 10 mg/mL | 0.2 mmol/10 mg[3] |
| Adrenaline 1 mg/1 mL | 0.2 mmol/mL[2] | Lignocaine 1% 5 mL | 0 mmol[1] |
| Adrenaline 1 : 10000 (0.1 mg/mL) | 0.1 mmol/mL[2] | Lincomycin 600 mg/2 mL | 0 mmol[1] |
| Amiodarone 150 mg/3 mL | 0 mmol[2] | Linezolid 2 mg/mL | 5 mmol/300 mL[1] |
| Aminophylline 250 mg/10 mL | 0 mmol[3] | Meropenem 1 g | 4.0 mmol/g[1] |
| Amoxycillin 1 g | 3.3 mmol/g[3] | Methylprednisolone Na succinate 1 g/16 mL | 2 mmol/g[1] |
| Ampicillin 1 g | 2.7 mmol/g[1,2] | Metoclopramide 10 mg/2 mL | 0.3 mmol/10 mg[1] |
| Atropine 1 mg/10 mL | 1.5 mmol/mg[3] | Metoprolol 5 mg/5 mL | 0.8 mmol/5 mL[1] |
| Azithromycin 500 mg | 5.0 mmol/500 mg[1] | Metronidazole 500 mg/100 mL | 13.5 mmol/500 mg[1] |
| Benztropine 2 mg/2 mL | 0.310 mmol/2 mg[1] | $MgSO_4$ 2.47 g/5 mL | 0 mmol[1] |
| Benzylpenicillin 1.2g/vial | 3.6 mmol/1.2 g[1] | Midazolam 5 mg/mL | 0.1 mmol/5 mg[1] |
| Betamethasone 5.7 mg/mL | 0.1 mmol/mL[3] | Milrinone 10 mg/10 mL | 0 mmol[1] |
| Bupivacaine 50 mg/20 mL vial | 0 mmol/vial[1] | Morphine | 0 mmol |
| Cefepime 1 g | 0 mmol/vial[1] | Moxifloxacin 400 mg/250 mL | 34 mmol/400 mg[1] |
| Cefotaxime 1 g | 2.2 mmol/g[1] | Naloxone 400 mg/mL | 0.2 mmol/400 mg[1] |
| Ceftriaxone 1 g/vial | 3.6 mmol/g[1] | Nimodipine 100 mg | 0 mmol[1] |
| Cephazolin 1 g | 2.0 mmol/g[1] | Noradrenaline 2 mg/2 mL | 0 mmol[1] |
| Chloramphenicol 1.2 g | 2.3 mmol/g[1] | Pantoprazole 40 mg | 0.1 mmol/40 mg[4] |
| Chlorpromazine 50 mg/2 mL | 0.2 mmol/50 mg[3] | Phenobarbitone sodium 200 mg/mL | < 1 mmol[1] |
| Ciprofloxacin 200 mg/100 mL (Ciproxin IV) | 15.4 mmol/200 mg[1] | Phenytoin 250 mg/5 mL | 1.0 mmol/250 mg[1] |
| Clonazepam 1 mg | 0 mmol[1] | Phytomenadione 10 mg | 0 mmol[1] |
| Clonidine 150 μg/1 mL | 0.2 mmol/150 μg[1] | Piperacillin 2 g | 3.7 mmol/2 g[1] |
| Desmopressin (DDAVP) | 0 mmol/vial[1] | Piperacillin 4 g + tazobactam 500 mg (Tazocin) | 11.1 mmol/vial[1] |
| Dexamethasone 8 mg/2 mL | 0 mmol[1] | Potassium | 0 mmol[1] |
| Diazepam 10 mg/2 mL | 0.7 mmol/10 mg[1] | Propofol | 0 mmol[1] |
| Dicloxacillin 1 g | 2.2 mmol/g[1] | Protamine 50 mg/5 mL | 0.8 mmol/50 mg[3] |
| Digoxin 500 μg/2 mL | 0 mmol[1] | Ranitidine 50 mg/2 mL | 0 mmol[1] |
| Dobutamine 250 mg | 0 mmol[1] | Rifampicin 600 mg | 0.1 mmol/vial[1] |
| Dopamine 200 mg/ 5 mL | 0 mmol/200 mg[1] | Rocuronium | < 1 mmol[1,4] |
| Ephedrine 30 mg/mL | 0.1 mmol/ 30 mg[1] | Sodium bicarbonate 10 mL | 10 mmol/10 mL[1] |
| Erythromycin 1 g | 0 mmol[1] | Sodium nitroprusside 50 mg/vial | 0.3 mmol/50 mg[1] |
| Esmolol 100 mg/10 mL | 0.3 mmol/100 mg[1] | Sotalol 40 mg/4mL | < 1 mmol/100 mg[1] |
| Flucloxacillin 1 g | 2.2 mmol/g[1] | Suxamethonium 100 mg/2 mL | 0 mmol[1] |
| Fluconazole 200 mg/100 mL (premix) | 15 mmol/200 mg[1] | Thiamine 100 mg/mL | 0 mmol[1] |
| Flumazenil 0.5 mg/5 mL | 0.8 mmol/0.5 mg[1] | Thiopentone 500 mg | 2.5 mmol/500 mg[1] |
| Frusemide 250 mg/25 mL | 0.8 mmol/250 mg[1] | Ticarcillin 3 g + potassium clavulanate 0.1 g (Timentin) 3.1 g in 100 mL normal saline | 31 mmol/3.1 g[1] |
| Frusemide 20 mg/2 mL | 0.3 mmol/ 20 mg[1] | Theophylline 200 mg/50 mL | 0 mmol[3] |
| Gentamicin 80 mg/2 mL | 0.1 mmol/80 mg[1] | Trimethoprim 80 mg + sulfamethoxazole 400 mg/5 mL | 0 mmol[1] |
| Glucagon 1 mg | 0 mmol[1] | Tropisetron 2 mg/2 mL | < 1 mmol[1] |
| Glucose IV 50% (25 g/50 mL) | 0 mmol[1] | Vancomycin | 0 mmol[1] |
| Glyceryl trinitrate 50 mg/10 mL | 0 mmol[1] | Vasopressin 20 unit/mL | 0.2 mmol/mL[1] |
| Haloperidol 5 mg/mL | 0 mmol[1] | Vecuronium 10 mg/vial | 0.1 mmol/10 mL[1] |
| Heparin Na | 155.2 mmol/L (if normal saline)[1] | Verapamil 5 mg/2 mL | 0.3 mmol/5 mg[1] |
| Hydralazine 20 mg/ampoule | 0 mmol[1] | Voriconazole 200 mg | 10 mmol[1] |

**Appendix 1 (continued)**

| | Sodium content |
|---|---|
| **Fluid** | |
| 0.9% normal saline | 155 mmol/L |
| 4% dextrose + 0.18% normal saline (default choice of fluid in FMC ICU) | 31 mmol/L |
| 20% saline | 3444 mmol/L |
| NSA (4% albumin) | 140 mmol/L[4] |
| 20% albumin | 74 mmol/L[4] |
| Gelofusin | 154 mmol/L[4] |
| Hartmann (CSL) | 131 mmol/L[4] |
| **Transfusion** | |
| Packed red blood cells | 31.3 mmol/U |
| Fresh frozen plasma | 44 mmol/U |
| Platelet | 30.5 mmol/U |
| **Nasogastric feeds** | |
| Nutrison Concentrated | 4.3 mmol/100 mL[5] |
| Nutrison Energy | 5.8 mmol/100 mL[5] |
| Nutrison Energy Multi Fibre | 5.8 mmol/100 mL[5] |
| Nutrison Low Sodium | 1.1 mmol/100 mL[5] |
| Nutrison Multi Fibre (default choice of feed in FMC ICU) | 4.3 mmol/100 mL[5] |
| Abbott Nepro | 3.7 mmol/100 mL[6] |
| Nutrison Standard | 4.3 mmol/100 mL[5] |
| **Flush** | |
| Heparin Na | 155.2 mmol/L (normal saline)[1] |
| Daily two lines (8 mL/h) | 29.8 mmol/day (normal saline) |

FMC = Flinders Medical Centre. ICU = intensive care unit. IV = intravenous.

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