Fluid bolus therapy in critically ill children: a survey of practice among paediatric intensive care doctors in Australia and New Zealand

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ABSTRACT

Objective: Fluid bolus therapy (FBT) is a widely used intervention in paediatric critical illness. The aim of this study was to describe the attitudes and practices towards FBT of paediatric intensive care doctors in Australia and New Zealand.

Design: An internet-based survey of paediatric intensive care doctors in Australia and New Zealand between 7 and 30 November 2016.

Setting: Paediatric intensive care units with greater than 400 admissions annually.

Participants: Paediatric intensive care specialists and junior medical staff.

Main outcome measures: Preferences for FBT and markers of fluid responsiveness.

Results: There were 106/175 respondents (61%); 0.9% saline and 4% albumin are used frequently or almost always by 86% and 57% of respondents respectively. The preferred volume and duration were 10 mL/kg in less than 10 minutes. The highest rated markers of fluid responsiveness were heart rate and blood pressure — rated as "good" or "very good" by 75% and 58% of respondents respectively. Central venous saturations and serum lactate were the highest rated biochemical markers. The most frequently expected magnitude of change for heart rate and blood pressure was 6–15% by 89% and 76% of respondents respectively. The preferred fluid composition for sepsis, trauma, traumatic brain injury and acute lung injury was 0.9% saline, and 4% albumin for post-operative cardiac surgery.

Conclusions: Paediatric intensive care doctors prefer 0.9% saline and 4% albumin for FBT. Heart rate and blood pressure are the most preferred markers to assess fluid responsiveness. Preferences for FBT in specific conditions exist.

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Fluid bolus therapy (FBT) remains one of the most commonly administered interventions in critical illness. The aim of FBT is to increase the volume of the circulation to improve venous return and hence cardiac output. Studies of FBT in children over the past two decades have been largely restricted to sepsis in low income countries or specific infections.[1-5] Fewer studies exist for trauma, acute lung injury or for congenital heart disease. Crystalloid and colloid are commonly administered to critically ill children, but preferences for fluid composition and response to therapy are not well described.

Current international guidelines for septic shock recommend administering 40–60 mL/kg and up to 200 mL/kg of FBT in the first hours,[6] but, despite being longstanding, these guidelines are based on limited evidence. An increasing number of retrospective studies report association between fluid overload, respiratory morbidity, and mortality.[7-9] The Fluid Expansion as Supportive Therapy (FEAST) study[10] showed increased mortality in African children with sepsis and impaired perfusion when administered FBT compared with no FBT. These findings have generated debate regarding the implications of this study in resource-rich settings.[11-13] Nonetheless, restrictive FBT strategies are now emerging [14,15] (eg, the SQEEZE trial [a study to determine whether septic shock reversal is quicker in paediatric patients randomised to an early goal-directed fluid-sparing strategy *v* usual care], ClinicalTrials.gov NCT 03080038). In order to inform future study design and variability of care, it is important to understand the attitudes of paediatric intensive care doctors to FBT.

Paediatric intensivists rely on vital signs and haemodynamic parameters to determine fluid responsiveness, yet, the reliability of these signs is questionable.[16] There are limited observational data on the physiological response to FBT and optimal markers of fluid responsiveness in children.[17,18] A systematic review of haemodynamic response to FBT in adults with sepsis shows heterogeneity in dose, triggers and physiological responses.[19] In children with congenital heart disease, dynamic measures such as pulse pressure variability and echocardiographic-derived indices have been shown to be more predictive of fluid responsiveness compared with vital signs, before and after an operation.[20,21] Therefore, assessing fluid responsiveness in children is challenging even in the presence of invasive haemodynamic monitoring.

Physician attitudes to FBT have been reported in adult critical care and paediatric emergency medicine.[22,23] There are no similar studies of paediatric intensive care doctors. Our aim was to describe the attitudes and practices of paediatric intensive care doctors in Australia and New Zealand towards FBT in terms of its composition, responses and disease-specific preferences.

Methods

We conducted a survey inviting paediatric intensive care medical staff (senior and junior medical staff) in Australia and New Zealand between 7 and 30 November 2016. The survey was conducted in intensive care units (ICUs) with over 400 admissions annually that contribute to the Australian and New Zealand Paediatric Intensive Care Registry. These hospitals included the Royal Children's Hospital, Melbourne; Monash Medical Centre, Melbourne; Princess Margaret Hospital, Perth; Women's and Children's Hospital, Adelaide; Children's Hospital at Westmead, Sydney; Sydney Children's Hospital, Sydney; Lady Cilento Children's Hospital, Brisbane; and Starship Children's Health, Auckland. Approval to conduct the study was provided by the Human Research and Ethics Committee at the Royal Children's Hospital in Australia (approval No. 35267A) and the Human Research and Ethics Committee at Starship Children's Health in New Zealand.

Survey development

The survey sought to determine individual preferences in relation to prescription and assessment of response to FBT (supplementary Appendix, Section 1; online at cicm.org.au/Resources/Publications/Journal). Part one examined participant demographics such as qualifications, years of experience and ICU type (paediatric intensive care unit [PICU] or mixed unit). The second part focused on preferred fluid composition, volumes and administration rate of FBT. A five-point Likert scale response was used and a preferred fluid composition was defined as the proportion selecting "frequently" or "almost always". The third part related to the minimum expected clinically significant physiological and biochemical responses to FBT. Similarly, a five-point Likert scale was used to rate markers of fluid responsiveness. The fourth part provided scenarios to gauge preferences in specific pathophysiological conditions, such as post-operative congenital heart disease, septic shock, trauma, traumatic brain injury and acute lung injury (supplementary Appendix, Section 2). Lastly, participants were asked whether they were familiar with the FEAST trial and whether the findings had altered their practice in regard to FBT. The survey was piloted at three study sites by a consultant, fellow and registrar at each site. Adjustments to the survey were made based on the pilot responses.

Survey conduct

The survey was distributed to site investigators who then distributed it to medical staff within each unit. It was constructed on an online proprietary survey website (www.surveymonkey.net.au). Reponses were anonymous and not identifiable by site. The survey was voluntary and consent was implied by its completion. Weekly reminders were distributed at each site.

Analysis

Statistical analyses were performed using STATA-IC (version 14.2; StataCorp, College Station, TX, USA). The data were summarised by frequency (n) and percentages (%) for both univariate and bivariate analysis. The difference in proportions for preferred fluid composition in specific pathophysiological conditions was tested using the test of proportions.

Results

The survey was distributed to 175 paediatric intensive care medical staff. There were 106 respondents (61%) including 49 consultants, 11 fellows and 46 registrars. At participating centres, the proportion of consultants who responded was 49/58 (84%). The profile of survey responders is described in the supplementary Appendix, Section 3.

Preferences for fluid boluses

When presented with a scenario of a 3-year-old child with tachycardia and hypotension, the most preferred fluid composition was 0.9% saline (90/105, 86%), followed by 4% albumin (58/102, 57%), then Hartmann's solution (Baxter Healthcare, Sydney, NSW) (12/102, 12%) (Figure 1). Plasma-Lyte (Baxter Healthcare) was "uncommonly" or "never used" by 72/103 respondents (70%); hydroxyethyl starch, dextran and Gelofusine (a colloidal plasma volume substitute; B Braun, Sydney, NSW) were reported as "never used" in 100/100 (100%), 97/101(96%) and 97/101 responses (96%), respectively. The most preferred volume for 0.9% saline and 4% albumin was 10 mL/kg for 68/102 (67%) and 57/72 respondents (79%), respectively (Figure 2). The preferred rate of FBT for 0.9% saline and 4% albumin was less than 10 minutes for 66/102 (65%) and 43/74 (58%) respondents respectively (Table 1). A rate of 11–30 minutes was preferred by a range of 33–39% of respondents for all crystalloids and 4% albumin.

Fluid responsiveness: haemodynamic, physiological and biochemical indices

The highest rated haemodynamic parameters to assess fluid responsiveness were decreasing heart rate and improving blood pressure. Table 2 describes the rating of haemodynamic,

Figure 1. Proportion of respondent's use of fluid composition as "frequently" or "almost always"

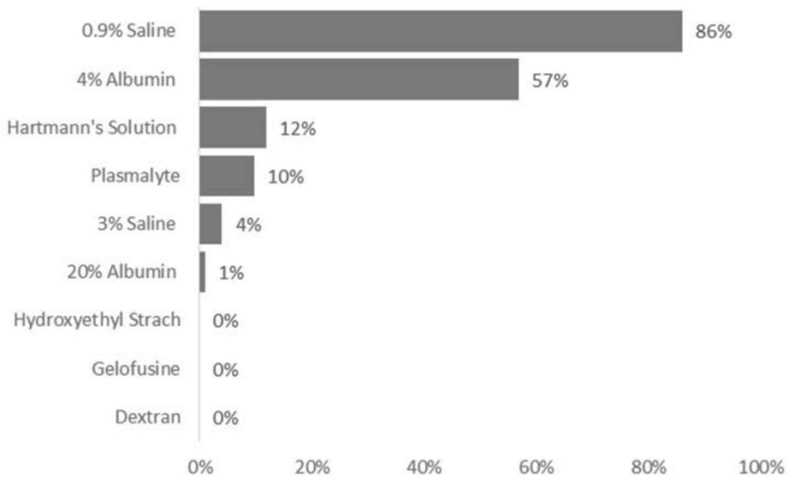

Figure 2. Preferred volume of fluid bolus therapy by most commonly prescribed fluid type

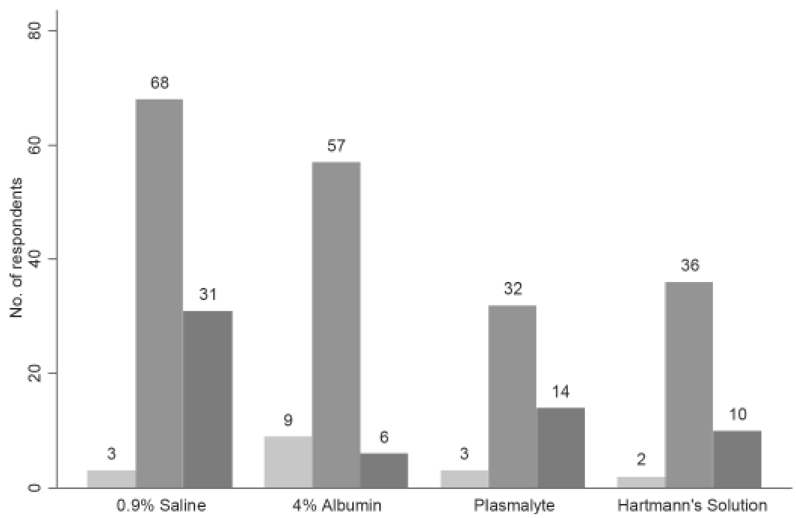

Table 1. Preferred duration of fluid bolus therapy by fluid composition

Fluid composition	Duration (min)			
	< 10	11–30	31–60	Total
0.9% saline	66 (65%)	34 (33%)	2 (2%)	102
4% albumin	43 (58%)	29 (39%)	2 (3%)	74
Hartmann's solution	27 (60%)	16 (36%)	1 (2%)	45*
PlasmaLyte	32 (65%)	16 (33%)	1 (2%)	49

* There was one respondent who indicated a preference for 120–240 minutes for Hartmann's solution.

physiological and biochemical markers of fluid responsiveness and the most preferred minimum expected magnitude of change to FBT. Point-of-care ultrasound was used by 70/106 respondents (66%), and rated as "good" or "very good" by 34/70 (49%). Dynamic tests such as the straight leg raise was used by 78/106 (74%), and rated as "good" or "very good" by 21/78 (27%). Respiratory rate and oxygen saturation were rated similarly by 15/106 (14%) and 11/106 (10%), respectively.

Eighty-one per cent of respondents (86/106) expected improved urine output after FBT, with 75/106 (71%) expecting an increase of 0.5–1 mL/kg in the following hour. A change in central venous pressure was expected by 87/106 (82%), and 57/106 (54%) expected a change of 2–3 cmH_2O. A change in central venous saturations was expected by 94/106 (89%), but only 48% rated this as a "good" or "very good" marker. For 73/106 (69%) of respondents, a minimum increase of 6% in central venous saturations was expected. A decrease in blood lactate was expected by 101/106 (95%), with 51% rating it as "good" or "very good" and 89/101 (84%) expecting a decrease of 0.6–1.5 mmol/L.

Preferences for specific pathophysiological conditions

For all scenarios, at least 90% of respondents selected either 0.9% saline or 4% albumin as their preferred fluid composition. For the post-operative cardiac surgical patient, 63/98 (64%) preferred 4% albumin and 41/63 (65%) of preferred 5 mL/kg. For the remaining scenarios, the most commonly preferred fluid was 10 mL/kg of 0.9% saline (supplementary Appendix, Section 4).

Other findings

In children with septic shock, 57% of respondents preferred commencing vasoactive medications after 40–60 mL/kg of FBT, and for 33% of respondents, after 20–40 mL/kg of FBT. Ninety-two per cent of participants were aware of the FEAST study and 36% reported to have changed their practice subsequently.

Table 2. Rating of markers of fluid responsiveness and minimum expected clinically significant response to fluid bolus therapy

Markers of fluid responsiveness	Respondents reporting use of the parameter *n* = 106	Rating as "good" or "very good"	Minimum expected clinically significant response	
Haemodynamic and physiological markers				
Heart rate	106	79 (75%)	94 (89%)	Decrease in heart rate of 6–15%
Blood pressure	106	62 (58%)	80 (76%)	Increase in MAP of 6–15%
Urine output	106	47 (44%)	75 (71%)	Increase in urine output of 0.5–1 mL/kg/h
Central venous pressure	106	41 (39%)	57 (54%)	Increase of 2–3 mmHg; 19 (18%); no change
Pulse pressure variability	99	45 (45%)		
Skin perfusion/capillary refill	106	44 (41%)		
Core to peripheral temperature gradient	96	20 (21%)		
Dynamic test (eg, straight leg raise)	78	21 (27%)		
Point-of-care ultrasound	70	34 (49%)		
Biochemical markers				
Serum lactate	106	54 (51%)	89 (84%)	Decrease of 0.6–1.5 mmol/L
Central venous saturations	103	49 (48%)	73 (69%)	Increase in $Scvo_2$ of 6% to > 8%
Base excess	101	19 (19%)		
Creatinine	104	6 (6%)		

MAP = mean arterial pressure. $Scvo_2$ = central venous oxygen saturation.

Discussion

Key findings

In this survey, we assessed the preferred fluid composition, volumes and rates as well as the preferred measures of fluid responsiveness of medical staff working in PICUs in Australia and New Zealand. The survey revealed preferences for the haemodynamic and physiological response assessment and therapy. The 0.9% saline and 4% albumin represent the most preferred fluid compositions, and the most preferred rate was less than 10 minutes. Clinicians rated heart rate and blood pressure highest as markers of fluid responsiveness. Other than for post-operative cardiac surgery, where 4% albumin was preferred, 0.9% saline represented the preferred fluid for FBT.

Comparing paediatric intensive care doctors with doctors from other disciplines

The findings from this survey show similarities to surveys of adult critical care physicians and paediatric emergency physicians[22,23] in terms of preferred fluid composition and markers of fluid responsiveness. Our study showed that 0.9% saline and 4% albumin were the most frequently used fluid compositions. Heart rate and blood pressure were highly rated by over three quarters and nearly 60% of respondents, respectively. In contrast, less than 50% rated pulse pressure variability, skin perfusion, central venous pressure and urine output similarly. For FBT in sepsis, 98% of surveyed paediatric emergency department (ED) physicians in Australia and New Zealand prefer 0.9% saline. The most highly regarded markers of fluid responsiveness included heart rate and blood pressure as well as skin perfusion. Sixty-two per cent preferred 20 mL/kg for every fluid bolus, whereas, in our study, 10 mL/kg is the preferred volume irrespective of fluid type. In comparison, in a survey of adult intensivists and ED physicians in Australia and New Zealand, the most commonly reported FBT was greater than 250 mL of 0.9% saline administered within 30 minutes. Differences in fluid type, preference and expected physiological responses were observed between intensivists and ED physicians.

Clinician preferences and guidelines in paediatric septic shock

In the present study, the approach of paediatric intensive care doctors to septic shock (and FBT generally) aligns with international guidelines in terms of rapid administration of crystalloid and consideration of vasoactive medications after 40–60 mL/kg of FBT. Specifically, clinicians reported an almost equal preference for FBT of 10 and 20 mL/kg of 0.9% saline for the initial bolus. The two recent editions of the American College of Critical Care Medicine

Pediatric Advanced Life Support guidelines maintain their recommendations of 20 mL/kg boluses up to 60 mL/kg be administered in the first 15 minutes of resuscitation, unless signs of fluid overload occur.[6,24] The foundation of these recommendations primarily stem from an observational cohort study from 1991, where subjects were categorised by administered volumes of FBT in the first 6 hours of septic shock.[25] The study suggested that those who received more than 40 mL/kg of FBT had improved survival compared with those who received less than 20 mL/kg.

While most participants in this survey were familiar with the FEAST study, only a third suggested their management had changed subsequently. This is intriguing, given the commonly held views about the applicability of this trial to children in resource-rich settings. At the very least, it does invite the intensive care community to investigate the role of FBT more thoroughly, particularly in view of the high mortality rate from septic shock of 17% in Australia and New Zealand.[26] The majority of studies of FBT in children relate to sepsis or septic shock, especially in diseases such as malaria,[1,3] dengue fever[4,5,27]and meningococcal sepsis.[28] The FEAST study, however, generated much debate as it showed increased mortality in children with sepsis and impaired perfusion who received FBT compared with those who did not.[10] The implication for children in resource-rich settings has been appropriately put into perspective,[12,13] but increasing interest in examining FBT has ensued.[29] There have only been three randomised controlled trials of FBT in children with septic shock and access to intensive care therapies — one in Brazil[30] and two in India.[31,32] None of these studies compared FBT with no FBT. A total of 309 children were randomised, and the Brazilian study showed improved survival using goal-directed therapy, but otherwise, no difference in shock reversal or patient-centred outcomes was identified.[33]

Fluid bolus therapy for cardiac surgery, trauma and acute lung injury in children

This survey shows that, aside from cardiac surgery for which 4% albumin was preferred, 0.9% saline is the preferred fluid composition for sepsis, trauma, traumatic brain injury and acute lung injury. One could speculate from these results that there is a perceived superior response to 4% albumin compared with 0.9% saline. Remarkably, few studies of the physiological effects of FBT in children undergoing surgery for congenital heart disease exist. Two small studies of fluid responsiveness using echocardiographic measures of stroke volume and pre- and post-surgical repair show that pulse pressure variation correlated most with measured stroke volume.[20,21]

The preferred fluid in trauma, acute lung injury and traumatic brain injury was 0.9% saline. There are no randomised studies in paediatrics to guide practice in relation to these conditions. However, there are data supporting fluid restriction. The Fluid and Catheter Treatment Trial (FACTT) — a randomised controlled study of a conservative versus liberal fluid strategy in adults with acute lung injury — showed a reduction in the duration of respiratory support in fluid-restricted patients.[34] Similarly, Day 3 positive cumulative fluid balance in children with acute lung injury is also associated with increased duration of ventilation.[35] However, the contribution of FBT to overall fluid balance in these circumstances is not clear. International consensus guidelines give no specific recommendation in relation to FBT in children with acute lung injury, but suggest a goal-directed fluid management approach.[36]

Fluid responsiveness

A high proportion of paediatric intensive care clinicians in Australia and New Zealand rate clinical signs such as heart rate and blood pressure as markers of fluid responsiveness. Less than half felt the same regarding urine output, central venous pressure and pulse pressure variability, and roughly half rated serum lactate and central venous saturations highly. Both dynamic and static measures of fluid responsiveness are unreliable in children.[16,37] Respiratory variation in aortic blood flow velocities appear better predictors of fluid responsiveness in children,[17,18] more so than systolic pressure variation and pulse pressure variability.[38] This survey, however, did not support the widespread use or high rating of point-of-care ultrasound. In practice, paediatric intensive care clinicians use a combination of vital signs, including the volume and quality of the peripheral pulse,[39] some invasive monitoring, and clinical judgement to guide fluid therapy.

Balanced solutions

Balanced solutions, such as Plasma-Lyte, are not commonly used as FBT in children. These solutions are attractive in that they aim to mitigate hyperchloraemia, metabolic acidosis and resultant impaired renal perfusion, which occurs with higher chloride-containing fluids.[40,41] Two randomised controlled trials in adults in intensive care comparing 0.9% saline and Plasma-Lyte for fluid therapy did not show a difference in renal complications.[42,43] An Indian study is currently recruiting children with septic shock, aiming to determine whether Plasma-Lyte compared with 0.9% saline reduces acute kidney injury (ClinicalTrials.gov identifier NCT02835157). Its role in fluid therapy in children, although promising, remains to be seen.[44]

Scope for further research: physiological response to fluid bolus therapy

Since FBT is one of many acute interventions within a complex myriad of haemodynamic responses to critical illness and imprecise measures of its requirement or response, it may prove difficult to investigate in isolation. There are few studies of the physiological and haemodynamic consequences of FBT in children. At the very least, describing the haemodynamic and physiological response to FBT may inform clinicians of the expected magnitude and duration of response, and possibly guide further interventional studies examining benefit or harm and how best to administer this common intervention.

Strengths and limitations

The strength of this study is that it provides insight into current attitudes to FBT of paediatric intensive care doctors from two high income countries. We were able to examine the attitudes towards fluid composition, volumes and rates in general and for a wide range of common conditions. We also gained insight into the expected response suggesting fluid responsiveness. The limitations are primarily inherent to the methodology of a survey. A response rate of just over 60% is good but may not reflect the opinion of a greater sample. The low numbers did not permit a comparison of responses based on discipline or ICU experience.

Conclusion

In a binational survey of FBT, clinicians in paediatric intensive care predominantly prescribe 0.9% saline or 4% albumin, and haemodynamic signs such as heart rate and blood pressure are considered the most valued measures of fluid responsiveness.

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Competing interests

None declared.

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