Maintenance fluid practices in intensive care units in Australia and New Zealand

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ABSTRACT

Background: Administration of maintenance fluid is common practice in the intensive care unit, contributing to daily fluid and sodium intake and balance. Despite this, there is little evidence to describe clinical practices relating to its administration to ICU patients.

Methods: We conducted a prospective, observational, point-prevalence study in 49 Australian and New Zealand ICUs in 2014. We aimed to document the type and volume of maintenance fluid administered to ICU patients, and to describe additional fluid received. We also assessed changes in maintenance fluid administration practices compared with our similar study conducted in 2011.

Results: Of 645 patients enrolled, 399 (62%) received maintenance fluid on the study day. A median volume of 630 mL (interquartile range [IQR], 272–1250 mL) was delivered, accounting for a median of 35% (IQR, 16%–56%) of total daily administered fluids. This was in addition to other fluids administered as fluid resuscitation, drug infusions and boluses, flushes and enteral or parenteral feeds, as well as oral intake. 0.9% saline was the most commonly used maintenance fluid (36%), followed by balanced salt solutions (30%). Compared with data from 2011, there has been a decrease in the median volume of maintenance fluid administered (2011, 860 mL [IQR, 360–1533 mL]; 2014, 630 mL [IQR, 287–1328 mL]; $P = 0.01$), although the proportion of patients receiving maintenance fluid remains unchanged. There has been no change in the types of fluids most commonly used for maintenance, but the use of balanced salt solutions has increased (2011, 24%; 2014, 30%; $P = 0.01$).

Conclusion: Administration of maintenance fluids to patients in Australian and New Zealand ICUs is common. Although the volume being delivered has decreased, maintenance fluids contribute over one-third of daily total fluid administration.

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The intravenous (IV) administration of maintenance fluids is a routine component of care for many critically ill adult patients,[1] originating from the practice of providing continuous IV hydration to fasting surgical patients[2,3] and extrapolation from the paediatric literature.[4] Recently, the administration of maintenance fluid to critically ill patients as standard practice has been called into question, due to its potentially significant contribution to overall fluid balance.[5] There are growing concerns about fluid administration and overload, due to evidence showing an association between cumulative positive fluid balance and poorer patient outcomes.[6-8]

It is not currently known to what extent maintenance fluid contributes to the overall fluid balance in critically ill patients. Recently, two large randomised controlled trials of fluid resuscitation in critically ill patients reported that a substantial amount of non-study fluid[9] and other fluid[10] was administered during the study period, with a high proportion of these fluids presumed to be maintenance fluids. Consistent with this, a point-prevalence study that we conducted in 2011, examining sodium intake, found that 30.9% of sodium intake was from maintenance fluids.[11] It is thus likely that maintenance fluids make a substantial contribution to overall fluid and sodium intake in critically ill patients.

We aimed to characterise maintenance fluid practices in Australian and New Zealand intensive care units in the context of all other administered fluids (parenteral and enteral), and to compare these findings to those of our previous study, conducted in 2011. The results of this study may assist in designing future interventional trials that restrict administration of other fluids in ICU patients.

Methods

We conducted a cross-sectional, multicentre, point-prevalence study on 24 September and 22 October 2014 in 49 Australian and New Zealand adult ICUs. Human research ethics committee approval was obtained, with the requirement for individual patient consent waived at all sites. The study included all adult patients (aged over 16 years) in participating ICUs at 10 am on the study day, and data were collected over 24 hours.

Demographic and clinical data collected for all patients included age, sex, weight (estimated or measured), Acute Physiology and Chronic Health Evaluation (APACHE) II score on ICU admission, Sequential Organ Failure Assessment (SOFA) score within the 24 hours preceding the study day, and ICU admission source. Data related to ICU admission diagnoses (eg, operative or trauma), specific diagnosis

Table 1. Patient demographics (*n* = 645)

Characteristic	Measure
Male, *n* (%)	386 (60%)
Mean age, years (SD)	59.8 (17.7)
Mean weight, kg (SD)	81.9 (23)
Mean APACHE II score (SD)	19 (12)
Median SOFA score (IQR)	7 (3–11)
Diagnoses, *n* (%)	
Post-operative	246 (38.1%)
Trauma	71 (11.0%)
Sepsis on study day	152 (23.5%)
Mechanical ventilation, *n* (%)	270 (41.8%)
Median ICU LOS, days (IQR)	3 (1–7)
Vasopressor or inotrope, *n* (%)	189 (29.3%)
Renal replacement therapy, *n* (%)	53 (8.2%)
ECMO, *n* (%)	5 (0.8%)
Bed blocked, *n* (%)	86 (13.3%)
28-day mortality, *n* (%)	64 (9.9%)

APACHE = Acute Physiology and Chronic Health Evaluation. SOFA = Sequential Organ Failure Assessment. IQR = interquartile range. ICU = intensive care unit. LOS = length of stay. ECMO = extra-corporeal membrane oxygenation.

on the study day (eg, sepsis) and bed block status were collected. Patients with a neurological, neurosurgical or head trauma diagnosis (based on APACHE III diagnostic codes) were examined separately because of the potential for specific requirements for isotonic fluids. Requirements for mechanical ventilation, renal replacement therapy and extracorporeal membrane oxygenation on the study day were also documented. Data on vital status 28 days after the study day were collected from hospital administrative databases. Study data were collected and managed using an electronic data capture system (REDCap) hosted at the George Institute for Global Health, Sydney, Australia.[12]

Data collected included:

- amount and type of maintenance fluids (continuous fluid administered for maintenance or to replace fluid losses; not for resuscitation purposes)
- resuscitation fluids (defined as a bolus of crystalloid; a crystalloid infusion of ≥ 5 mL/kg/h (or ≥ 400 mL/h) for 1 or more hours; a colloid bolus; any colloid by infusion; or transfusion of whole blood, packed red blood cells, fresh frozen plasma or platelets)
- fluids administered as a diluent or vehicle for drug infusions and boluses
- enteral and parenteral feeds
- IV flushes associated with haemodynamic monitoring
- data for patients receiving an oral diet (estimated as ≥ 50% of dietary requirements met by normal oral intake, without supplementation by enteral or parenteral feeds)
- daily total fluid administration, urine output and fluid balance.

We compared results with data from our separate point-prevalence study conducted in 2011.[11] In the 2011 study, patients receiving an oral diet were excluded from the analysis, so comparisons between the 2011 and 2014 studies are restricted to the subset of patients not receiving oral feeds.

Statistical analysis

We report means with SDs, medians with interquartile ranges (IQRs), or proportions and percentages, as appropriate. We used χ^2 tests, Mann–Whitney *U* tests and independent sample *t* tests, as appropriate, to compare data from 2011 and 2014. For all analyses, a two-sided $P < 0.05$ was considered significant. Statistical analysis was performed using SPSS, version 21.0 (IBM).

Results

Patient characteristics

A total of 645 adult patients from 49 ICUs (22 tertiary referral, 16 metropolitan, seven regional or rural and four private hospitals) were enrolled (Appendix). The mean age of participants was 59.8 years (SD, 17.7 years), mean APACHE II score was 19 (SD, 12) and 386 patients (60%) were men (Table 1). There were 246 post-operative patients (38.1%) enrolled. The median length of ICU stay was 3 days (IQR, 1–7 days). A 24-hour study chart was available for 445 patients (69%), and for the remaining 200 patients, data were available for a median of 14 hours (IQR, 8–18 hours).

Maintenance fluids

On the study day, 399 patients (62%) received maintenance fluids and 190 patients (29%) were given resuscitation

Table 2. Fluids administered and fluid balance, all patients (*n* = 645)

Fluid	Measure
Resuscitation fluids, *n* (%)	190 (29%)
Maintenance fluids, *n* (%)	399 (62%)
Enteral feeding, *n* (%)	234 (36%)
Parenteral feeding, *n* (%)	34 (5%)
Predominantly oral diet, *n* (%)	303 (47%)
Median total fluid, mL (IQR)	2155 (1350–2845)
Median urine output, mL (IQR)	1480 (790–2332)
Median fluid balance, mL (IQR)	336 (–236 to 1078)

IQR = interquartile range.

Table 3. Fluid intake in patients receiving maintenance fluids (*n* = 399)

Fluid	*n* (%)	Median volume, mL (IQR)
Maintenance fluids	399 (100%)	630 (272–1250)
Resuscitation fluids	136 (34%)	578 (300–1000)
Drug infusions, boluses	345 (86%)	235 (52–617)
Flushes	319 (80%)	100 (100–200)
Enteral feeds	131 (33%)	965 (490–1960)
Parenteral feeds	17 (4%)	1440 (285–1776)
Predominantly oral feeds*	183 (46%)	–
Total fluid administered	399 (100%)	2305 (1535–2990)
Urine output	399 (100%)	1480 (893–2350)
Fluid balance	399 (100%)	459 (–155 to 1184)

IQR = interquartile range. * Volume of oral feeds was not measured.

fluids. Data relating to other fluids or feeds and fluid balance are shown in Table 2. The median total amount of fluid administered on the study day was 2155 mL (IQR, 1350–2845 mL). In patients who received maintenance fluids (*n* = 399), the median volume of fluid administered for maintenance was 630 mL (IQR, 272–1250 mL) (Table 3). The most common type of maintenance fluid administered was 0.9% saline (36%), followed by balanced salt solutions (compound sodium lactate or Hartmann's, and Plasmalyte) (30%), 5% glucose (14%) and 4% glucose with 0.18% saline (12%).

Additional fluid in patients receiving maintenance fluids

Of the patients who received maintenance fluids, 136 (34%) also received fluid administered as fluid resuscitation on the study day (Table 3). The median volume of additional fluid received for resuscitation was 578 mL (IQR, 300–1000 mL). Drug boluses and infusions accounted for an additional median 235 mL (IQR, 52–617 mL). The median volume of fluid administered as flushes for arterial and central line catheters was 100 mL (IQR, 100–200 mL). Of the 399 patients who received maintenance fluids, 131 patients (33%) also received enteral nutrition (median, 965 mL [IQR, 490–1960 mL]) and 17 patients (4%) received parenteral nutrition (median, 1440 mL [IQR, 285–1776 mL]) on the study day. A total of 183 patients (46%) were also receiving an oral diet. Overall, patients who received maintenance fluids received an additional median volume of 984 mL of fluid (IQR, 347–1847 mL) and nutrition from other sources. Maintenance fluids contributed a median of 35% (IQR, 16%–56%) of the total volume of overall daily fluid intake.

Neurological and neurosurgical patients

Of 99 patients with a neurological or neurosurgical admission diagnosis, 67 patients (68%) received maintenance fluids on the study day. Of these patients, 32 (47%) received 0.9% saline, 22 (33%) received a balanced salt solution, four (6%) received 5% glucose and three (4%) received 4% glucose with 0.18% saline.

Comparison with data from 2011

Because data relating to fluids received were not collected for patients on an oral diet in 2011 (*n* = 46 ICUs), we excluded patients receiving predominantly oral feeds during the 2014 study (*n* = 57) from the comparative analysis. From 2011 to 2014, there was no change in the proportion of patients receiving maintenance fluids (2011, 225/356 [63%]; 2014, 216/342 [63%]) or resuscitation fluids (2011, 110/356 [31%]; 2014, 113/342 [33%]) (Table 4). There was a significant decrease in the median total volume of fluid administered between 2011 and 2014 (2011: 3157 mL [IQR, 2703–4328 mL]; 2014: 2475 [IQR, 1830–3175 mL]; *P* = 0.01), but urine output and fluid balance remained unchanged.

There was a significant decrease in median volume of maintenance fluid administered to patients between 2011 and 2014 (2011: 860 mL [IQR, 360–1533 mL]; 2014: 630 mL [IQR, 287–1328 mL]; *P* = 0.01) and a significant decrease in the median total volume of fluid administered (2011: 2935 mL [IQR, 2118–3947 mL]; 2014: 2539 mL

Table 4. Comparison of fluids administered, current study (2014, *n* = 342*) v previous study (2011, *n* = 356)

Fluid	Current study	Previous study	*P*
Resuscitation fluids, *n* (%)	113 (33%)	110 (31%)	0.63
Maintenance fluids, *n* (%)	216 (63%)	225 (63%)	0.71
Enteral feeds, *n* (%)	218 (63%)	233 (65%)	0.64
Parenteral feeds, *n* (%)	34 (9%)	37 (10%)	0.51
Median total fluid administered, mL (IQR)	2475 (1830–3175)	3157 (2703–4328)	0.01
Median urine output, mL (IQR)	1636 (928–2411)	1699 (909–2555)	0.48
Median fluid balance, mL (IQR)	419 (–58 to 1215)	682 (509–1574)	0.16

IQR = interquartile range. * Patients on oral feeds were excluded for this comparison.

[IQR, 2048–3317 mL]; $P < 0.01$) (Table 5). There was also a trend towards a less positive fluid balance on the study day. There was little variation in the type of fluid administered as maintenance fluid, with 0.9% saline the most commonly used fluid on both study days, although the use of balanced salt solutions has increased significantly (2011, 24%; 2014, 30%; $P = 0.01$) (Table 5).

Discussion

Key findings

In Australian and New Zealand ICUs, 62% of patients were administered maintenance fluids. Maintenance fluids accounted for a median volume of 630 mL of fluid per day in these patients, and 35% of the total daily fluid intake. Between 2011 and 2014, we found a decrease in the volume of maintenance fluid administered, from a median of 860 mL to 630 mL. Despite increased use of balanced salt solutions between 2011 and 2014, 0.9% saline continues to be the most commonly used maintenance fluid.

We found that non-maintenance sources of fluid contributed a median daily fluid volume of 984 mL (IQR, 347–1847 mL) in patients receiving maintenance fluids. Administration of maintenance fluids was common in patients receiving enteral (33%) and parenteral (4%) feeds. Finally, we found that 46% of patients who received maintenance fluid were also allowed to eat and drink orally, further adding to the total daily administered fluid volume.

Comparison with previous studies

We found that a median of more than 35% of daily administered fluids (IQR, 16%–56%) were in the form of maintenance fluids, accounting for more than the total fluid administered as fluid resuscitation (medians: maintenance fluids, 630 mL; fluid resuscitation, 578 mL). The finding that non-resuscitation fluids contribute substantially to total fluid administration is consistent with the findings of larger fluid studies. In the trial comparing saline versus albumin (the SAFE trial), non-study fluids were administered in a higher volume than study fluids (resuscitation fluids) on Days 2 to 4 of the study.[9] Similarly, other fluids contributed more than the trial fluids (study and open-label fluids) on Days 1 to 3 in the study comparing starch versus Ringer's acetate (the 6S study).[10] A further study from our group found that resuscitation fluids only contributed one-third of the daily fluid balance in critically ill patients with sepsis,[13] with the rest coming from other sources of fluids. In addition to the significant volumes of fluid administered as maintenance fluid, the current findings also show that a higher proportion of patients routinely received maintenance fluids (62%). In comparison, only 29% of patients received resuscitation fluids.

Clinical implications

A positive fluid balance may be associated with poor lung and kidney function, delayed return of gastrointestinal function after surgery and an increased risk of mortality.[6,8,14,15] This has led researchers to consider whether a conservative fluid administration strategy might result in improved outcomes. So far, clinical trials have focused on the delivery of resuscitation fluids.[9,10,16,17] The results of this study suggest that the contribution of other fluids to daily fluid intake should be considered in trials of conservative fluid resuscitation strategies, and that maintenance fluid may provide an important target for intervention.

Despite an increase in the use of balanced salt solutions, 0.9% saline remains the most commonly used maintenance fluid. The change in practice shown by an increase in the use of balanced salt solutions compared with our previous study in 2011 is probably in response to increasing evidence suggesting harm associated with the use of chloride-rich fluids, in terms of causing renal[18,19] and respiratory dysfunction.[20] Similar changes can be seen in a larger

Table 5. Comparison of fluids administered to patients receiving maintenance fluids, current study (2014, *n* = 216) v previous study (2011, *n* = 225)

Fluid	Current study	Previous study	*P*
Median total fluid administered,* mL (IQR)	2539 (2048–3317)	2935 (2118–3947)	< 0.01
Median urine output,* mL (IQR)	1660 (1000–2425)	1700 (933–2543)	0.10
Median fluid balance,* mL (IQR)	491 (9–217)	656 (114–1678)	0.06
Median maintenance fluid,* mL (IQR)	630 (287–1328)	860 (360–1533)	0.01
Maintenance fluid type, *n* (%)			
0.9% saline	78 (36%)	76 (34%)	0.15
Balanced salt solutions	65 (30%)	55 (24%)	0.01
5% glucose	30 (14%)	34 (15%)	0.55
4% glucose and 0.18% saline	22 (10%)	21 (9%)	0.48

* Patients on oral feeds were excluded for these comparisons.

observational time series in Australia and New Zealand across six time points (which includes the patients reported in our current more detailed analysis).[21] Use of other fluids, such as 5% glucose, and 4% glucose with 0.18% saline, which contribute a small or no sodium and chloride load, is low. It is possible that this is because of traditional teaching that an increase in the risk of hyponatraemia is associated with hypotonic fluids,[1] which is based mostly on data from the paediatric literature. With the significant contribution of maintenance fluids to overall fluid administration, the type of fluids used for maintenance should be considered in future studies.

Maintenance fluids are the largest contributor to the sodium load[11] in critically ill patients. An increased sodium load contributes to a high sodium balance[22,23] and extracellular volume expansion,[22] and is associated with peripheral oedema[22] and respiratory dysfunction.[22,23] It is unclear whether sodium load, or fluid balance regardless of sodium load, is the greater contributor to adverse outcomes in these patients, and this hypothesis needs to be tested in clinical trials.

Strengths and limitations

Our single-day, point-prevalence study conducted across multiple ICUs in Australia and New Zealand represents a snapshot of current practice relating to administration of IV maintenance fluids for critically ill patients. It is supported by comparison to our previously published study using similar methodology, from 3 years earlier.[11]

Despite our best efforts to record all fluids administered, it is possible that some sources were not included. The indications for prescribing maintenance fluids were not collected, and it is possible that some maintenance fluid may have been a dministered as replacement for ongoing losses. Patients who were on the first day of their ICU stay on the study day had less than 24 hours' data collected, meaning that the true volume of maintenance fluid administered is likely to have been underestimated. Because it was a simple observational study, no inferences can be made about patient outcomes, and results cannot be generalised outside Australia and New Zealand, where the data were collected. Finally, we compared patient data from 2011 (from 46 ICUs) with 2014 (from 49 ICUs), and even though the study in 2014 is inclusive of 45 ICUs previously examined in 2011 and there is no change in the major diagnostic groups, there is a possibility that the casemix changed in the time frames assessed.

Conclusion

A high proportion of patients in Australian and New Zealand ICUs receive IV maintenance fluids. Although there has been a reduction in the volume of maintenance fluids delivered to patients since 2011, maintenance fluids still account for over one-third of the total volume of daily administered fluids. There is an increase in the use of balanced salt solution as maintenance fluid, but 0.9% saline remains the most commonly used fluid.

Our results suggest that fluid resuscitation trials should consider the contribution of maintenance fluids, and potentially other non-resuscitation fluids, as they can be a substantial source of fluid and sodium. Our findings provide important information about maintenance fluid practices in Australian and New Zealand ICUs. They may also have significant implications for future clinical trial design, particularly for studies evaluating a conservative fluid resuscitation strategy.

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References

1 Moritz ML, Ayus JC. Maintenance intravenous fluids in acutely ill patients. *N Engl J Med* 2015; 373: 1350-60.

2 Shidler FP. Considerations of postoperative electrolyte and fluid replacement. *Calif Med* 1950; 73: 309-11.

3 Macfie J. Nutrition and fluid therapy. In: Williams NS, Bulstrode CJK, O'Connell PR, editors. Bailey and Love's short practice of surgery. London: Edward Arnold, 2008: 226.

4 Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics* 1957; 19: 823-32.

5 Gattas DJ, Saxena MK. Is maintenance fluid therapy in need of maintenance? *Crit Care Resusc* 2013; 15: 255-6.

6 Boyd JH, Forbes J, Nakada TA, et al. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. *Crit Care Med* 2011; 39: 259-65.

7 Maitland K, Kiguli S, Opoka RO, et al; FEAST Trial Group. Mortality after fluid bolus in African children with severe infection. *N Engl J Med* 2011; 364: 2483-95.

8 Bouchard J, Soroko SB, Chertow GM, et al; Program to Improve Care in Acute Renal Disease (PICARD) Study Group. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. *Kidney Int* 2009; 76: 422-7.

9 SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 2004; 350: 2247-56.

10 Perner A, Haase N, Guttormsen AB, et al; 6S Trial Group; Scandinavian Critical Care Trials Group. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. *N Engl J Med* 2012; 367: 124-34.

11 Bihari S, Peake SL, Seppelt I, et al. Sodium administration in critically ill patients in Australia and New Zealand: a multicentre point prevalence study. *Crit Care Resusc* 2013; 15: 294-300.

12 Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap) — a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; 42: 377-81.

13 Bihari S, Prakash S, Bersten AD. Post resuscitation fluid boluses in severe sepsis or septic shock: prevalence and efficacy (price study). *Shock* 2013; 40: 28-34.

14 Wiedemann HP, Wheeler AP, Bernard GR, et al; National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006; 354: 2564-75.

15 Lobo DN, Bostock KA, Neal KR, et al. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet* 2002; 359: 1812-8.

16 Myburgh JA, Finfer S, Bellomo R, et al; CHEST Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med* 2012; 367: 1901-11.

17 Young P, Bailey M, Beasley R, et al; SPLIT investigators and the ANZICS CTG. Effect of a buffered crystalloid solution vs saline on acute kidney injury among patients in the intensive care unit. *JAMA* 2015; 314: 1701-10.

18 Yunos NM, Bellomo R, Hegarty C, et al. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA* 2012; 308: 1566-72.

19 Chowdhury AH, Cox EF, Francis ST, Lobo DN. A randomized, controlled, double-blind 534 crossover study on the effects of 2-L infusions of 0.9% saline and plasma-lyte 148 on renal blood flow velocity and renal cortical tissue perfusion in healthy volunteers. *Ann Surg* 2012; 256: 18-24.

20 Bihari S, Wiersema UF, Schembri D, et al. Bolus intravenous 0.9% saline, but not 4% albumin or 5% glucose, causes interstitial pulmonary edema in healthy subjects. *J Appl Physiol* 2015; 119: 783-92.

21 Hammond NE, Taylor C, Saxena M, et al; George Institute for Global Health and Australian and New Zealand Intensive Care Society Clinical Trials Group. Resuscitation fluid use in Australian and New Zealand intensive care units between 2007 and 2013. *Intensive Care Med* 2015; 41: 1611-9.

22 Bihari S, Baldwin CE, Bersten AD. Fluid balance does not predict estimated sodium balance in critically ill mechanically ventilated patients. *Crit Care Resusc* 2013; 15: 89-96.

23 Bihari S, Peake SL, Prakash S, et al. Sodium balance, not fluid balance, is associated with respiratory dysfunction in mechanically ventilated patients: a prospective, multicentre study. *Crit Care Resusc* 2015; 17: 23-8. ❑