JOP. J Pancreas (Online) 2008; 9(4):440-448.

ORIGINAL ARTICLE

Nasogastric Tube Feeding in Predicted Severe Acute Pancreatitis. A Systematic Review of the Literature to Determine Safety and Tolerance

Maxim S Petrov[1], M Isabel TD Correia[2], John A Windsor[3]

[1]Department of Surgery, Nizhny Novgorod State Medical Academy. Nizhny Novgorod, Russia. [2]Department of Surgery, Federal University of Minas Gerais. Belo Horizonte, Brazil. [3]Department of Surgery, University of Auckland. Auckland, New Zealand

ABSTRACT

Context Nasogastric tube feeding is safe and well tolerated in most critically ill patients. However, its safety and tolerance in the setting of severe acute pancreatitis is debatable.

Objective We aimed to review all available studies on nasogastric feeding in patients with severe acute pancreatitis to determine the safety and tolerance of this approach. A further aim was to perform a meta-analysis of the available randomized controlled trials regarding nasogastric *versus* nasojejunal feeding.

Methods Three electronic databases (Cochrane Central Register of Controlled Trials, EMBASE and MEDLINE) and the abstracts of major gastroenterological meetings were reviewed. Meta-analysis was performed using the random effects model.

Main outcome measures The summary estimates were reported as risk ratio (RR) with 95% confidence interval (95% CI).

Results A total of four studies on nasogastric tube feeding in 92 patients with predicted severe acute pancreatitis were identified. Documented infected pancreatic necrosis developed in 11 patients (16.9%) and multiple organ failure in 10 (15.4%) out of 65 patients with available data. Overall, there were 15 deaths (16.3%). An exacerbation of pain after initiation of feeding occurred in 3 (4.3%) out of 69 patients with available data. Full tolerance was achieved in 73 (79.3%) patients who did not require temporary reduction, stoppage or withdrawal of nasogastric feeding. The results of nasogastric feeding as compared to nasojejunal feeding, were no worse in terms of mortality (RR=0.77; 95% CI: 0.37 to 1.62; P=0.50) or intolerance of feeding (RR=1.09; 95% CI: 0.46 to 2.59; P=0.84).

Conclusion Nasogastric feeding appears safe and well tolerated in patients with predicted severe acute pancreatitis. An adequately powered randomized trial on nasogastric *versus* nasojejunal feeding is required to support this approach as routine clinical management.

INTRODUCTION

Nutritional support plays an important role in the management of patients with severe acute pancreatitis [1, 2, 3]. It has been convincingly demonstrated in numerous studies that enteral nutrition is preferable to parenteral nutrition as it leads to significantly better glycemic control and decreases infectious complications and mortality [4, 5, 6, 7]. With these apparent benefits, the question has been to determine the most optimal site of tube feeding administration. The alternatives include nasojejunal and nasogastric tube

placement. The former requires the assistance of an endoscopist or a radiologist which may result in a delay in commencing enteral nutrition. This delay may have an impact on the clinical outcome as it is now believed that enteral nutrition should commence as soon as possible after hospital admission in order to maximize clinical benefits [8]. In contrast, a nasogastric feeding tube can be inserted immediately and with ease so that pre-pyloric feeding can be started without delay.

A number of randomized controlled trials (RCTs) and the latest meta-analysis [9] have demonstrated the equivalence of nasogastric and nasojejunal tube feeding in terms of safety and tolerance in critically ill patients. While this may be true for this group of patients in general, it is recognized that patients with severe acute pancreatitis are particularly prone to gastric ileus because of the subjacent inflamed pancreas [10]. This has been given as a reason for providing enteral nutrition into the jejunum [1, 11]. Another reason given to avoid the provision of enteral nutrition proximal to the jejunum has been the concern that pancreatic exocrine stimulation will result in an increased severity of the acute pancreatitis [12]. Most studies reveal that the majority of patients receiving enteral nutrition for severe acute pancreatitis have received nasojejunal tube feeding, but there are some studies of successful nasogastric feeding [13, 14, 15].

The only review on nasogastric feeding in acute pancreatitis [16] attempted to define the feasibility of this route of nutrition by meta-analyzing the data from RCTs on nasogastric *versus* 'conventional' nutrition. The pooled estimates and variance of the treatment effect were based on the statistical aggregation of the results from studies with essentially different comparators (i.e., total parenteral and nasojejunal tube feeding). Such an approach might be misleading as nasojejunal, but not parenteral, nutrition is now considered the therapy of choice in severe acute pancreatitis. Moreover, there was a marked heterogeneity in baseline risk among the studies involved in that meta-analysis, particularly in regards to age and gender ratio [15, 17], and incorrect pooled estimates were presented due to inaccurate data input [14, 15]. Furthermore, the previous review [16] did not determine the efficacy of nasogastric tube feeding alone.

The aim of this systematic review was to assess the relative efficacy of nasogastric *versus* nasojejunal feeding in severe acute pancreatitis, and to determine the safety and tolerance of nasogastric tube feeding. This was done by analyzing all of the literature (randomized and non-randomized studies) relating to acute pancreatitis and nasogastric tube feeding.

METHODS

A computerized literature search of the Cochrane Central Register of Controlled Trials, EMBASE and MEDLINE through December 1st, 2007 was conducted. The key words for Cochrane Central Register of Controlled Trials were "acute pancreatitis" and "nutrition". The key words for EMBASE included the terms "acute pancreatitis" and "enteral nutrition" or "enteral feeding". The same key words used for EMBASE were used for MEDLINE. No language restrictions were applied. The bibliographies of all selected articles found which included information on nasogastric tube feeding in acute pancreatitis were reviewed in an attempt to find other relevant articles. The abstracts of major pancreatology meetings (Digestive Disease Week (DDW), United European Gastro-enterology Week (UEGW), International Hepato-Pancreato-Biliary Association (IHPBA), and European Pancreatic Club (EPC)) until 2007 were also manually screened.

The following selection criteria were used to identify published studies for inclusion in this systematic review: study design: cohort study or RCT; population: patients with predicted severe acute pancreatitis; intervention: nasogastric tube feeding; outcome: at least one of the following: tolerance, organ failure, infectious complications, and mortality.

The records extracted by the initial search were scanned to exclude obviously irrelevant studies. Full-text articles were retrieved and reviewed by two authors (MSP, MITDC)

Table 1. Methodological quality score.

		Criteria	Score
Patients	*Selection*	- Random patients	2
		- Consecutive patients	1
		- Selected patients or not reported	0
	Baseline comparability	- Groups comparable on 5-6 items	2
		- Groups comparable on 3-4 items	1
		- Groups comparable on 0-2 items	0
		Items:	
		Age: mean (median) differs <10%	
		Sex: proportion of men differs <10%	
		Aetiology: biliary and/or alcohol differs <10%	
		Severity score on admission: mean (median) differs <10%	
		CRP concentration on admission: mean (median) differs <10%	
		Time between onset of symptoms and commencement of treatment differs <10%	
	Withdrawals	- No	2
		- <10%	1
		- >10% or not reported	0
Intervention	*Concealment of allocation*	- Adequate concealment	2
		- Inadequate concealment	1
		- No concealment or not reported	0
	Method of allocation	- Valid randomization	2
		- Quasi-randomization	1
		- No randomization or not reported	0
	Blinding	- Double-blind	2
		- Single-blind	1
		- Unblinded or not reported	0
	Protocol of intervention	- Reproducibly reported	2
		- Poorly reported	1
		- Not reported	0
	Co-interventions	- Reported and equal between groups	2
		- Reported but not equal between groups	1
		- Not reported	0

independently with the aim of applying inclusion criteria. All differences found between the two reviewers were resolved by discussion among the three authors of this paper.

The methodological quality of the randomized studies included was estimated using a modification of the previously published quality score [18]. It consists of 8 parameters with a quality score range from 0 to 16 points (Table 1).

Chosen *a priori*, a meta-analysis (Review Manager - RevMan (Computer program); Version 5.0. Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2008) was carried out on the data from the RCTs of nasogastric *versus* nasojejunal feeding. The outcome data were combined to determine the risk ratio (RR), with its 95% confidence interval (95% CI). The presence of heterogeneity was assessed using the I^2 measure, with I^2 greater than 25% indicating significant heterogeneity [19]. Irrespective of the degree of heterogeneity of effect among the trials included, a random effects model was used.

RESULTS

A total of 396 publications were identified using the above-mentioned search strategy. Of these, 392 articles did not meet the inclusion criteria and were subsequently excluded. Figure 1 details the selection process. A total of 4 studies were included in

Table 2. Characteristics of the studies included.

Study	Setting	Design	Control group	APACHE II score	Feeding start	Feeding formula	Duration of nutrition (days)	Quality of the study [c]
Eatock *et al.*, 2000 [13]	UK	Cohort study	N/A	10 (4-28) [a]	<48 h of admission	Semi-elemental	Not stated	N/A
Eatock *et al.* 2005 [14]	UK	RCT	Nasojejunal	10 (7-18) [a]	<72 h after onset	Semi-elemental	5	14
Kumar *et al.* 2006 [15]	India	RCT	Nasojejunal	10.5±3.8 [b]	48-72 h of admission	Semi-elemental	7	13
Eckerwall *et al.*, 2006 [17]	Sweden	RCT	Parenteral	10 (8-13) [a]	<24 h of admission	Polymeric	6 (5-9) [a]	14

[a] Values are median (range)
[b] Values are mean ± standard deviation
[c] The range of the quality score is 0 to16 (Table 1)

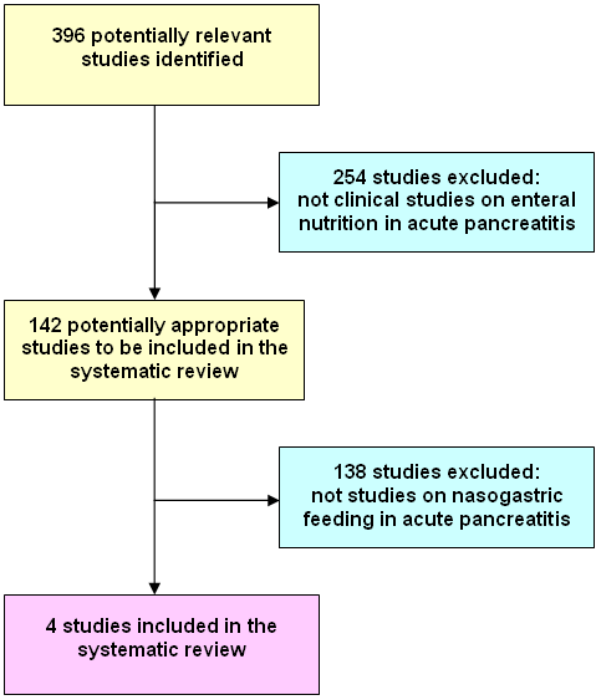

Figure 1. Selection of eligible studies.

this review [13, 14, 15, 17]. One study was a cohort study [13] whereas the other three studies were RCTs [14, 15, 17]. The control groups for the RCTs were nasojejunal feeding in two [14, 15] and parenteral feeding in the third one [17]. Table 2 demonstrates the characteristics of the studies included in this systematic review, including the assessment of study quality. Overall, 93 patients with predicted severe acute pancreatitis were enrolled in these trials. The severity of the patients at admission was comparable in all 4 cohorts, based on APACHE II scoring. Table 3 presents the baseline characteristics of the patients who received nasogastric tube feeding. One patient had a protocol violation; therefore, the results were available in 92 patients (the characteristics of the protocol violator are unknown).

The main clinical outcomes of the studies are summarized in Table 4. Thirty-five of the 92

Table 3. Characteristics of patients receiving nasogastric tube feeding.

Study	No. of patients	Age (years)	Male:female ratio	Etiology		
				Biliary	Alcohol	Other
Eatock *et al.*, 2000 [13]	26	47 (27-96) [a]	12:14	18	5	3
Eatock *et al.*, 2005 [14]	27	63 (47-74) [a]	14:13	16	6	5
Kumar *et al.*, 2006 [15]	16	43.3±12.8 [b]	14:2	8	4	4
Eckerwall *et al.*, 2006 [17] [c]	24	71 (58-80) [a]	10:14	14	3	7
Total [c]	**93**	**-**	**50:43**	**56**	**18**	**19**

[a] Values are median (range)
[b] Values are mean ± standard deviation
[c] Before exclusion of one protocol violator

Table 4. Outcomes of nasogastrically-fed patients in the studies included.

Study	No. of patients	Patients on ventilatory support	Patients with MOF	Infected pancreatic necrosis	Surgery	Mortality	LOS (days)
Eatock *et al*., 2000 [13]	26	11 (42.3%)	6 (23.1%)	5 (19.2%)	10 (38.5%)	4 (15.4%)	17.5 (3-82) [a]
Eatock *et al*., 2005 [14]	27	7 (25.9%)	Not stated	Not stated	Not stated	5 (18.5%)	16 (10-22) [a]
Kumar *et al*., 2006 [15]	16	15 (93.8%)	3 (18.8%)	5 (31.3%)	1 (6.3%)	5 (31.3%)	24.1±14.4 [b]
Eckerwall *et al*., 2006 [17]	23	2 (8.7%)	1 (4.3%)	1 (4.3%)	1 (4.3%)	1 (4.3%)	9 (7-14) [a]
Total	**92**	**35/92 (38.0%)**	**10/65 (15.4%)**	**11/65 (16.9%)**	**12/65 (18.5%)**	**15/92 (16.3%)**	**-**

[a] Values are median (range)
[b] Values are mean ± standard deviation
LOS: length of hospital stay
MOF: multiple organ failure

patients (38.0%) required ventilatory support. There was no evidence of aspiration pneumonia in any of the patients. The other outcomes were available in 3 studies only (65 cases): infected pancreatic necrosis was revealed in 11 patients (16.9%), multiple organ failure developed in 10 patients (15.4%), and 12 patients underwent surgery (18.5%). The mortality rate was 16.3% (15 cases).

Nasogastric feeding-related outcomes, including safety and tolerance, are presented in Table 5. Full tolerance was achieved in 73 of the 92 (79.3%) patients who did not require temporary reduction, stoppage or withdrawal of nasogastric feeding. The 19 patients who had a modification of the nasogastric tube feeding regimen presented signs of gastric ileus (n=6), diarrhea (n=10), or repeatedly removed their feeding tube (n=3). Three patients out of 69 (4.3%) experienced an exacerbation of pain after commencement of nutrition, although it was not a reason for the discontinuation of tube feeding in any of the cases.

The meta-analysis was restricted to the randomized studies of nasogastric *versus* nasojejunal feeding. In two eligible trials [14, 15], a total of 43 patients received enteral nutrition via the nasogastric route and 36 patients via the nasojejunal route. The use of nasogastric feeding resulted in a non-significant reduction in the risk of death (RR=0.77; 95% CI: 0.37 to 1.62; P=0.50) (Figure 2). The number of nutrition-associated adverse events was similar

Table 5. Tolerance of nasogastric tube feeding in the studies included.

Study	No. of patients	Diarrhea	Tube removal	Gastric retention	Exacerbation of pain following feeding	Achievement of nutritional goal	Full tolerance of feeding [a]
Eatock *et al*., 2000 [13]	26	3 (11.5%)	1 (3.8%)	3 (11.5%)	0	Not stated	19 (73.1%)
Eatock *et al*., 2005 [14]	27	3 (11.1%)	1 (3.7%)	0	2 (7.4%)	21 patients (77.8%) after 60 h	23 (85.1%)
Kumar *et al*., 2006 [15]	16	4 (25%)	1 (6.3%)	0	1 (6.3%)	16 patients (100%) by day 7 [b]	11 (68.8%)
Eckerwall *et al*., 2006 [17]	23	0	0	3 (13%)	Not stated	15 patients (65.2%) by day 7	20 (86.9%)
Total	**92**	**10/92 (10.9%)**	**3/92 (3.3%)**	**6/92 (6.5%)**	**3/69 (4.3%)**	**52/66 (78.8%)**	**73/92 (79.3%)**

[a] Did not require temporary reduction, stoppage or withdrawal of feeding
[b] Six patients were supplemented by parenteral nutrition during the commencement of feeding

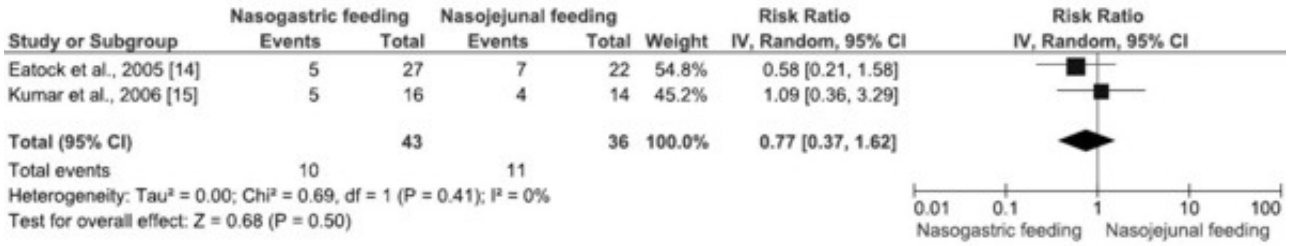

Figure 2. Random effects model of the risk ratio of death associated with nasogastric feeding in comparison with nasojejunal feeding.

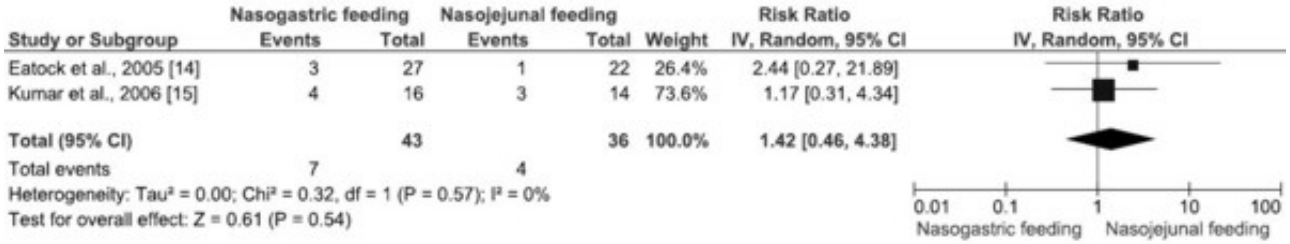

Figure 3. Random effects model of the risk ratio of diarrhea associated with nasogastric feeding in comparison with nasojejunal feeding.

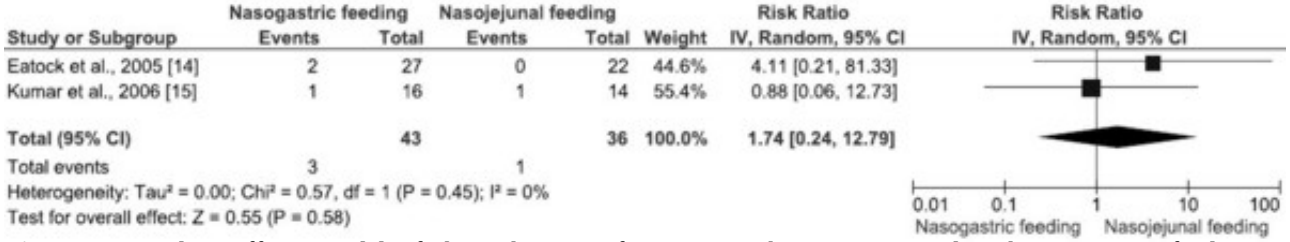

Figure 4. Random effects model of the risk ratio of pain exacerbation associated with nasogastric feeding in comparison with nasojejunal feeding.

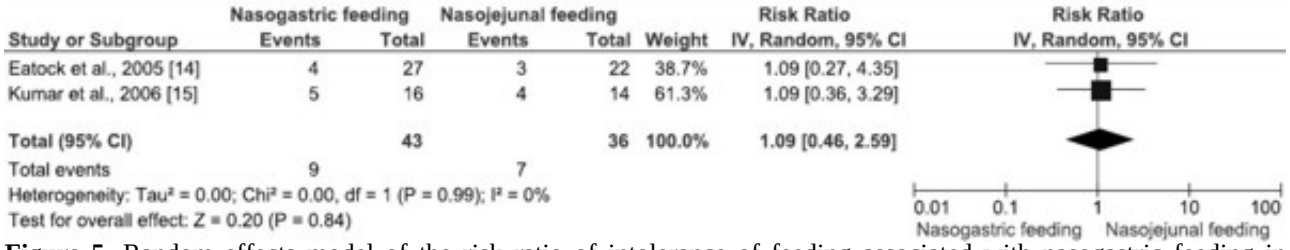

Figure 5. Random effects model of the risk ratio of intolerance of feeding associated with nasogastric feeding in comparison with nasojejunal feeding.

between the two groups. As a consequence, nasogastric feeding was associated with non-significant increases in the risk of diarrhea (RR=1.42; 95% CI: 0.46 to 4.38; P=0.54) (Figure 3) and the exacerbation of pain following feeding (RR=1.74; 95% CI: 0.24 to 12.79; P=0.58) (Figure 4). Overall, patients in both groups did not differ significantly in terms of an intolerance to feeding (RR=1.09; 95% CI: 0.46 to 2.59; P=0.84) (Figure 5). There was no heterogeneity between the study results for all comparisons (I^2=0%).

DISCUSSION

This systematic review of the literature demonstrates the safety and tolerance of nasogastric tube feeding in 4 out of 5 patients with predicted severe acute pancreatitis. The clinical outcomes were within the expected range. Nasogastric tube feeding-related problems occurred in about 20% of patients, but they were relatively minor. The meta-analysis also demonstrated that there was no difference between nasogastric and nasojejunal tube feeding with respect to safety and tolerance in the two available RCTs. However, there were limitations in both the RCTs. Some data on certain essential clinical outcomes were not presented in the RCT from the United Kingdom [14]. In addition, it was noted that it is likely that jejunal tube feeding in this trial was probably duodenal (because

true jejunal placement would have been difficult with the types of feeding tubes and placement techniques used) meaning that both feeding arms may have been equally pro-inflammatory [20]. The defect of the RCT from India [15] was that there was a considerable delay (7.8±6.5 and 5.7±4.7 days after symptom onset in the nasogastric and nasojejunal groups, respectively) in commencing enteral nutrition. Apart from these concerns, both trials were insufficiently powered to detect any difference or to prove equivalence between the groups studied in terms of any clinical outcome. For example, an adequately powered RCT would need to enrol 153 patients per arm in order to show a decrease in mortality from 16% (average rate in the nasogastric group in the present review) to 6% (best results in the nasojejunal group of RCTs on enteral *versus* parenteral nutrition [21, 22]) with 80% power and alpha value equal to 0.05 (two-sided).

One of the most important issues in considering tube feeding in acute pancreatitis is the effect of nutrition on pancreatic exocrine function. It was shown by O'Keefe *et al*. [23] that all forms of enteral nutrition stimulate pancreatic secretion. In particular, when compared to placebo-saline, an oral liquid polymeric diet resulted in a significantly higher level of amylase ($P<0.01$) and lipase ($P<0.01$); a duodenal polymeric enteral formula led to an increased level of amylase ($P<0.01$), lipase ($P<0.01$) and trypsin ($P<0.01$); a duodenal elemental feeding formula resulted in an elevated level of lipase ($P<0.05$). The same research group also compared pancreatic secretory response to tube feeding delivered into the duodenum, mid jejunum (40-60 cm distal to the ligament of Treitz), and distal jejunum (100-120 cm distal to the ligament of Treitz) [24]. Even though the authors did not find a direct relationship between the decrease in enzyme secretion and the distance to the mid-distal jejunum, they demonstrated a significantly lower secretion of trypsin ($P<0.01$) and lipase ($P<0.05$) in response to the elemental formula delivered into the jejunum (40 cm or more distal to the ligament of Treitz) in comparison with the duodenum. Moreover, the trypsin and lipase secretory response in the mid-distal jejunum group was as low as in the control group (fasting).

It should be noted, however, that these studies [23, 24] on the effects of enteral feeding on pancreatic exocrine function were in healthy subjects. There is now convincing evidence [25] that patients with acute pancreatitis have significantly lower rates of pancreatic enzyme secretion into the duodenum as compared to healthy subjects. Furthermore, when patients with mild/moderate acute pancreatitis were compared to those with severe acute pancreatitis, a lower secretion of trypsin (6-fold), amylase (22-fold) and lipase (42-fold) was found in the latter group, suggesting that duodenal secretion of pancreatic enzymes is inversely related to the severity of acute pancreatitis [25]. In line with this finding, another study [26] showed 86% rate of pancreatic exocrine insufficiency (measured by fecal pancreatic elastase-1) in patients recovering from severe attacks of acute pancreatitis. Moreover, the severity of pancreatic exocrine insufficiency correlated with the extent of pancreatic necrosis. These data suggest that injured acinar cells are not able to fully respond to the physiological stimuli of secretion into the duodenum and this may be of some help in explaining the findings of this review, namely, that nasogastric tube feeding does not appear to aggravate the severity of acute pancreatitis.

In conclusion, the present review has appraised the current evidence regarding nasogastric tube feeding to patients with predicted severe acute pancreatitis. The evidence base is small but does show that enteral nutrition administered by means of the nasogastric route is safe and well tolerated in 79% of patients with predicted severe acute pancreatitis. The statistically aggregated data from two randomized trials on the direct comparison of nasogastric and nasojejunal nutrition are encouraging as they demonstrate no difference in safety and tolerance between these routes. An adequately powered randomized trial on nasogastric *versus* nasojejunal feeding is required to support this

approach before early nasogastric tube feeding can be established as the standard of care.

Received January 28th, 2008 - Accepted April 15th, 2008

Keywords Enteral Nutrition; Pancreatitis, Acute Necrotizing /complications

Abbreviations RCT: randomized controlled trials

Conflict of interest The authors have no potential conflicts of interest

Correspondence
Maxim S Petrov
PO Box 568
Nizhny Novgorod
603000 Russia
Phone: +7-910.383.3963
Fax: +1-801.788.7383
E-mail: max.petrov@gmail.com

Document URL: http://www.joplink.net/prev/200807/04.html

References

1. Forsmark CE, Baillie J; AGA Institute Clinical Practice and Economics Committee; AGA Institute Governing Board. AGA Institute technical review on acute pancreatitis. Gastroenterology 2007; 132:2022-44. [PMID 17484894]

2. Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006; 101:2379-400. [PMID 17032204]

3. Pezzilli R, Fantini L, Morselli-Labate AM. New approaches for the treatment of acute pancreatitis. JOP. J Pancreas (Online) 2006; 7:79-91. [PMID 16407625]

4. Marik PE, Zaloga GP. Meta-analysis of parenteral nutrition versus enteral nutrition in patients with acute pancreatitis. BMJ 2004; 328:1407-13. [PMID 15175229]

5. Petrov MS, Zagainov VE. Influence of enteral versus parenteral nutrition on blood glucose control in acute pancreatitis: a systematic review. Clin Nutr 2007; 26:514-23. [PMID 17559987]

6. McClave SA, Chang WK, Dhaliwal R, Heyland DK. Nutrition support in acute pancreatitis: a systematic review of the literature. JPEN J Parenter Enteral Nutr 2006; 30:143-56. [PMID 16517959]

7. Petrov MS, van Santvoort HC, Besselink MG, van der Heijden GJ, Windsor JA, Gooszen HG. Enteral nutrition reduced the risk of mortality and infectious complications in patients with severe acute pancreatitis: a meta-analysis comparing enteral and parenteral nutrition. Arch Surg 2008 (In press).

8. Dervenis C. Enteral nutrition in severe acute pancreatitis: future development. JOP. J Pancreas (Online) 2004; 5:60-3. [PMID 15007186]

9. Marik PE, Zaloga GP. Gastric versus post-pyloric feeding: a systematic review. Crit Care 2003; 7:46-51. [PMID 12793890]

10. Maykel JA, Bistrian BR. Is enteral feeding for everyone? Crit Care Med 2002; 30:714-6. [PMID 11990947]

11. Pandol SJ, Saluja AK, Imrie CW, Banks PA. Acute pancreatitis: bench to the bedside. Gastroenterology 2007; 132:1127-31 [PMID 17383433]

12. Grant JP, James S, Grabowski V, Trexler KM. Total parenteral nutrition in pancreatic disease. Ann Surg 1984; 200:627-31. [PMID 6435552]

13. Eatock FC, Brombacher GD, Steven A, Imrie CW, McKay CJ, Carter R. Nasogastric feeding in severe acute pancreatitis may be practical and safe. Int J Pancreatol 2000; 28:23-9. [PMID 11185707]

14. Eatock FC, Chong P, Menezes N, Murray L, McKay CJ, Carter CR, Imrie CW. A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis. Am J Gastroenterol 2005; 100:432-9. [PMID 15667504]

15. Kumar A, Singh N, Prakash S, Saraya A, Joshi YK. Early enteral nutrition in severe acute pancreatitis: a prospective randomized controlled trial comparing nasojejunal and nasogastric routes. J Clin Gastroenterol 2006; 40:431-4. [PMID 16721226]

16. Jiang K, Chen XZ, Xia Q, Tang WF, Wang L. Early nasogastric enteral nutrition for severe acute pancreatitis: a systematic review. World J Gastroenterol 2007; 13:5253-60. [PMID 17876897]

17. Eckerwall GE, Axelsson JB, Andersson RG. Early nasogastric feeding in predicted severe acute pancreatitis: A clinical, randomized study. Ann Surg 2006; 244:959-65. [PMID 17122621]

18. de Vries AC, Besselink MG, Buskens E, Ridwan BU, Schipper M, van Erpecum KJ, Gooszen HG. Randomized controlled trials of antibiotic prophylaxis in severe acute pancreatitis: relationship between methodological quality and outcome. Pancreatology 2007; 7:531-8. 17901714]

19. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003; 327:557-60. [PMID 12958120]

20. O'Keefe SJ, McClave SA. Feeding the injured pancreas. Gastroenterology 2005; 129:1129-30. [PMID 16143153]

21. Oláh A, Pardavi G, Belágyi T, Nagy A, Issekutz A, Mohamed GE. Early nasojejunal feeding in acute pancreatitis is associated with a lower complication rate. Nutrition 2002; 18:259-62. [PMID 11882400]

22. Petrov MS, Kukosh MV, Emelyanov NV. A randomized controlled trial of enteral versus parenteral feeding in patients with predicted severe acute pancreatitis shows a significant reduction in mortality and in infected pancreatic complications with total enteral nutrition. Dig Surg 2006; 23:336-44. [PMID 17164546]

23. O'Keefe SJ, Lee RB, Anderson FP, Gennings C, Abou-Assi S, Clore J, et al. Physiological effects of enteral and parenteral feeding on pancreaticobiliary secretion in humans. Am J Physiol Gastrointest Liver Physiol 2003; 284:G27-36. [PMID 12488233]

24. Kaushik N, Pietraszewski M, Holst JJ, O'Keefe SJ. Enteral feeding without pancreatic stimulation. Pancreas 2005; 31:353-9. [PMID 16258370]

25. O'Keefe SJ, Lee RB, Li J, Stevens S, Abou-Assi S, Zhou W. Trypsin secretion and turnover in patients with acute pancreatitis. Am J Physiol Gastrointest Liver Physiol 2005; 289:G181-7. [PMID 15705659]

26. Boreham B, Ammori BJ. A prospective evaluation of pancreatic exocrine function in patients with acute pancreatitis: correlation with extent of necrosis and pancreatic endocrine insufficiency. Pancreatology 2003; 3:303-8. [PMID 12890992]