

Sodium administration in critically ill patients in Australia and New Zealand: a multicentre point prevalence study

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Critically ill patients are at risk of sodium retention due to activation of the renin–angiotensin–aldosterone system¹ and impaired activity of dopamine in the proximal tubule of the kidney² where dopamine normally inhibits sodium reabsorption.³ Depending upon concomitant water balance, the administration of large amounts of sodium, combined with the propensity for sodium retention, may have important clinical implications such as hypernatraemia,⁴ which has been associated with poor outcomes,^{5,6} and changes in extracellular and intracellular fluid volumes.

Two of us (SB and AB) were involved in running a single-centre study⁷ that reported that the amount of sodium administered to intensive care patients receiving invasive mechanical ventilation for more than 5 days was over twice the recommended daily intake of 100 mmol.⁸ We also found that the main sources of sodium administration were intravenous (IV) maintenance fluids, flushes and drugs.⁷ However, the results of a single-centre study reflect local practice and are not generalisable to other centres. To confirm these results, a multicentre, single-day point prevalence study was undertaken in conjunction with the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group (CTG) and the George Institute for Global Health.

The primary aim of the study was to determine the total amount of sodium administered in critically ill patients in Australian and New Zealand intensive care units and to determine the most common sources of administration.

Methods

All Australian and New Zealand CTG-affiliated ICUs were invited to participate. Approval was obtained, when required, from the individual research ethics committees of participating sites. The study was a prospective, cross-sectional, observational audit and, as such, the requirement for individual patient consent was waived at all sites.

All adult patients (≥ 16 years) present in participating ICUs at 10 am on the study day (Wednesday 21 September 2011, with a back-up day, 19 October 2011) were enrolled. Routine survey data for all patients included age, sex, weight (estimated or measured), Acute Physiology and Chronic Health Evaluation (APACHE) II score on ICU admis-

ABSTRACT

Background: Inadvertent sodium administration in excess of recommended daily requirements has been reported during routine care of critically ill patients.

Aim: To determine the amount and sources of sodium administered in Australian and New Zealand intensive care units.

Design, setting and participants: Prospective, observational, single-day, point prevalence survey conducted in 46 Australian and New Zealand ICUs on 21 September 2011. All patients present in ICU at 10 am and not receiving an oral diet on the study day were evaluated. Demographic data, ICU admission diagnosis, Acute Physiology and Chronic Health Evaluation (APACHE) II score and sources of sodium administration over the study day were recorded.

Results: 356 patients (64% male) were enrolled. Mean (SD) age and weight were 58.5 years (18.0 years) and 81.6 kg (24.0 kg), respectively. Mean ICU admission APACHE II score was 20 (SD, 8). Overall median (interquartile range [IQR]) sodium administration was 224.5 mmol (IQR, 144.9–367.6 mmol), or 2.8 mmol/kg (IQR, 1.6–4.7 mmol/kg). Among patients who were on Day 2–10 of their ICU admission on the study day, sodium sources and amounts administered were: i) maintenance or replacement intravenous (IV) infusions, 69.3 mmol; 30.9% of all sodium sources; ii) IV fluid boluses, 36.5 mmol; 16.3%; iii) IV drug boluses, 27.6 mmol; 12.3%; iv) enteral nutrition, 26.5 mmol; 11.8%; v) IV drug infusions, 19.3 mmol; 8.6%; vi) IV flushes, 16.6 mmol; 7.4%; vii) blood products, 13.5 mmol; 6%; viii) IV antimicrobials, 11.2 mmol; 5%; and ix) parenteral nutrition, 4.3 mmol; 1.9%. Factors associated with sodium administration were site ($P=0.04$), age ($P<0.001$), administered fluid ($P=0.03$) and day of ICU stay ($P=0.01$) (multiple linear regression).

Conclusion: This point prevalence study suggests that sodium administration in excess of recommended daily requirements may be common in Australia and New Zealand ICUs. The main sodium source was IV maintenance fluids, followed by fluid boluses and drug boluses.

Table 1. Patient characteristics (n = 356)

Characteristic	No. of patients (%) [*]
Age, years [†]	58.5 (18)
Male sex	229 (64.3%)
Weight, kg ^{†‡}	81.6 (24)
APACHE II score [†]	20 (8)
Intensive care unit admission source	
Emergency department	110 (30.8%)
Hospital ward	75 (21.1%)
Operating theatre	109 (30.6%)
Other	62 (17.4%)
APACHE III diagnosis categories	
Cardiovascular	40/247 (16.2%)
Respiratory	65/247 (26.3%)
Gastrointestinal	15/247 (6.0%)
Neurological	39/247 (15.8%)
Sepsis	35/247 (14.2%)
Trauma	22/247 (8.9%)
Other	29/247 (11.7%)
SOFA score on study day [§]	7 (4–11)
Respiratory SOFA score on study day [§]	2 (1–3)
Sepsis on study day	127 (35.6%)
ALI/ARDS on study day	38 (10.6%)
Renal replacement therapy	41 (11.5%)
Hospital length of stay, days [§]	5.0 (2.0–13.0)
28-day mortality	45 (12.6%)

APACHE = Acute Physiology and Chronic Health Evaluation. SOFA = Sequential Organ Failure Assessment. ALI = acute lung injury. ARDS = acute respiratory distress syndrome. * Unless otherwise specified. † Mean (SD). ‡ Weight estimated or actual. § Median (interquartile range).

sion, Sequential Organ Failure Assessment (SOFA) score within the 24 hours preceding the study day, and ICU admission source. Data related to ICU admission diagnoses (operative v non-operative, burns, trauma) and specific diagnoses on the study day (acute lung injury [ALI], acute respiratory distress syndrome [ARDS], sepsis) were collected. Requirement for renal replacement therapy (RRT) on study day was also collected. The highest serum sodium level on the study day was recorded, and patients were defined as having hypernatraemia (≥ 150 mmol/L⁶) or hyponatraemia (< 130 mmol/L⁹). Vital status 28 days after study day was ascertained using hospital administrative databases.

Patients receiving an oral diet (at least 50% of dietary requirements met by oral intake, and enteral and/or

Table 2. Sodium administration according to diagnostic category

Diagnostic category [*]	No. (%)	Sodium administered, mmol [†]
Postoperative	109 (30.6%)	224.3 (142.0–368.5)
Trauma	61 (17.0%)	256.7 (165.1–445.0)
Burns	3 (0.8%)	464.9 (168.6–686.5)
Sepsis	127 (35.6%)	224.3 (142.0–368.5)
ALI or ARDS	38 (10.6%)	200.8 (140.9–367.7)

* Postoperative, trauma (operative and non-operative) and burns diagnostic categories were at intensive care unit admission. Sepsis and ALI/ARDS diagnoses were on study day. † Data expressed as median (interquartile range). ALI = acute lung injury. ARDS = acute respiratory distress syndrome.

parenteral nutrition not administered on the study day) were excluded for the purposes of ascertaining the sources of sodium administration.

Data on all remaining patients included:

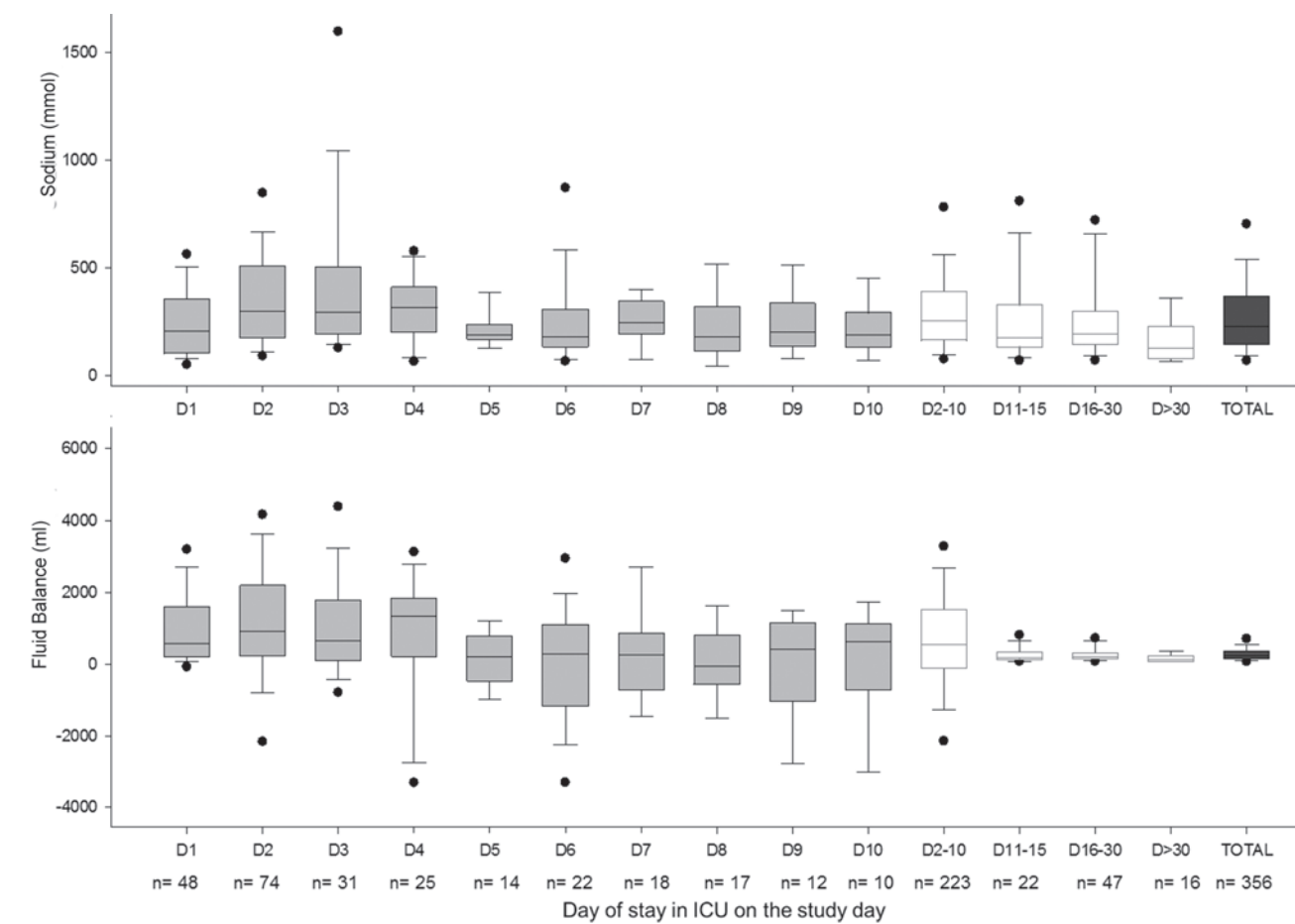
- IV bolus fluids administered for volume expansion or “fluid resuscitation” (ie, crystalloid infusion ≥ 5 mL/kg/h or ≥ 400 mL/h or any colloid bolus or infusion);
- blood products (ie, red blood cells, platelets, fresh frozen plasma);
- IV maintenance or replacement fluids (ie, crystalloids given by continuous infusion);
- IV drug infusions (ie, drugs administered by continuous infusion) together with their vehicles;
- IV drug boluses together with their vehicles;
- IV flushes associated with haemodynamic monitoring (eg, intra-arterial or central venous catheter);
- enteral nutrition;
- parenteral nutrition.

For all IV fluids and blood products, the type and volume administered over the 24-hour study day were recorded and the amount of sodium administered was calculated based on published sodium concentrations.⁷ For drug infusions and boluses, sodium content was calculated from both the sodium content of the drug and the type and volume of carrier fluid or diluent. For enteral and parenteral nutrition, information on the type and volume of feed was recorded and the sodium content was calculated accordingly. For custom parenteral nutrition, the sodium content was recorded. No data on oral sodium intake were collected.

Statistical analysis

Variables are reported as mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Sources

Figure 1. Sodium and fluid balance on study day according to day of stay in the intensive care unit after ICU admission*



* Data presented as box plot representing median, upper and lower quartile with the 10th and 90th percentile either side, dots are 95th and 5th percentiles. Day 1 has 14 h (median; IQR 11–18 h) of data. "n=" represents the total number of patients according to the day of stay in ICU on study day.

of sodium administration are reported as percentages with 95% CI. Antimicrobials were analysed separately to other IV drugs due to the high sodium load of some agents.⁷

Pearson correlation was used to test for the association between sodium administered (log transformed for normal distribution) and the following factors: age, weight, APACHE II score and day of ICU stay, SOFA score, serum sodium, fluid administered and 24-hour fluid balance on study day. Predictor variables for sodium administration (age, sex, APACHE II score, site, and variables significant at $\alpha \leq 0.10$) were analysed using multiple linear regression (SPSS version 2.0). Day 1 data were not included in the model as 24-hour data were incomplete (median [IQR] ICU length of stay, 14 [11–18] hours). In addition, the amount of sodium administered during routine care as opposed to the initial resuscitation phase that occurs at ICU admission is potentially different.

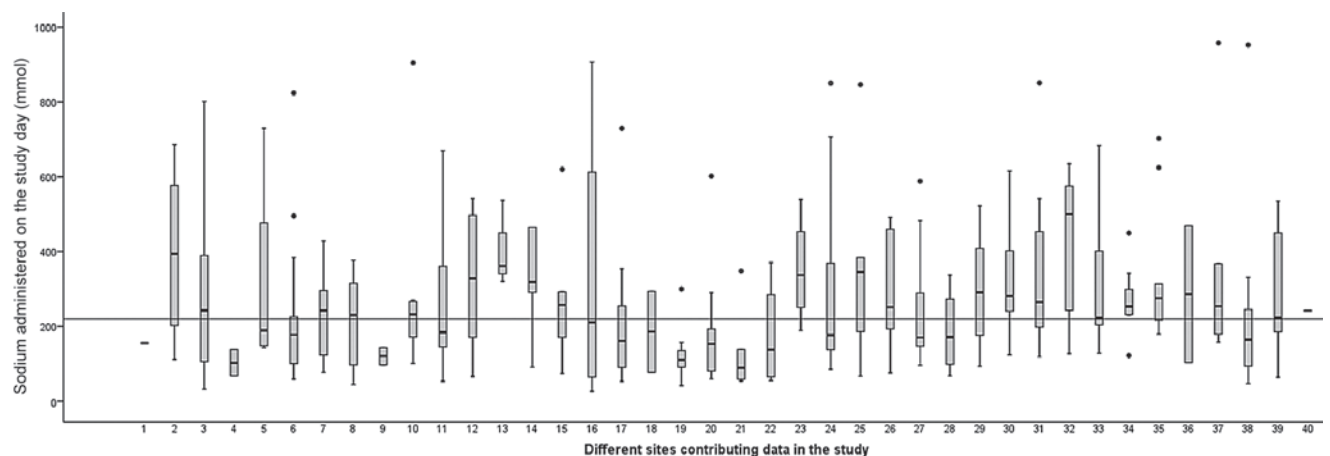
For all analyses, a *P* value of less than 0.05 was considered significant.

Results

Patient characteristics

Five hundred and eleven patients from 46 tertiary referral, metropolitan and rural hospital ICUs were enrolled in the point prevalence survey (Appendix). One hundred and fifty-five patients (30.3%) were excluded, either because of oral intake (148; 28.9%) or missing data (7; 1.4%).

Of the remaining 356 patients (40 sites), 64.3% (229) were men and the mean (SD) age and estimated body weight (on study day) were 58.5 years (18.0 years) and 81.6 kg (24.0 kg), respectively. Twenty-eight-day mortality was 12.6%. Other patient characteristics are shown in Table 1.

Figure 2. Sodium administration on study day at different sites*

* Box plot representing median, upper and lower quartile with the 95 and 5 percentile either side; dots are outliers. Horizontal line represents the median level of administered sodium, 224.5 mmol.

Serum sodium

Mean (SD) serum sodium level on study day was 140.5 mmol/L (5.0 mmol/L). Sixty-nine patients (19.3%) had a serum sodium ≥ 145 mmol/L and 18 (5.1%) were hypernatraemic (serum sodium, ≥ 150 mmol/L). Fifty-seven patients (16.0%) had a serum sodium < 135 mmol/L and 6 (1.7%) were hyponatraemic (serum sodium, ≤ 130 mmol/L) on study day.

Sodium and fluid administration

The median (IQR) total amount of sodium administered at individual study sites ranged from 90.0 mmol (56.5–243.3 mmol) to 500.1 mmol (199.5–604.1 mmol). Overall sodium administration across all the sites was 224.5 mmol (144.9–367.6 mmol) or 2.8 mmol/kg (1.6–4.7 mmol/kg). Twenty-four hour fluid balance was +503.5 mL (+2.5 to +1345 mL). Sodium administration according to diagnostic category is shown in Table 2. Sodium administration and fluid balance according to the day of stay in ICU is shown in Figure 1.

Among patients for whom the study day was Day 1 (median [IQR] ICU length of stay 14 h [11–18 h]) of their ICU admission (48/356; 13.4%), 202.9 mmol (101.5–352.9 mmol) of sodium was administered. The main sodium source was IV maintenance or replacement fluids (77.5 mmol; 38.2% [95% CI, 37.3%–39.0%] of all sodium administered). Other sources included IV fluid boluses (44.4 mmol; 22.0% [95% CI, 21.3%–22.7%]), IV drug boluses other than antimicrobials (22.9 mmol; 11.3% [95% CI, 10.7%–11.8%]), IV drug infusions (19.1 mmol; 9.4% [95% CI, 8.9%–9.9%]), IV flushes (12.6 mmol; 6.2% [95% CI, 5.8%–6.6%]), blood products (12.4 mmol; 6.1% [95%

CI, 5.6%–6.5%]), IV antimicrobials (7.2 mmol; 3.5% [95% CI, 3.2%–3.8%]), enteral nutrition (6.2 mmol; 3.1% [95% CI, 2.7%–3.3%]), and parenteral nutrition (0.3 mmol; 0.1% [95% CI, 0.0–0.1%]). The total amount of fluid administered as a bolus on Day 1 was 800 mL (467–1048 mL).

Among patients for whom the study day was Day 2–10 of their ICU admission (223/356; 62.6%), 255.1 mmol (163.2–390.5 mmol) of sodium was administered. Twenty-four hour fluid balance was +550 mL (–126 to +1515 mL) (Figure 1). The main source of sodium administration was IV maintenance or replacement fluids (69.3/224.5 mmol; 30.9% [95% CI, 30.6%–31.2%] of all sodium administered). Of the 225 patients receiving IV maintenance or replacement fluids, 33.7% (76/225) received 0.9% saline. The four other most common fluids infused were Hartmann's solution (in 55/225 patients; 24.4%), 5% dextrose (34/225; 15.1%) and 4% dextrose and 0.18% saline (21/225; 9.3%).

Other sodium sources included IV fluid boluses (36.5 mmol; 16.3% [95% CI, 16.0%–16.4%]), IV drug boluses other than antimicrobials (27.6 mmol; 12.3% [95% CI, 12.1%–12.5%]), enteral nutrition (26.5 mmol; 11.8% [95% CI, 11.5%–12.0%]), IV drug infusions (19.3 mmol; 8.6% [95% CI, 8.4%–8.8%]), IV flushes (16.6 mmol; 7.4% [95% CI, 7.2%–7.5%]), blood products (13.5 mmol; 6% [95% CI, 5.8%–6.4%]), IV antimicrobials (11.2 mmol; 5% [95% CI, 4.8%–5.1%]) and parenteral nutrition (4.3 mmol; 1.9% [95% CI, 1.8%–2.0%]). Saline 0.9% was the most commonly used vehicle for IV drug boluses (177/234; 75.6%) and IV drug infusions (152/236; 64.4%). Heparinised saline was the most commonly used IV flush fluid (214/218; 98.1%).

The highest proportion of sodium administered from IV fluid boluses occurred on Days 2 and 3 of ICU admission. Seventy-four patients (20.8%) received a fluid bolus on Day 2 (513 mL [332–1637 mL]) that delivered 66.0 mmol of sodium (22.3% [95% CI, 21.8%–22.8%]) of all sodium administered). Patients for whom the study day was Day 3 of their ICU admission (31/356; 20.8%), received 467 mL (257–1971 mL) as fluid boluses, amounting to 55.2 mmol (18.8% [95% CI, 18.1%–19.4%]) of administered sodium. Overall, albumin (4% or 5%) was the most commonly administered bolus fluid (46/125 fluid boluses; 36.8%), followed by 0.9% saline (30/125; 24%) and Hartmann solution (16/125; 12.8%).

Sodium administration was weakly correlated with study day total SOFA score ($P=0.001$; $r=0.19$), the respiratory component of the SOFA score ($P=0.032$; $r=0.14$), 24-hour administered fluid ($P=0.038$; $r=0.11$) and fluid balance ($P<0.001$; $r=0.45$). Using multiple linear regression modelling ($R^2=0.115$), factors associated with administered sodium were site (standardised β coefficient, 0.105; $P=0.044$) (Figure 2), age (-0.227 ; $P<0.001$), administered fluid on study day (0.121; $P=0.03$) and day of stay in ICU (-0.167 ; $P=0.01$) (Figure 1).

Discussion

In this multicentre point prevalence study of Australian and New Zealand ICUs, the median sodium administration was greater than 220 mmol on the study day. In contrast, fluid balance on the study day was only 500 mL positive, suggesting that ICU patients, despite a small positive fluid balance, receive a high sodium load in excess of recommended daily requirements for a healthy population⁸ (albeit there is no recommended daily intake for critically ill patients in ICU).

The principal source of sodium administration was not IV fluid resuscitation as one may have presupposed, but was IV infusions — in particular, maintenance fluids — as well as IV drug infusions, boluses and flushes. These sources of sodium are inadvertent and potentially modifiable, depending on clinician choice for “routine” IV fluid administration. These findings are also similar to the results of our single-centre study.⁷ A high level of non-dietary sodium administration has been similarly reported in cardiac patients.¹⁰ Furthermore, although the selection of fluid type varied between participating sites, 0.9% saline was the most common IV fluid, contributing to 59.2% of all sodium administered. While the reason(s) for choosing 0.9% saline cannot be ascertained from this point prevalence survey, it is noteworthy that recent studies have indicated that after a bolus of 0.9% saline, excretion of both water and sodium is

slower¹¹ and may result in reductions in renal blood flow velocity and renal cortical tissue perfusion.¹²

Sodium retention might be more relevant in critically ill patients owing to activation of the renin–angiotensin–aldosterone system.¹ This is especially so in mechanically ventilated patients, where positive pressure ventilation and positive end-expiratory pressure both raise intrathoracic pressure, which results in reduced venous return and consequent complex neurohumoral responses^{13,14} leading to sodium¹⁵ and water retention. As seen in this current study, sodium administration on the study day had a weak correlation with the SOFA score and with a net positive fluid balance. Importantly, a positive fluid balance has been shown to be associated with poor lung and kidney function,^{16,17} delayed return of gastrointestinal function after surgery¹⁸ and an increased risk of mortality.¹⁹ The adverse effects of positive fluid balance are probably due to extracellular fluid expansion. Therefore, both water and sodium may be important because water distributes to both intracellular and extracellular spaces. In contrast, sodium distributes into the extracellular spaces leading to cellular dehydration and interstitial oedema in both the lungs¹⁵ and the systemic circulation. Current strategies using conservative fluid balance therapy without attention to concomitant sodium balance could potentially lead to intracellular dehydration, and it could have been one of the mechanisms contributing to abnormal neurocognitive effects in patients with lung injury managed with conservative fluid balance.²⁰

Sodium administration is often coupled with chloride, usually as a 1 : 1 ratio except for fluids such as Hartmann solution, where the ratio is 1.2 : 1. Although chloride administration was not directly measured in our study, it can be hypothesised that high sodium administration would have accompanying high chloride administration, which may have adverse effects; effects of chloride restriction on the acid–base status of ICU patients has recently been investigated,²¹ and implementation of a chloride-restrictive strategy in a tertiary ICU was associated with a significant decrease in the incidence of kidney injury and the requirement for dialysis in ICU.²² Irrespective of these considerations, the issue of sodium restriction is increasingly recognised as important in ICU patients.²³

Large amounts of administered sodium, together with the propensity for sodium retention and a conservative fluid balance, can lead to hypernatraemia. Hypernatraemia is not uncommon in the critically ill;⁴ in our study, 19.3% of patients had a serum sodium ≥ 145 mmol/L and 5% had hypernatraemia (≥ 150 mmol/L). This rate of hypernatraemia is consistent with the literature⁶ and has previously been associated with poor outcomes.^{5,6}

Limitations

Our single-day point prevalence study conducted across multiple ICUs in Australia and New Zealand represents a snapshot of current practices for critically ill patients not receiving oral nutrition on study day. Despite our best efforts to record all IV and enteral fluids administered, it is possible that other sources of sodium were not included. Formal sodium balance and the indications for the prescription of high-sodium fluids such as 0.9% saline were also not collected. Finally, inferences regarding sodium administration on Day 1 are limited, as data collection covered less than 24 hours.

Future directions

Inadvertent high levels of sodium administration are potentially modifiable as IV sodium sources are primarily maintenance fluids, vehicles for infusions and drug boluses, and flushes. Future studies should include both prospective observational studies examining the relationship between sodium administration, sodium balance and important clinical outcomes (eg, mortality) and interventional trials to assess whether it is desirable and/or safe to modify daily sodium administration in critically ill patients, and can be coupled with simultaneous measurement of chloride administration and balance.

Conclusion

We have shown high levels of sodium administration in multiple ICUs across Australia and New Zealand in a large cohort of patients. Most administered sodium is from inadvertent sources. However, there is wide variability in the use of infusions and vehicles for drug infusions and boluses.

Competing interests

None declared.

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Appendix. List of participating sites and investigators

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