Enteral nutrition in Australian and New Zealand intensive care units: a point-prevalence study of prescription practices

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ABSTRACT

Background: Enteral nutrition (EN) is widely accepted as the preferred method for providing nutrition therapy to critically ill patients. However, optimal energy goals and the best way to achieve those goals are ill defined.

Objective: To determine the type and energy concentration of commonly prescribed EN formulations and whether energy-dense formulations (> 1 kcal/mL) are used.

Design: Prospective, observational, multicentre, single-day, point-prevalence study.

Participants and setting: All patients present in 38 Australian and New Zealand intensive care units at 10:00 on 17 November 2010.

Main outcome measures: Demographic data, admission diagnosis and information on EN administration were collected.

Results: 522 patients were enrolled. Mean age was 58.7 (SD, 17.3) years, 65% were male and 79% were mechanically ventilated. On study day, 220/522 patients received EN (43%; 95% CI, 39%–48%). ICU admission source, Acute Physiology and Chronic Health Evaluation (APACHE) III diagnostic category, APACHE II score and ventilation on study day predicted receipt of EN. Of those receiving EN, 111/220 (51%; 95% CI, 44%–57%) received a 1 kcal/mL formulation and the remainder received an energy-dense formulation — 2 kcal/mL, 39/220 (18%; 95% CI, 13%–23%); and 1.5 kcal/mL, 32/220 (15%; 95% CI, 10%–20%). There were no significant predictors for receipt of energy-dense versus 1 kcal/mL EN.

Conclusions: 1 kcal/mL and energy-dense formulations are administered with about equal frequency in Australian and New Zealand ICUs. This finding supports future research into the evaluation of optimal nutritional delivery amounts using EN formulations with differing energy concentrations.

Crit Care Resusc 2012; 14: 148–153

Enteral nutrition (EN) is widely accepted as the preferred method for nutrition therapy in critically ill patients.[1-3] Reported benefits include maintenance of gut integrity[4] and function,[5] reduced infectious complications,[6-8] decreased incidence of hyperglycaemia[9] and reduced hospital length of stay.[10]

To prevent the complications of undernutrition (eg, malnutrition, infection, prolonged ventilation) and overnutrition (eg, increased gastric residual volumes, aspiration, pneumonia, hyperglycaemia, fatty liver), the traditional approach is to deliver sufficient energy to meet measured expenditure using indirect calorimetry[1,11] or estimated expenditure, based on either predictive equations developed in the non-critically ill (eg, the Harris–Benedict equation, the Schofield equation)[12,13] or on fixed weight-based prescriptions (generally 20–25 kcal/kg/day).[14] Irrespective of the method, clinical practice typically results in critically ill patients receiving only 50%–70% of prescribed energy.[15-19] In an international survey of nutritional practices conducted in 167 intensive care units across 37 countries, 69% of patients received EN alone.[19] The mean daily energy prescribed was 24.0 kcal/kg (SD, 5.8 kcal/kg) (1794 kcal [SD, 364 kcal]), but only a mean of 14.0 kcal/kg (SD, 7.6 kcal/kg) (1034 kcal [SD, 514 kcal]; 59% of prescribed energy)[19] was delivered.

Multiple observational studies have shown an association between low energy intake and poor clinical outcomes.[19-21] However, recent small comparative studies have suggested that hypocaloric nutrition may not be associated with inferior outcomes.[22,23] Given the lack of large, multicentre, randomised controlled trials (RCTs) demonstrating an association between a specific energy delivery amount and improved outcomes, some clinicians consider permissive hypocaloric nutrition to be warranted. Conversely, others have focused on determining reliable methods to match energy delivery to recommended isocaloric goals. Although promotility drugs[24-27] and small intestinal delivery[3,28] are frequently initiated in ICU patients with EN intolerance, another technique that may increase delivery is to administer energy-dense formulations (> 1 kcal/mL). This strategy has only successfully increased energy delivery in one small study in non-critically ill children;[29] and its safety has been questioned.[30]

As preliminary research for conducting a large, multicentre, double-blind, RCT to determine if delivery of different energy amounts to critically ill adults affects clinically

Table 1. Patient characteristics

Characteristic	All patients	Any type of EN	1 kcal/mL EN	> 1 kcal/mL EN
No. of patients	522	220	111	109
Mean age, years (SD)	58.7 (17.3)	58.0 (17.5)	58.9 (17.4)	57.1 (17.7)
Male sex no. (%)	337/522 (64.6)	153/219 (69.9)	73/110 (66.4)	80/109 (73.4)
Mean weight,* kg (SD)	80.7 (19.3)	81.6 (19.8)	80.0 (19.1)	83.1 (20.5)
Mean APACHE II score (SD)	17.4 (7.3)	19.5 (7.6)	20.0 (7.9)	19.2 (7.2)
ICU admission source, no. (%)				
Emergency department	145/521 (27.9)	67/219 (30.6)	36/110 (32.7)	30/108 (27.8)
Hospital ward	110/521 (21.1)	57/219 (26.0)	25/110 (22.7)	32/108 (29.6)
Operating theatre	203/521 (39.0)	59/219 (27.0)	30/110 (27.3)	29/108 (26.9)
Other	63/521 (12.1)	36/219 (16.4)	19/110 (17.3)	17/108 (15.7)
APACHE III diagnostic categories, no. (%)				
Cardiovascular	116/477 (24.3)	37/203 (18.2)	21/103 (20.4)	16/99 (13.2)
Respiratory	78/477 (16.4)	44/203 (22.2)	20/103 (19.4)	23/99 (23.2)
Gastrointestinal	79/477 (16.6)	31/203 (15.3)	17/103 (16.5)	14/99 (14.1)
Neurological	65/477 (13.6)	36/203 (17.7)	21/103 (20.4)	15/99 (15.2)
Sepsis	44/477 (9.2)	17/203 (8.4)	9/103 (8.7)	8/99 (8.1)
Trauma	47/477 (9.9)	29/203 (14.3)	11/103 (10.7)	18/99 (18.2)
Other	48/477 (10.1)	9/203 (4.4)	4/103 (3.9)	5/99 (5.1)
Mechanical ventilation on study day, no. (%)	237/301 (78.7)	168/184 (91.1)	85/93 (50.6)	83/91 (49.4)
Mean SOFA score on study day (SD)	2.2 (0.9)	2.2 (0.8)	2.1 (0.8)	2.2 (0.8)
Median hospital length of stay, days (IQR)	4.0 (1.0–11.0)	7.0 (3.0–15.0)	6.0 (2.0–14.0)	7.0 (4.0–16.0)
Mortality 28 days after study day, no (%)†	66/465 (14.2)	36/199 (18.1)	25/105 (23.8)	13/100 (13.0)

APACHE = Acute Physiological and Chronic Health Evaluation. EN = enteral nutrition. IQR = interquartile range. SOFA = Sequential Organ Failure Assessment.
* Weight estimated or actual. † Risk difference, 10.8% (95% CI, – 0.3 to – 21.3%) for > 1 kcal/mL v 1 kcal/mL EN.

important outcomes, a single-day point-prevalence survey was undertaken on 17 November 2010 in conjunction with the Australian and New Zealand Intensive Care Society Clinical Trials Group (CTG)-endorsed Point Prevalence Program and conducted by the George Institute for Global Health. The primary aim was to determine the most commonly prescribed EN formulations in critically ill patients in Australian and New Zealand ICUs and to determine whether energy-dense formulations are commonly used for patients prescribed EN.

Methods

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

All adult patients (⩾ 16 years) present in participating ICUs at 10:00 on the study day were enrolled. Routine survey data included age, sex, weight, ICU admission Acute Physiology and Chronic Heath Evaluation (APACHE) II score, Sequential Organ Failure Assessment score within the preceding 24 hours, ICU admission source and APACHE III diagnostic category and requirement for invasive or non-invasive ventilation on the study day. Vital status 28 days after study day was ascertained using hospital administrative databases. Specific information on enteral formulations included the number of patients receiving EN on the study day and the type of formulation prescribed, including energy concentration.

Statistical analysis

Variables are reported as mean (SD) or median (interquartile range [IQR]) as appropriate. EN proportions (n/N) are reported as percentages with 95% confidence intervals. Differences between patients receiving 1 kcal/mL versus energy-dense EN were analysed using the Student *t* test for continuous variables or χ^2 for categorical variables, as appropriate. Predictor variables (age, sex, weight, APACHE II score, APACHE III diagnostic category, mechanical ventilation, ICU admission source, ICU readmission) for EN prescription and for the prescription of energy-dense versus 1 kcal/mL EN

Table 2. Predictor variables for receipt of enteral nutrition

	Logistic regression model ($n = 234$)		Final logistic regression model with multiple imputations ($n = 522$, $m = 150$)*	
Variable	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Age	1.02 (0.996–1.043)	0.096	0.998 (0.984–1.013)	0.831
Sex	0.839 (0.447–1.489)	0.58	1.5 (0.965–2.332)	0.072
Weight	1.004 (0.989–1.018)	0.778	1.005 (0.994–1.016)	0.353
APACHE II score	1.029 (0.981–1.080)	0.242	1.072 (1.030–1.117)	0.001
ICU admission source†				
Emergency department	1.157 (0.531–2.452)	0.717	1.018 (0.516–2.007)	0.959
Hospital ward	1.62 (0.635–4.132)	0.313	2.044 (1.091–3.30)	0.026
Other	2.04 (0.856–4.866)	0.108	1.886 (0.939–3.788)	0.075
ICU readmission	0.864 (0.243–3.078)	0.778	1.538 (0.617–3.834)	0.356
APACHE III diagnostic category†				
Respiratory	6.132 (0.959–2.089)	0.001	2.919 (1.400–6.083)	0.004
Gastrointestinal	0.969 (0.392–2.394)	0.945	1.473 (0.726–2.986)	0.283
Neurological	3.062 (0.932–10.062)	0.065	4.121 (1.737–9.778)	0.001
Sepsis	1.353 (0.460–3.980)	0.583	0.796 (0.381–1.661)	0.543
Trauma	7.015 (2.456–20.033)	< 0.001	5.375 (2.286–12.634)	< 0.001
Other	0.591 (0.148–2.368)	0.458	0.512 (0.225–1.166)	0.111
Mechanical ventilation	9.511 (4.166–21.713)	< 0.001	8.377 (4.202–16.70)	< 0.001

APACHE = Acute Physiology and Chronic Health Evaluation. AUC = area under the (non-parametric) receiver operator characteristic curve. ICU = intensive care unit.
* All missing data < 3% except for APACHE II score (14%), mechanical ventilation (42%) and APACHE III diagnostic categories (8%). Monte Carlo error estimates all < 0.02 except for mechanical ventilation (0.14). Logistic regression model: complete-case analysis, AUC, 0.79; Hosmer–Lemeshow test, $P = 0.59$; imputed AUC, 0.85; Hosmer–Lemeshow test, $P = 0.05$. † Reference category: ICU admission source, operating theatre; APACHE III diagnostic category, cardiovascular.

were analysed using complete-case logistic regression (clustering of patients within ICUs and robust variance) and with multiple imputation to adjust for missing data.

Multiple imputation[31] was undertaken using the chained equation approach,[32] and was implemented using Stata version 12 (StataCorp 2011, College Station, Tex, USA) and guided by a reduction in Monte Carlo error.[33] Imputation fidelity was checked after the recommendations of Marchenko and Eddings;[34] in particular, summary estimates and the distribution of key continuous variables were compared between the imputed datasets and the complete-case dataset. Statistical significance was ascribed at $P \leqslant 0.05$.

Results

Thirty-eight tertiary referral, metropolitan and regional hospitals participated (Appendix 1) and 522 patients were enrolled. Patient characteristics are displayed in Table 1. Sixty-five per cent (337/522) were male and the mean age was 58.7 years (SD, 17.3 years). On the study day, 220 of 508 patients (43%; 95% CI, 39%–48%) for whom data were available received EN. Of these, 91% (168/184) received invasive or non-invasive ventilation, median hospital length of stay was 7.0 days (IQR, 3.0–15.0 days) and 28-day mortality was 18% (36/199) (Table 1). In the complete-case analysis, the predictors for receipt of EN were APACHE III diagnostic category (respiratory, trauma) and mechanical ventilation on study day (Table 2). Adjusting for missing data, the predictors were ICU admission source (hospital ward), APACHE II score, APACHE III diagnostic category (respiratory, neurological, trauma) and mechanical ventilation (Table 2). Although there was no attempt to further model the logistic regression predictors (eg, non-linear covariate effects and interactions), a small increment in area under the curve (AUC) (0.79 to 0.85) was evident with the imputed model using the same covariate predictors as in the complete-case analysis. The proportion ventilated and the mean APACHE II score were similar for both the imputed datasets (0.72 v 0.79) and the complete-case analysis dataset (17.4 v 18.8).

The most common formulation prescribed was Jevity (36/220, 16%; 95% CI, 12%–22%) (1 kcal/mL). Overall, 51% (95% CI, 44%–57%) of patients (111/220) received a 1 kcal/mL EN formulation. Thirty-two patients (15%; 95% CI,

Table 3. Number of patients prescribed various enteral nutrition formulations

1 kcal/mL ($n = 111$)		1.2 or 1.25 kcal/mL ($n = 32$)		1.5 kcal/mL ($n = 32$)		2 kcal/mL ($n = 39$)	
Formulation	No. (%)	Formulation	No. (%)	Formulation	No. (%)	Formulation	No. (%)
Jevity	36 (16.4)	Jevity plus	10 (4.6)	Nutrison energy multifibre	11 (5.0)	Nepro	20 (9.1)
Nutrison 1 cal	17 (7.7)	Nutrison protein plus multifibre	9 (4.1)	Jevity hical	5 (2.3)	Twocal HN	8 (3.6)
Promote with fibre	15 (6.8)	Fibersource HN	7 (3.2)	Isosource 1.5	3 (1.4)	Nutrison concentrated	7 (3.2)
Glucerna	14 (6.4)	Isosource HN	4 (1.8)	Nutrison energy	3 (1.4)	Novasource 2.0	4 (1.8)
Nutrison multifibre	12 (5.5)	Nutrison protein plus	2 (0.9)	Ensure plus	2 (0.9)		
Osmolite	12 (5.5)			Impact 1.5	1 (0.5)		
Fibersource	3 (1.4)						
Nutrison low sodium	1 (0.5)						
Peptisorb	1 (0.5)						

Other enteral nutrition formulations (no. of patients): Fresubin original fibre (1), Perative (1), Diabetic resource (1), Pulmonary nutrison (1), Resource 2 (2).

10%–20%) received EN formulations containing 1.5 kcal/mL and 39 patients (18%; 95% CI, 13%–23%) 2.0 kcal/mL. The remaining patients received either 1.2 or 1.25 kcal/mL formulations (32/220, 15%; 95% CI, 10%–20%) or other formulation types (6/220, 3%; 95% CI, 1%–6%) (Table 3). There were no significant differences in patient characteristics (Table 1) and no predictor variables ($P \geqslant 0.11$ with complete-case analysis, $P \geqslant 0.18$ for the multiple imputation dataset; logistic regression AUC, 0.63 and 0.61, respectively) for those receiving energy-dense versus 1 kcal/mL EN. Patients receiving an energy-dense formulation tended to have a lower mortality 28 days after the study day (13.0% v 23.8%; risk difference − 10.8% [95% CI, −0.3% to −21.3%]; $P = 0.05$).

Discussion

This Australian and New Zealand point-prevalence study indicates that about 40% of critically ill patients received EN on the study day. Just over 50% of those patients received a 1 kcal/mL EN formulation, and the rest received an energy-dense formulation containing more than 1 kcal/mL.

The common use of energy-dense EN has not been previously reported. It is unclear why these formulations were used, as this was not investigated. There were no significant clinical predictors (demographics, severity of illness, mechanical ventilation) for determining the energy content of the EN formulation. It is not surprising, however, that illness severity (as indicated by APACHE II score) and requirement for mechanical ventilation predicted prescription of EN. Similarly, patients transferred to ICU from the hospital ward versus direct from the ED may have had several days of undernutrition before ICU admission, and hence, may have been more likely to receive nutritional therapy in ICU.

The most likely reasons for prescribing an energy-dense formulation were either an attempt to administer full energy requirements while restricting fluid intake or to achieve nutritional goals in patients who had not tolerated a 1 kcal/mL EN formulation. EN intolerance is commonly manifest by large gastric residual volumes that are believed to be due to delayed gastric emptying.[35] This appears to be due to an exaggerated feedback response to the presence of nutrient (1 kcal/mL) in the small intestine.[36] Although energy-dense formulations could result in a further enhancement of small intestinal feedback and a further slowing of gastric emptying,[37] studies have specifically examined the relationship between EN energy concentration and delivery in critically ill patients.

Furthermore, although energy-dense formulations may have been prescribed to increase energy delivery, the more fundamental question of whether increasing energy delivery actually improves clinical outcomes such as mortality or functional recovery remains unanswered. We found a trend to improved survival in patients prescribed an energy-dense formulation; however, this may simply reflect the non-randomised nature of this single-day point-prevalence study, selection bias and that patients were at different stages of critical illness.

Given limited and conflicting evidence regarding optimal energy delivery in the critically ill,[10,19-21,38,39] further research on the delivery of different energy amounts is needed. As EN is the standard nutrition therapy in Australia and New Zealand, allocation of patients to different amounts of energy delivery from EN (either a 1 kcal/mL EN formulation or an energy-dense formulation) in a large-scale, multicentre, blinded RCT seems optimal.

Our results represent a snapshot of EN prescription practices and must be interpreted with caution. Thirty-eight

hospitals participated and the results may not be applicable to other ICUs. The reasons for delivery of specific EN formulations, the rate of delivery and whether or not the EN was tolerated were also not examined.

The degree of individual variable missing data was relatively modest, but multiple imputation was indicated, as the overall effect of the missing data was to reduce the analysable data in the logistic regression models by 54% (EN versus no EN prescription) and 33% (energy-dense versus 1 kcal/mL EN). As adjudged by summary estimates and the distribution of key continuous variables, the imputation process was accepted as being satisfactory;[40] and compared with the complete-case analysis, the imputation analysis was more efficient (reflected in a decreased width of the 95% CI).

Conclusions

This point-prevalence survey suggests that energy-dense EN formulations are commonly administered in Australian and New Zealand ICUs and that there are no obvious patient-specific predictors for their administration. This supports the conduct of an RCT to assess clinical outcome effects of a 1 kcal/mL compared with an energy-dense EN formulation. Missing data in observational studies is a frequent problem and principled methods of imputation should always be considered.

Competing interests

None declared.

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Middlemore Hospital, Auckland, New Zealand: T Williams, J Tai, A Tilsley

Nepean Hospital, Sydney, NSW, Australia: I Seppelt, L Weisbrodt

North Shore Private Hospital, Sydney, NSW, Australia: A Delaney, S Ash, DL Hogben

Royal Adelaide Hospital, Adelaide, SA, Australia: M Chapman, S O'Connor

Royal Darwin Hospital, Darwin, NT, Australia: D Stephens, J Thomas

Royal Melbourne Hospital, Melbourne, VIC, Australia: C Macisaac, T Caf, D Barge

Royal Perth Hospital, Perth, WA, Australia: S Webb, G McEntaggart, J Chamberlain

Royal Prince Alfred Hospital, Sydney, NSW, Australia: D Gattas, D Rajbhandari, H Buhr

Sir Charles Gairdner Hospital, Perth, WA, Australia: S Baker, B Roberts

St George Hospital, Sydney, NSW, Australia: J Myburgh, V Dhiacou

St Vincent's Hospital, Melbourne, VIC, Australia: J Santamaria, R Smith

St Vincent's Hospital, Sydney, NSW, Australia: P Nair, C Burns, C Reynolds

The Queen Elizabeth Hospital, Adelaide, SA, Australia: S Peake, P Williams, C Kurenda

Townsville Hospital, Townsville, QLD, Australia: G Gordon, L Jones

Wellington Regional Hospital, Wellington, New Zealand: D Dinsdale, D Mackle, L Andrews

Westmead Hospital, Sydney, NSW, Australia: A Bannerjee, C Skelly

Wollongong Hospital, Sydney, NSW, Australia: M Sterba, B Johnson, R Xu.