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Transpyloric enteral nutrition in the critically ill child with renal failure

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Abstract *Objective:* To study the efficacy and tolerance of transpyloric enteral nutrition (TEN) in the critically ill child with acute renal failure (ARF). *Design:* Prospective observational study. *Setting:* Paediatric intensive care unit. *Patients:* Critically ill children with ARF who received TEN were included in the study. They were compared with the remaining 473 critically ill children receiving TEN in this period. Tolerance of nutrition and gastrointestinal complications were assessed. *Intervention:* Transpyloric enteral nutrition. *Measurements and results:* Fifty-three critically ill children with ARF aged between 3 days and 17 years received TEN. Children with ARF more frequently received parenteral nutrition before TEN (56.6%) than the other patients (17.5%). The incidence of shock, hepatic alterations and mortality was significantly higher in patients with ARF than in the remaining children. In children with ARF the mean duration of the TEN was 16.5 ± 27.3 days and the maximum caloric intake was 77 ± 26.7 kcal/kg/day. Thirteen patients (24.5%) presented gastrointestinal complications, 9 (17%) abdominal distension and/or excessive gastric residue, 5 (9.4%) diarrhoea, 1 necrotising enterocolitis and 1 duodenal perforation. The frequency of gastrointestinal complications was significantly higher in children with ARF. TEN was definitive suspended in five patients due to gastrointestinal complications. Four of these patients were treated with continuous renal replacement therapy. Thirty percent of patients died during TEN. In only one patient was the death related to complications of the nutrition. *Conclusions:* Critically ill children with ARF tolerate TEN, although the incidence of gastrointestinal complications is higher than in other critically ill children.

Keywords Acute renal failure · Continuous renal replacement therapy · Enteral nutrition · Critically ill children · Transpyloric enteral nutrition · Gastrointestinal complications

Introduction

Critically ill adults and children with acute renal failure have a high mortality [1, 2, 3, 4]. Malnutrition is a common finding in patients with acute renal failure and leads to an increase in the risk of complications and mortality [5]. Nutrition is a fundamental factor in the treatment of the critically ill patient with acute renal failure and can improve the prognosis [6, 7].

Enteral nutrition is the best feeding method in the critical patient as it favours intestinal trophism, stimulates the immune system, reduces bacterial translocation and the incidence of sepsis and multisystem failure, and has few side effects [8, 9, 10]. However, oral or nasogastric feeding is sometimes poorly tolerated, particularly in those patients on mechanical ventilation, due to the reduced gastric motility secondary to the administration of drugs or to the disease itself, with the onset of distension,

the accumulation of gastric residues, and a higher risk of pulmonary aspiration [11]. Duodeno-jejunal enteral nutrition has been shown to be a good alternative route in critically ill adults [12, 13] and children [14, 15]. Acute renal failure could reduce the tolerance to enteral nutrition due to the gastrointestinal motility disorders associated with the uraemia [16]. For this reason, many critically ill patients who develop acute renal failure have been treated with parenteral nutrition [17, 18]. Very few studies exist that have analysed the tolerance and adverse effects of enteral nutrition in adult patients with acute renal failure [19], and no studies exist in children. The objective of the present study was to analyse the tolerance of transpyloric enteral nutrition (TEN) in children with ARF compared with other critically ill children who received TEN.

Patients and methods

A prospective observational study was performed that included all critically ill children admitted to the paediatric intensive care unit (PICU) between 1 March 1994 and 31 December 2004 who received TEN. We compared patients with renal failure with the remaining children. Acute renal failure was defined as an acute increase in the creatinine levels to more than twice the upper limit of normal level for age, with or without a change in the diuresis, and/or the need for renal replacement therapy. In our PICU venovenous continuous renal replacement therapy is the preferred method of depuration [20]. However, the indication for and type of renal replacement therapy, decided by the paediatric intensive care assistant, was individualised according to the age and diagnosis of the patients, haemodynamic status, diuresis, and levels of urea and creatinine.

TEN was held to be indicated in children requiring acute mechanical ventilation and sedatives, those with an altered consciousness level and/or respiratory failure without mechanical ventilation and/or children without mechanical ventilation with a risk of aspiration, and in those who did not tolerate gastric nutrition because of vomiting or important abdominal distension. The transpyloric tube was inserted by the nursing staff following a protocolised method [21]. Confirmation of the position of the tube was initially performed by aspiration and measurement of the pH and this was subsequently confirmed radiologically. All the tubes were situated between the 1st and 4th portions of the duodenum. A second tube was inserted via the same nasal orifice for drainage of the gastric contents and for measurement of the gastric residue every 3–4 h.

The type of nutrition administered depended on the age of the patient. In children under 2–3 years, an infant formula was administered (700 kcal/l, × 18 g protein/l); this was substituted by protein hydrolysate in patients with milk-protein intolerance or a suspicion of intestinal damage. Calorie supplements in the form of dextrin-maltose, medium-chain triglycerides or cereals were added in some patients. In children over 2–3 years of age, isocaloric (1.2 kcal/ml), normoproteic (26 g proteins/l) paediatric liquid formulae were administered. The alimentation was started at a rate of 0.5–1 ml/kg per hour, with increases of 0.5–1 ml/kg every 3–4 h if the gastric residues were less than 25% of the volume administered, until a normal calorie intake according to the age [22] was achieved in the first 24 to 48 h. Failure of the enteral nutrition was considered to have occurred when complications secondary to the nutrition developed that required its interruption; these included significant abdominal distension, residues of the nutrition in the gastric aspirate with a volume greater than 50% of the volume administered in the previous 4 h due to duodenogastric reflux, severe diarrhoea (more than 5 loose stools/day) and necrotising enterocolitis. Table 1 shows data prospectively registered.

The characteristics of the nutrition were compared between the patients with ARF and the remaining critically ill children. Comparisons were also performed between the patients with ARF requiring renal replacement therapy and those who were treated with conservative treatment.

The statistical analysis was performed using the SPSS version 12 statistical programme, expressing the quantitative variables as means and standard deviations or medians and range when data are not normally distributed, and

Table 1 Data prospectively registered

Epidemiological data
Age
Sex
Weight
Diagnosis
Surgery
Nutritional data
Parenteral nutrition and duration
Indication for TEN
Duration of stay before starting TEN
Maximum volume of enteral nutrition and calories administered
Duration of TEN
Indications for withdrawal and subsequent type of nutrition
Gastrointestinal complications
Renal data
Urea and creatinine
Need for renal replacement therapy and technique used
Treatments and organ failures
Doses of vasoactive drugs during TEN
Doses of sedatives and muscle relaxants administered during the TEN
Mechanical ventilation and its duration
Shock, defined as a mean blood pressure more than 2 SD less than the mean for age and/or administration of dopamine (> 15 μg/kg/min and/or adrenaline > 0.3 μg/kg/min) to maintain normal blood pressure
Altered liver function: defined as an elevation of AST to more than twice the upper limit of normal and/or of bilirubin above 2 mg/dl
Nosocomial pneumonia after starting TEN [35]

the qualitative variables as percentages. Uni- or bivariate analyses were used to study statistical associations. The chi-squared test was used for the analysis of the qualitative variables and Fisher's exact test for the quantitative variables when n was less than 20 or when any theoretical value was less than 5. Student's t-test was used to compare quantitative variables between independent groups with normal distribution. The limit of significance was set at $p < 0.05$.

Results

Of the 4769 patients admitted to the PICU during the study period, 526 (11%) received TEN. Fifty-three (10%) of the patients with TEN presented acute renal failure, and 38 of these patients (71.6%) required continuous venovenous renal replacement therapy (CRRT). The causes of the renal failure are summarised in Table 2. The indication for TEN was mechanical ventilation in 46 patients (86.7%), respira-

Table 2 Patients' diagnoses

Diagnosis	ARF Number and percentage of patients	Rest of patients Number and percentage of patients
Postoperative: cardiac surgery	34 (64.1%)	266 (56.2%)
Renal diseases	6 (11.3%)[a]	0 (0%)
Other medical causes	11 (20.7%)[b]	87 (18.3%)
Postoperative: other surgery	0 (0%)	51 (10.8%)
Acute respiratory failure	2 (3.7%)	69 (14.5%)
Total	53	473

[a] Haemolytic–uraemic syndrome, glomerulonephritis, other nephropathies
[b] Septic shock 6 (11.3%), oncological 5 (9.4%)

Table 3 Comparison between the children with acute renal failure and the remainder of the critically ill patients who received transpyloric enteral nutrition

Parameter	ARF	Other patients	p
Number of patients	53	473	
Age (months), median (range)	18 (0.6–264)	5 (0.1–216)	**0.001**
Weight (kg), median (range)	10 (2.8–70)	5.5 (2.1–70)	**0.001**
Sex (male/female)	30/23 (1.3/1)	262/211 (1.2/1)	0.866
Cardiac surgery	34 (64.1%)	266 (56.2%)	0.391
Shock	26 (49%)	39 (8.2%)	**0.000**
Dopamine	44 (83%)	325 (68.7%)	**0.031**
Mean (SD) µg/kg/min	7.8 (5.9)	5.7 (5.8)	**0.016**
Epinephrine	33 (62.2%)	89 (18.8%)	**0.000**
Mean (SD) µg/kg/min	0.3 (0.3)	0.1 (0.6)	**0.049**
Milrinone	30 (56.6%)	222 (46.9%)	0.282
Mean (SD) µg/kg/min	0.3 (0.3)	0.3 (0.3)	0.162
Hepatic disturbances	4 (7.5%)	4 (0.8%)	**0.001**
Nosocomial pneumonia	9 (16.9%)	42 (8.8%)	0.799
Mortality	16 (30.1%)	34 (7.1%)	**0.000**
Midazolam	48 (90.5%)	400 (84.5%)	0.244
Mean (SD) µg/kg/min	4.6 (3.5)	5 (3.9)	0.449
Fentanyl	48 (90.5%)	370 (78.2%)	0.080
Mean (SD) µg/kg/h	4.4 (3.1)	4.6 (3.7)	0.647
Vecuronium	29 (54.7%)	201 (42.5%)	0.089
Mean (SD) mg/kg/h	0.1 (0.02)	0.1 (0.08)	0.111
Parenteral nutrition	30 (56.6%)	83 (17.5%)	0.086
Mean (SD) days	9.4 (9)	8.2 (7.8)	0.598
Days before TEN	4.5 (5.6)	3.5 (6.2)	0.236
Initiation of TEN within 48 h of admission	28 (52.8%)	297 (62.7%)	0.275
Maximum calorie intake (kcal/kg/day)	77 (26.7)	85 (24.9)	**0.029**
TEN duration (days)	16.5 (27.3)	14 (20.9)	0.245
Gastrointestinal complications	13 (24.5%)	47 (9.9%)	**0.008**
Abdominal distension/excessive gastric residues	9 (17%)	24 (5%)	**0.003**
Diarrhoea	5 (9.4%)	29 (6.1%)	0.372
Necrotising enterocolitis	2 (3.7%)	1 (0.2%)	–
Duodenal perforation	1 (1.9%)	0	–
Suspension of TEN	5 (9.4%)	6 (1.2%)	**0.000**

Table 4 Comparison between the children with ARF requiring continuous renal replacement therapy and the remaining ARF patients

Parameter	ARF with CRRT	ARF without CRRT	*p*
Number of patients	38	15	
Age (months), median (range)	21.5 (0.4–264)	7 (0.3–228)	0.938
Weight (kg), median (range)	10.2 (2.8–70)	5.2 (2.8–66)	0.604
Sex (male/female)	19/19	11/4	0.140
Cardiac surgery	20 (52.6%)	13 (86.6%)	0.059
Shock	23 (60.5%)	3 (20%)	**0.014**
Dopamine	31 (81.5%)	13 (86.6%)	1
Mean (SD) μg/kg/min	7.7 (5.8)	8 (6.2)	0.888
Epinephrine	26 (68.4%)	5 (33.3%)	**0.030**
Mean (SD) μg/kg/min	0.3 (0.4)	0.08 (0.1)	**0.001**
Milrinone	17 (44.7%)	10 (66.6%)	0.363
Mean (SD) μg/kg/min	0.3 (0.3)	0.5 (0.5)	0.112
Hepatic disturbances	4 (10.5%)	0	0.306
Nosocomial pneumonia	4 (10.5%)	1 (6.6%)	1
Mortality	11 (28.9%)	5 (33.3%)	0.751
Days before TEN	4.6 (6.2)	4.4 (4.1)	1
Midazolam	36 (94.7%)	12 (80%)	0.131
Mean (SD) μg/kg/min	5.1 (4.2)	3.2 (3.2)	0.074
Fentanyl	37 (97.3%)	11 (66.6%)	**0.019**
Mean (SD) μg/kg/h	5.1 (3.1)	2.6 (2.5)	**0.009**
Vecuronium	24 (63.1%)	5 (33.3%)	0.069
Mean (SD) mg/kg/h	0.1 (0.02)	0.1 (0.02)	0.887
Parenteral nutrition	10 (26.3%)	7 (46.6%)	0.197
Mean (SD) days	12.4 (10.5)	5.1 (4.2)	0.07
Initiation of the TEN within the first 48 h after admission	20 (52.6%)	8 (53.3%)	1
Maximum caloric intake (kcal/kg/day)	75.1 (27.3)	81.9 (25.5)	0.407
TEN duration (days)	18.3 (31)	11.8 (13.5)	0.442
Abdominal distension/excessive gastric residues	6 (15.8%)	3 (20%)	0.701
Diarrhoea	5 (13.1%)	0	0.305
Necrotising enterocolitis	1 (2.6%)	1 (6.6%)	–
Duodenal perforation	1 (2.6%)	0	–
Suspension of TEN	4 (9.5%)	1 (6.6%)	0.307

tory failure without mechanical ventilation in 2 (3.7%) and intolerance to gastric nutrition in 5 (9.4%).

A comparison of the characteristics of the patients and the nutrition between the children with ARF and the remainder of the critically ill patients who received TEN in this period is presented in Table 3. Twenty-four children (45%) were under 1 year of age. The children with acute renal failure had a significantly higher age and weight than the remainder of the critically ill children who received TEN. The haemodynamic disturbances were more marked in the children with ARF, with a significantly higher incidence of shock, and a significantly higher proportion of patients received dopamine and epinephrine infusions. The dose of dopamine and epinephrine was also significantly higher in children with ARF than in the rest of patients. The children with ARF also presented a higher incidence of other hepatic alterations and a higher mortality (Table 3). The percentage of patients with ARF treated with continuous infusions of sedatives (midazolam and fentanyl) and muscle relaxants (vecuronium) was higher than in the children without ARF, though the differences did not reach statistical significance. With respect to the characteristics of the nutrition, the children with ARF had received parenteral nutrition prior to the TEN more frequently than the other patients, although there were no significant differences in the time between the admission of the patient to the PICU and the time of starting the TEN. The TEN was started within 48 h after admission of the patient to the PICU in 52.8% of the patients with ARF versus 62.7% of the children without ARF (non-significant difference). The maximum calorie intake achieved was lower in the children with ARF than in the other children (Table 3). With regard to the type of nutrition received, 24 children with ARF (45.2%) were administered infant formula, 5 (9.4%) received protein hydrolysate, 18 (3.6%) were given paediatric liquid formulae and 4 (7.5%) were administered specific enteral formulae for renal failure. The incidence of gastrointestinal complications was significantly higher in the children with ARF than in the remainder of the patients. There are no differences in the time of the initiation of the nutrition, the volume of nutrition or the quantity of calories administered between children with gastrointestinal complications and the remaining patients. The enteral nutrition had to be sus-

pended in eight patients with ARF due to gastrointestinal complications. In three of them, the TEN was reinitiated later with good tolerance. The definitive withdrawal of the nutrition was necessary in five children (9.4%) due to digestive tract complications (duodenal perforation caused by the reinsertion of transpyloric tube [23], gastrointestinal bleeding, necrotising enterocolitis secondary to severe shock in two patients and abdominal distension with diarrhoea). The frequency of definitive suspension of enteral nutrition was higher in children with ARF than in the other patients (Table 3). Death was related to the complications of the nutrition (duodenal perforation) in only one patient, and none of the deaths were caused by complications directly related to the renal failure.

A comparison between the patients with renal failure requiring renal replacement therapy (CRRT) and those who did not require this treatment is shown in Table 4. No differences in age or weight were observed between the two groups. The incidence of shock and the need for epinephrine and hepatic disturbances were significantly higher in the children requiring CRRT than in the other children. The incidence of nosocomial pneumonia was also higher, but the differences were not statistically significant. However, the mortality in the two groups was similar. The proportion of patients with ARF treated with continuous infusions of sedatives (midazolam and fentanyl) and muscle relaxants (vecuronium) was higher in the CRRT group than in the group which did not require this therapy, although only with fentanyl were the differences statistically significant. With respect to the characteristics of the nutrition, there were no differences in the time of PICU admission and the time of starting TEN, in the percentage of patients starting the nutrition within the first 48 h after admission, or in the maximum number of calories delivered. The duration of the previous parenteral nutrition in the children with CRRT was higher than in the remainder of the patients with ARF (Table 4). With respect to the complications of the enteral nutrition, the incidence of diarrhoea was higher in the children with CRRT than in the other children, but the difference did not reach statistical significance. Four of the five patients in whom the TEN had to be permanently withdrawn due to digestive tract complications were in the CRRT group (Table 4).

Discussion

Enteral nutrition is the best method of alimentation in critically ill patients, and the majority of critically ill children can receive this nutrition safely and effectively [24, 25]. A number of studies have demonstrated that TEN is particularly indicated in the most severely ill children, who have a lower tolerance to gastric nutrition, principally patients with deep sedation and relaxation [14, 15]. We have not found any previous studies that have prospectively analysed the tolerance to enteral nutrition in children with acute renal failure; and there is only one recent study in adults [19].

Our study shows that critically ill children with renal failure can be fed by TEN. In the majority of children with ARF, the volume of the nutrition was rapidly increased to reach the target calorie intake within the first 48 h. However, initiation of the nutrition in children with ARF was later and the percentage of previous PN was higher than in other critically ill children receiving TEN. This finding is probably related to the more severe clinical situation of children suffering ARF, although a limitation of our study has been that the severity indices and specific risk of mortality were not calculated. Moreover, children with and without ARF have different age and weight and this could influence the results.

It is generally accepted that in most critically ill children, except those with burns and head trauma, the energy expenditure is similar. However, there are no specific studies that analyse the energy expenditure in children with acute renal failure, and the ideal calorie intake is not known. In adult patients with renal failure who are on dialysis, the calorie and protein intake should be similar to that of other critically ill patients [26, 27, 28]. An insufficient calorie intake would lead to a reduction in body reserves, whereas an excessive calorie intake would lead to metabolic overload. Some authors have suggested adapting the calorie delivery to daily measurements of energy expenditure by indirect calorimetry [29, 30], although this method is technically complex and is not available in the majority of paediatric intensive care units. As we were unable to perform indirect calorimetry in our patients, we attempted to administer a normal caloric intake in relation to the age. This calorie intake was usually achieved within 24–48 h and was maintained for a long period of time, and we did not observe any significant increase in the urea, blood glucose or lactic acid levels. However, we are therefore unable to state whether the calorie and protein intake was adequate for the needs of each patient.

The frequency of digestive tract complications in the children with ARF was significantly higher than in the patients without ARF, as also found by Fiaccadori et al. in adults with ARF [19]. However, definitive withdrawal of the TEN due to digestive tract complications was required in only 9.4% of the children. The higher incidence of complications is probably related to the greater severity of the patients (reflected by a higher incidence of shock, the failure of other organs and mortality).

The incidence of abdominal distension, vomiting and gastric residues in our study was 17%, similar to that found in the only study published in adults with ARF (19.7%) [19]. The incidence of excessive residues and/or abdominal distension varies between 5% and 70% in critically ill adults and children receiving enteral nutrition [31, 32, 33], and it is usually caused by the existence of gastrointestinal paresis with a slowing of

intestinal transit. Gastroparesis is also common in patients with uraemia [16]. In our study, abdominal distension and/or gastric residues were not the cause for withdrawal of the TEN in any of our patients with ARF. Probably, the transpyloric administration avoids the problems of gastric emptying and improves tolerance.

A high proportion of our patients with ARF required the administration of large doses of vasoactive drugs. Some of these drugs, such as adrenaline and high doses of dopamine, can theoretically reduce intestinal perfusion and affect the tolerance to nutrition [11]. However, the majority of our patients presented an adequate tolerance to the transpyloric nutrition without gastrointestinal complications despite a large proportion of them receiving high doses of sedatives and muscle relaxants, with the reduced gastrointestinal motility caused by these drugs [11, 34]. Our study shows that TEN can be used in children with acute renal failure even if they require treatment with vasoactive drugs, sedatives and muscle relaxants at high doses.

The incidence of diarrhoea in our study was 9.4%, lower than that found in the study in adults with ARF (16.4%) [19]. The diarrhoea in our patients was generally mild and improved after modification of the diet. It could be assumed that the incidence of diarrhoea would be higher in patients fed by transpyloric nutrition as the processes of gastric digestion are bypassed and the feed is administered directly into the duodenum or jejunum. However, comparative studies have found no differences [12]. A relationship between the shock and the diarrhoea has been described in critically ill children fed with enteral nutrition [34]. In our study, the patients with ARF who required CRRT presented a higher frequency of shock, and this was associated with a higher incidence of diarrhoea. The low incidence of diarrhoea in our study confirms these findings and allows it to be stated that TEN is generally well tolerated.

Necrotising enterocolitis occurred in two patients with ARF and severe shock, namely a neonate with cardiogenic shock following cardiac surgery and *Klebsiella pneumoniae* infection and an infant with septic shock who needed high doses of vasoactive drugs. In both patients shock was the most important factor related to necrotising enterocolitis. Another infant with alveolar interstitial pneumopathy suffered duodenal perforation. The perforation was produced by the mechanical force involved in the reinsertion of the transpyloric tube. We think that ARF was not a risk factor for these complications.

On comparison of the patients requiring CRRT with those treated conservatively, we found that tolerance to the TEN was adequate in both groups, although the low number of patients with CRRT hampered statistical comparisons. This suggests that TEN should be the initial method of choice for critically ill children with ARF, whether or not they require renal replacement therapy.

We conclude that TEN is a safe and effective method of nutrition for the critically ill child with renal failure, although the incidence of digestive tract complications is higher than in other critically ill patients. Further studies are necessary to evaluate the calorie and protein requirements in critically ill children with acute renal failure and the metabolic response to the enteral nutrition.

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