Loop diuretic therapy in the critically ill: a survey

Sarah L Jones, Johan Mårtensson, Neil J Glassford, Glenn M Eastwood and Rinaldo Bellomo

ABSTRACT

Objectives: To describe the self-reported practice of loop diuretic therapy (LDT) administration by intensivists in Australia and New Zealand and to ascertain the anticipated clinical and physiological effects of LDT for several common clinical indications.

Design: Structured online questionnaire distributed to intensivists via the Australian and New Zealand Intensive Care Society Clinical Trials Group email contact list. Descriptive statistics were used to analyse the results.

Participants: Intensivists in Australia and New Zealand.

Results: A total of 146 intensivists responded to the survey with most (99 [67.8%]) being Fellows of the College of Intensive Care Medicine or the Joint Faculty of Intensive Care Medicine. Overall, 88 (60.2%) had worked in ICUs for 10 years or more. A positive fluid balance, acute pulmonary oedema (APO) and acute lung injury (ALI) were considered key indications for LDT (> 80.0% positive response), in contrast to an elevated central venous pressure (CVP) (20.3%) and acute kidney injury (AKI) (3.8%), which were not. LDT by bolus therapy was preferred (by 60.0%–89.4%, according to indication) over continuous infusion (3.6%–11.1%, according to indication). The dominant initial LDT dose was furosemide 40 mg as an intravenous (IV) bolus. There was a lack of consensus regarding what would be an adequate response, and for many of the clinical indications, no target was specified.

Conclusions: Australian and New Zealand intensivists typically give frusemide as a 40 mg IV bolus for a positive fluid balance, ALI and APO, but not for an elevated CVP or AKI. However, such therapy is given without explicit definitions of an adequate response under these different clinical circumstances.

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The use of loop diuretic therapy (LDT) in critically ill patients remains controversial. Worldwide, LDT is given for several indications[1], including reducing oedema, improving gas exchange, correcting oliguria and attenuating acute kidney injury (AKI).[2] Loop diuretics such as furosemide may also be used to exert non-renal physiological effects, including venodilatation[3] and reduction of pulmonary arterial wedge pressure.[4]

In critically ill patients, the haemodynamic effects of LDT remain poorly understood. However, considerable evidence exists showing that fluid accumulation during intensive care unit admission is associated with detrimental outcomes,[5-9] suggesting a potential role for LDT. Also, in patients with AKI and acute lung injury (ALI), LDT has been associated with a protective effect on patient survival,[10] which is likely to be attributable to a reduction in positive fluid balance.[11] Despite this, little is known about why and how clinicians use LDT in the ICU, and the aims and expectations of such therapy remain poorly defined.

We aimed to describe the self-reported practice of LDT administration by intensivists in Australia and New Zealand, and ascertain the anticipated physiological and clinical effects after an intravenous (IV) bolus or IV infusion when giving LDT, for some clinical indications.

Methods

We obtained ethics committee approval for the study (approval LNR/14/Austin/291), and as the survey was anonymous and internet protocol addresses were not stored, there were no privacy problems.

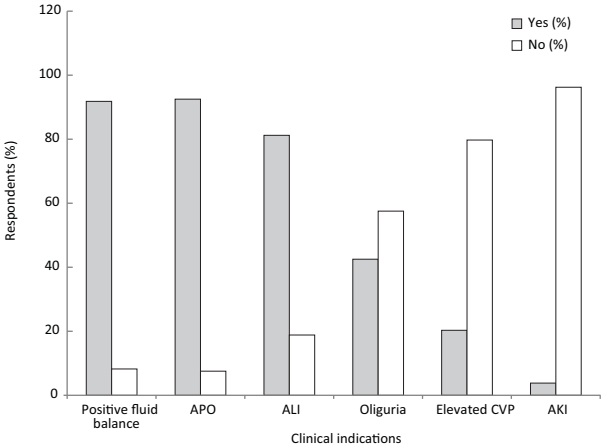
Survey design and distribution

We used a succinct, structured, multiple choice, online questionnaire to survey intensivists in Australia and New Zealand (see Appendix 1 online at cicm.org.au/Resources/Publications/Journal). Three senior intensivists reviewed the survey design.

The target population for the survey was intensivists working in Australia or New Zealand. All 71 member units of the Australian and New Zealand Intensive Care Society Clinical Trials Group were approached and asked to invite their specialists to participate in the survey. An invitation was sent by email containing a link to the questionnaire. Participation was voluntary and anonymous. Responses were obtained over a 2-week period in July 2014. A response to the email was taken as implied consent.

The clinical indications for LDT which were investigated in the survey were a markedly positive fluid balance, oliguria (defined as a urine output of < 0.5 mL/kg/h for ⩾ 6 h), ALI, elevated central venous pressure (CVP), acute pulmonary oedema (APO) and AKI. Descriptive statistics were used to analyse the results.

Figure 1. Surveyed clinical indications for loop diuretic therapy and percentage of respondents who would give it



APO = acute pulmonary oedema. ALI = acute lung injury. CVP = central venous pressure. AKI = acute kidney injury.

Results

Cohort and demographics

We received a total of 146 responses. The greatest number, 41 (28.1%), was from New South Wales.

Overall, 99 respondents (67.8%) were Fellows of the College of Intensive Care Medicine or the Joint Faculty of Intensive Care Medicine, and 20 (13.7%) were advanced trainees. The remaining 27 respondents (18.5%) were Fellows of the College of Anaesthetists, the College of Emergency Medicine or the College of Physicians. Most respondents were experienced ICU specialists with 88 (60.2%) having worked in ICUs for 10 years or more, and only 23 (15.8%) for fewer than 5 years.

Table 1. Preferred method for giving loop diuretic therapy, by clinical indication

	Loop diuretic therapy method preferred (%)		
Indication (*n*)	IV bolus	IV infusion	No preference
+ve fluid balance (130)	74.6%	10.7%	14.6%
Oliguria (61)	75.4%	8.2%	16.4%
ALI (108)	75.9%	11.1%	13.0%
↑ CVP (28)	82.1%	3.6%	14.3%
APO (123)	89.4%	4.1%	6.5%
AKI (5)	60.0%	0	40.0%

IV = intravenous. ALI = acute lung injury. CVP = central venous pressure. APO = acute pulmonary oedema. AKI = acute kidney injury.

Clinical indications, preferred administration method and preferred dose of LDT

Figure 1 shows the six clinical indications for LDT investigated in the survey, and the percentage of respondents who would give LDT for these indications. A positive fluid balance, APO and ALI were overwhelmingly considered to be key indications for giving LDT, in contrast to an elevated CVP and AKI, which only a small minority considered to warrant LDT.

Table 1 shows the preferred method for giving LDT for each of the clinical indications and shows the dominance of IV bolus therapy over continuous IV infusion. Table 2 shows the preferred LDT dose for each of the clinical indications and shows the dominance of the 40 mg IV bolus and the preferred starting dose of 10 mg/h for a continuous infusion. Table 3 shows the three most commonly expected clinical responses after LDT. It shows the widespread lack of precise and explicit definitions of what an "adequate response" would be in different circumstances, with the partial exception of the urinary output.

Discussion

Key findings

In our survey, we found that Australian and New Zealand intensivists overwhelmingly reported using LDT for a positive fluid balance, APO and ALI but not for an elevated CVP or AKI. An IV bolus (typically 40 mg) was clearly preferred over an infusion. However, with the partial exception of urinary output, the expected adequate clinical responses to such treatment remained undefined.

Relationship to previous studies

Some of our findings are in accordance with the results of a previous multinational study investigating LDT in the man-

Table 2. Preferred starting dose for loop diuretic therapy (furosemide), by clinical indication

	Preferred dose (%)	
Indication (*n*)	IV bolus*	IV infusion (per hour)
+ve fluid balance (124)	40 mg (50.0%)	10 mg (64.8%)
Oliguria (54)	40 mg (45.1%)	10 mg (38.9%) 20 mg (38.9%)
ALI (101)	40 mg (45.6%)	10 mg (73.0%)
↑ CVP (24)	20 mg (60.9%)	10 mg (42.9%)
APO (122)	40 mg (65.8%)	10 mg (50.0%)
AKI (4)	80 mg (50.0%)	50 mg (100%)

IV = intravenous. ALI = acute lung injury. CVP = central venous pressure. APO = acute pulmonary oedema. AKI = acute kidney injury.
* Dose options: 20 mg, 40 mg, 80 mg, 100 mg or more.

Table 3. The three most commonly expected clinical responses to loop diuretic therapy, by clinical indication

Indication (*n*)	Expected adequate clinical response (%)		
	Most common	2nd most common	3rd most common
+ve fluid bal. (130)	–ve fluid bal.; 1 L in 24 h (34.6%)	–ve fluid bal.; no set target (27.7%)	–ve fluid bal.; 1.5 L in 24 h (21.5%)
Oliguria (61)	UO > 1 mL/kg/h (37.7%)*	UO > 0.5 mL/kg/h (32.8%)*	Improved UO; no set target (11.5%)
ALI (108)	↓ PaO_2/FiO_2; no set target (91.7%)	PaO_2/FiO_2 > 200 (5.6%)	PaO_2/FiO_2 > 300 (1.9%)
↑ CVP (28)	↓ CVP; no set target (75%)	↓ CVP by 2 mmHg (17.9%)	↓ CVP by 4 mmHg (7.1%)
APO (122)	↓ FiO_2 (58.5%) and ↓ RR (66.7%); no set targets	↓ FiO_2 by 20% (22%) and ↓ RR by 8 bpm (16.7%)	↓ FiO_2 by 10% or 30% (8.5%) and ↓ RR by 4 bpm (10.8%)
AKI (5)	↓ serum creatinine, no set target (80%)	↓ serum creatinine by 10% (20%)	–

bal. = balance. UO = urine output. ALI = acute lung injury. CVP = central venous pressure. APO = acute pulmonary oedema. RR = respiratory rate. bpm = breaths per minute. AKI = acute kidney injury. * Actual urine output (not increase over baseline).

agement of AKI, which generated 331 responses from 16 countries.[1] In that study, clinicians also reported using diuretics as IV boluses in preference to infusion. This is perhaps surprising, given that lower doses of furosemide are generally required to achieve the same clinical effect when given as an infusion.[12] As in our study, diuretics were "frequently" or "almost always" given for APO, but "rarely" given for AKI. Over 75% of respondents targeted a urine output of ⩾ 0.5 mL/kg/h or ⩾ 1 mL/kg/h when giving diuretics for AKI. Nearly 18% of respondents did not specifically target a given fluid balance when using diuretics for AKI, although 35.9% targeted a negative daily balance of 0.5–1 L. No information was obtained on expected effects or definitions of an adequate response.

Study implications

Our study implies that in general, there is broad consensus among Australian and New Zealand intensivists on when to give LDT, the use of bolus therapy and the preferred LDT dose, but the expected physiological and clinical responses are poorly defined. These observations imply that, in many patients, LDT given in the ICU may be given without clear physiological and/or clinical targets.

Strengths and limitations

Our study has strengths and limitations. The method selected to sample respondents was efficient and expedient, and the survey was subject to thorough assessment by experienced intensivists before distribution

With regards to limitations, to optimise the number of respondents, questions were kept deliberately simple. To have focussed on more specific details for each clinical indication would have made it lengthier and reduced the number of respondents willing to participate. It is appreciated that when prescribing LDT for a critically ill patient, several factors are considered, including the patient's renal function, whether they usually take a diuretic, and the response seen when a dose has previously been given. Because of the way the survey was distributed, we could not impute an appropriate denominator to calculate a response rate.

Conclusions

Australian and New Zealand intensivists report giving LDT for a positive fluid balance, APO and ALI but not for an elevated CVP or for AKI. LDT is most commonly given as an IV bolus, typically at a dose of 40 mg. However, the clarity of reported practice is lost when defining the expected physiological and clinical effects. These observations suggest the need to conduct prospective observational studies to define the typical response to LDT in critically ill patients. Future work should also enquire about the concomitant administration of albumin ("push–pull" therapy) and the frequency of electrolyte replacement, notably potassium and magnesium, when giving LDT.

Competing interests

None declared.

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Appendix 1. This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors

Introduction

Diuretic use in critically ill patients, along with fluid bolus therapy remains a topic of controversy. Many of you have recently completed a survey designed to further understand fluid bolus therapy practice in the Intensive Care Unit (ICU). To understand another key intervention for fluid balance in critically ill patients, a second survey has been designed in an attempt to further clarify frusemide use in the ICU, particularly focussing on its expected clinical effects.

This short voluntary practice survey should take at most 5 minutes to complete.

The survey first asks about your location and duration of your intensive care practice. It then asks you to specify the clinical circumstances in which you would give frusemide, the dose and method of frusemide that you would give, followed by the anticipated clinical response.

This project has been reviewed by the Austin Health Human Research Ethics Committee (Project No. LNR/14/Austin/291). Your participation is voluntary and your responses will remain anonymous. All responses will be stored electronically and accessible only by the investigators. Only aggregated findings will be published or presented in peer-reviewed critical care journals.

Questionnaire version 3 (19/06/2014)

Respondent Details

* 1. Please indicate your State/Territory of Practice

- North Island, New Zealand
- South Island, New Zealand
- Queensland, Australia
- Western Australia
- New South Wales, Australia
- Tasmania, Australia
- Victoria, Australia
- South Australia
- Australian Capital Territory
- Northern Territory, Australia

* 2. Which of the following Fellowships do you hold at present?

- FCICM/JFICM
- FANZCA
- FACEM
- FRACP
- None - trainee

* 3. How long have you worked in Intensive Care?

- Less than 5 years
- 5-10 years
- 10-15 years
- 15-20 years
- More than 20 years

Frusemide and Positive Fluid Balance

* 4. Would you give frusemide to a critically ill patient with a markedly positive cumulative fluid balance?

- Yes
- No

* 5. What would be your preferred method for giving frusemide in this instance?

- IV bolus
- IV infusion
- No preference

6. Please specify what dose of frusemide you would typically give for this indication

	IV bolus	IV infusion
Dose		

* 7. What would constitute an adequate clinical response when administering frusemide for a markedly positive cumulative fluid balance?

- Negative fluid balance of 500mls in 24 hours
- Negative fluid balance of 1 Litres in 24 hours
- Negative fluid balance of 1.5 Litres in 24 hours
- Negative fluid balance of 2 Litres or more in 24 hours
- A negative fluid balance but no specific target

Frusemide and Oliguria

* 8. Would you give frusemide to an oliguric critically ill patient (urine output <0.5mls/kg/hr for 6 hours or more)?

- Yes
- No

* 9. What would be your preferred method for giving frusemide in this instance?

- IV bolus
- IV infusion
- No preference

10. Please specify what dose of frusemide you would typically give for this indication

	IV bolus	IV infusion
Dose		

* 11. What would constitute an adequate clinical response when administering frusemide for oliguria?

- Urine output > 0.5mls/kg/hour
- Urine output >1ml/kg/hour
- Urine output >1.5mls/kg/hour
- Urine output >2mls/kg/hour
- An improvement in urine output but no specific target

Frusemide in Acute Lung Injury

* 12. Would you give frusemide to a critically ill patient with Acute Lung Injury?

- Yes
- No

* 13. What would be your preferred method for giving furosemide in this instance?

- IV bolus
- IV infusion
- No preference

14. Please specify what dose of frusemide you would typically give for this indication

	IV bolus	IV infusion
Dose		

* 15. What would constitute an adequate clinical response when administering frusemide in Acute Lung Injury?

- PaO2/FiO2 ratio > 100
- PaO2/FiO2 ratio >200
- PaO2/FiO2 ratio >300
- PaO2/FiO2 ratio >400
- An improvement in the PaO2/FiO2 ratio but no specific target

Furosemide and Elevated CVP

16. Would you give furosemide to a critically ill patient with what you consider to be an elevated central venous pressure (CVP)?

- Yes
- No

* 17. What would be your preferred method for giving frusemide in this instance?

- IV bolus
- IV infusion
- No preference

18. Please specify what dose of furosemide you would typically give for this indication

	IV bolus	IV infusion
Dose		

* 19. What would constitute an adequate clinical response when administering furosemide for what you consider to be an elevated CVP?

- A reduction in CVP by 2mmHg
- A reduction in CVP by 4mmHg
- A reduction in CVP by 6mmHg
- A reduction in CVP but no specific target

Frusemide in Acute Pulmonary Oedema

* 20. Would you give frusemide to a critically ill patient with acute pulmonary oedema?

- Yes
- No

* 21. What would be your preferred method for giving frusemide in this instance?

- IV bolus
- IV infusion
- No preference

22. Please specify what dose of frusemide you would typically give for this indication

	IV bolus	IV infusion
Dose		

23. What would constitute an adequate clinical response when administering frusemide for pulmonary oedema?

	FiO2	Respiratory Rate
Reduction in		

Furosemide in Acute Kidney Injury

* 24. Would you give furosemide to a critically ill patient with Acute Kidney Injury based on serum creatinine alone?

- Yes
- No

25. What would be your serum creatinine threshold for frusemide administration in Acute Kidney Injury?

- > 1.5 x baseline serum creatinine (KDIGO AKI stage 1)
- > 2 x baseline serum creatinine (KDIGO AKI stage 2)
- > 3 x baseline serum creatinine (KDIGO AKI stage 3)
- No specific serum creatinine threshold

* 26. What would be your preferred method for giving frusemide in this instance?

- IV bolus
- IV infusion
- No preference

27. Please specify what dose of frusemide you would typically give for this indication

	IV bolus	IV infusion
Dose		

* 28. What would constitute an adequate clinical response when administering frusemide for Acute Kidney Injury?

- Fall in serum creatinine by 10%
- Fall in serum creatinine by 20%
- Fall in serum creatinine by 30%
- Fall in serum creatinine by 40%
- Fall in serum creatinine by 50% or more
- A reduction in serum creatinine, but no specific target

Survey Finish

Thank you for taking the time to complete this survey. It is much appreciated.

Please e-mail any comments your have regarding the survey to sarah.jones@austin.org.au