Research Article

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Intolerance to Early Nasogastric and Nasojejunal Enteral Nutrition in Patients with Moderately Severe Acute Pancreatitis

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RELEVANCE Early enteral nutrition is an essential element of intensive care for acute pancreatitis. Its intolerance is manifested by high gastric residual volumes, pain syndrome, bloating, diarrhea, nausea and vomiting. The relevance of our study is determined by the lack of information on how the routes of nutrient delivery affect its tolerability considering the gradual «as-per-protocol» increase in nutrition volumes for patients with moderately severe acute pancreatitis.

THE AIM OF THE STUDY Was to identify the key factors that determine intolerance to early nasogastric and nasojejunal enteral feeding in ICU patients with the early phase of moderately severe acute pancreatitis.

MATERIAL AND METHODS We conducted an open randomized controlled trial. Out of 64 patients with predicted severe course of acute pancreatitis, we identified a cohort with moderately severe acute pancreatitis, in which 17 (51.5%) patients received early enteral nutrition through a nasogastric tube, and 16 (48.5%) via an endoscopically placed nasojejunal tube. The criteria for nutrition intolerance were as follows: nasogastric tube discharge of more than 500±100 ml at a time or more than 500 ml/day in comparison with the enterally administered during this period, increased pain, bloating, diarrhea, nausea and vomiting. Using the method of logistic regression, indicators with prognostic significance were determined. The null hypothesis was rejected at $p<0.05$.

RESULTS

Regardless of the nutrition route, the progression of multiple organ failure increases the incidence of high gastric residual volumes (SOFA — OR (odds ratio) — 1.337, 95% CI (confidence interval) 1.001–1.787; p = 0.049). Pain syndrome is less common on the day of surgery (OR 0.258, 95% CI 0.110–0.606; p=0.002). Nasojejunal feeding was associated with a lower incidence of nausea and vomiting (OR 0.168, 95% CI 0.06–0.473; p=0.001), but with more diarrhea (OR 6.411, 95% CI 1.274–32.262; p=0.024).

CONCLUSION The progression of multiple organ failure increases the incidence of high gastric residual volumes. The pain syndrome is less pronounced on the day of surgery and more intense in case of nasogastric nutrition. Postpyloric nutrition reduces the incidence of nausea and vomiting, but increases diarrhea.

Key words: acute pancreatitis, enteral nutrition, intolerance, residual, volume, stomach, nausea, vomiting, bloating, nasogastric, nasojejunal, small intestine

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CI – confidence interval
GIT– gastrointestinal tract
MV – mechanical ventilation
NG – nasogastric
NJ – nasojejunal
ENI – enteral nutrition intolerance
GRV – gastric residual volume
AP – acute pancreatitis
ICU – intensive care unit
OR – odds ratio
MOD – multiple organ dysfunction
EEN – early enteral nutrition
MSAP — moderately severe acute pancreatitis
SAP – severe acute pancreatitis
EN – enteral nutrition
C-RP – C-reactive protein
SIRS – Systemic Inflammatory Response Syndrome

RELEVANCE

Acute pancreatitis (AP) is a disease that in 80-90% of cases occurs in a mild form. In other cases, moderately severe acute pancreatitis (MSAP) or severe acute pancreatitis (SAP) develops, both are characterized by systemic inflammatory response syndrome (SIRS), multiple organ dysfunction (MOD), and, as a rule, the development of pancreatic necrosis and increased mortality [1, 2].

The main criterion separating MSAP from SAP is the duration of MOD. There is evidence that MOD for more than 48 hours in SAP increases mortality to 55%, but if it does not exceed 48 hours, as in patients with MSAP, then mortality decreases to 3% [3, 4]. Early enteral nutrition (EEN) is a mandatory element of AP intensive care, as it improves clinical outcome [5, 6].

For EEN, a nasogastric (NG) or nasojejunal (NJ) tube is used. A number of small prospective randomized trials have shown that NG nutrition is not inferior to postpyloric nutrition in terms of the incidence of infectious complications, changes in the concentration of inflammatory markers, and the use of analgesics [7, 8]. To date, there have been no convincing data proving the superiority, disadvantage, or equivalence of NG and NJ enteral feeding regimens in SAP [9].

Enteral nutrition intolerance (ENI) is a condition characterized by an inability to maintain adequate nutrition or fluid and electrolyte balance due to an anatomical problem (bowel resection) or a physiological disorder of the gastrointestinal tract (GIT) [14].

ENI in AP is common and manifests itself as high gastric residual volumes (GRV), pain, bloating, diarrhea, nausea and vomiting [10], which may be the reason for a longer period to achieve nutritional support goals. In a recent study, factors influencing the development of ENI in patients with MSAP were identified: hypertriglyceridemia, SIRS, grade III acute gastrointestinal injury syndrome, pancreatic infection, as well as the time from admission to the hospital to the start of enteral nutrition (EN) [11].

In addition, it is known that an increase in the level of lipase by more than 2.5 times is a predictor of intolerance to oral nutrition [12]. The lack of information on the effect of EN delivery methods, the severity of MOD and surgical trauma on the development of ENI in patients in the early phase of MSAP determines the relevance of our study.

The aim of the study was to identify the key factors that determine intolerance to NG and NJ EEN in intensive care unit (ICU) patients in the early phase of MSAP.

MATERIAL AND METHODS

Our open randomized controlled cohort trial was performed in the ICU of JSC Neftyanik Hospital, Tyumen, from November 2012 to October 2018. Eligibility criteria were as follows: the diagnosis of AP, the early phase of the disease, and the presence of at least one predictor of the severe course.

Exclusion criteria: age over 80 years, chronic diseases in the terminal stage, pancreatogenic shock – a lactate level above 4 mmol/L, the need to use adrenomimetics to maintain mean arterial pressure more than 70 mm Hg. The diagnosis of AP was established on the basis of a characteristic clinical picture, confirmed by laboratory and instrumental research methods [1].

C-reactive protein (C-RP) over 150 mg/l, Acute Physiology and Chronic Health Evaluation (APACHE) II score over 8, and the Sequential Organ Failure Assessment (SOFA) score over 2 were used as predictors associated with the development of SAP [13]. The patient assignment to 2 groups was done using the randomization envelope method in the ratio of 1:1. Subsequently, a cohort of patients with MSAP was identified from the 64 patients included in the study. Of these, 17 patients received NG EEN in the first 12–24 hours from the moment of admission, and 16 patients received NJ EEN with a 7 CH tube installed using fibrogastroduodenoscopy to a depth of 30–50 cm distal to the ligament of Treitz. The follow-up period was 5 days.

The EN formula was standard isocaloric fiber enriched (Nutricomp Standard Fiber, BBrown, Germany). In the second group the nasojejunal route was supplemented with the nasogastric one. The nutrient mixture was administered into the tube as a continuous drip using a perfusor. In the NG nutrition group, every 6 hours its administration was stopped for 1–2 hours, the tube remained open to monitor gastric residual volume (GRV), and in the NJ nutrition group, the inserted into the stomach tube was always open. The initial rate of feeding was 15 ml/h, and then every subsequent day it was increased by 15 ml/h. The required volume of enteral nutrition for the first day was 250 ml/day, and every subsequent day it was increased by 250 ml/day depending on tolerance. The criteria for EEN intolerance were defined as NG tube discharge >500 ml at one time or more than 500 ml/day, increased pain, bloating, diarrhea (loose stools more than 3 times per day), nausea and vomiting. When these symptoms occurred, the rate of mixture administration was reduced by 50% or completely stopped.

Later, after symptoms of feeding intolerance subsided, the rate was gradually increased to the previous values according to the above protocol. During the observation period, all those operated on underwent a surgery - abdominal drainage via laparoscopic access under total intravenous anesthesia with myoplegia and mechanical ventilation (MV). Statistical analysis was performed using the SPSS-22 software package. After checking for distribution normality using the Shapiro–Wilk's test, the results were presented as means with standard deviation $M \pm \sigma$ or medians with quartiles Me, (Q25; Q75). Parametric and nonparametric criteria were used for group comparison. The null hypothesis was rejected at $P<0.05$.

RESULTS

Clinical and laboratory characteristics of the groups are given in Table 1.

Table 1

Clinical and laboratory characteristics of patients with moderately severe acute pancreatitis

Parameter	Total patient number (n=33)	Nasogastric administration (n=17)	Nasojejunal administration (n=16)	p
Sex, male/female	18/15	9/8	9/7	-
Age, years	42.16±12.9	41.93±9.78	44.86±15.03	0.535e
Shapiro–Wilk's test, p	0.09	0.5	0,152	-
CRP24, mg/l	78 (23.4; 125)	87.57±63.04	79.0±65.65	0.917f
Shapiro–Wilk's test, p	0.016	0.241	0.084	
CRP48, mg/l	181 (141.4; 203.5)	195 (130;207)	181 (152; 188.5)	1,0f
Shapiro–Wilk's test, p	0.001	0.002	0.033	-
Operations, %	63.63	70.58	56.25	0.894g
APACHE-II, points (the first day)	4 (3; 7)	4 (3; 5)	4 (3; 7.5)	0.753f
Shapiro–Wilk's test, p	0.001	0.008	0.022	-
SOFA, points (the first day)	2 (1; 2)	2 (1; 2)	1.5 (1; 2)	0.991f
Shapiro–Wilk's test, p	0.001	0.024	0.027	-
MVh for more than 12, but less than 24 hours, patients	4	3	1	-

Notes: MV — mechanical ventilation; C-RP — C-reactive protein; a — MSAP — moderately severe acute pancreatitis; 24 — the first day of admission; 48 — second day; c — Acute Physiology And Chronic Health Evaluation; d — Sepsis-related Organ Failure; e — ANOVA; f — the Kruskal–Wallis test; g — Pearson's chi-square test; h - mechanical ventilation, not associated with anesthesia, lasting more than 12 hours, but less than 24 hours

The formed groups with NG EEN and NJ EEN were comparable in age, C-RP concentration in the first two days, the severity of the condition on the day of admission (see Table 1), and in the next 5 days (Table 2). The number of operated patients did not differ statistically significantly between the groups (see Table 2). Abdominal drainage via laparoscopic access under total intravenous anesthesia with myoplegia and mechanical ventilation was more often performed on the 2nd and 3rd days after hospitalization in the ICU (Table 3).

Table 2

Percentage of patients with symptoms of enteral nutrition intolerance and severity of the condition during the entire observation period

Group	Surgeries	a	Pain	Nausea, vomiting	Bloating	Diarrhea	Shapiro–Wilk's test, p	APACHE IIb	Shapiro–Wilk's test, p	SOFAc
e nutrition, %	70.58	64.7	76.47	58.82	60	17.64	0.001	4 (2; 6)	0.001	1 (0; 2)
f nutrition, %	56.25	25	31.25	37.5	37.5	43.75	0.001	4 (2; 6)	0.001	0 (0; 1.5)
p=	0.646g	0.048g	0.003g	0.213g	0.335g	0.269g	–	1.0h	–	0.267h
NG and NJ nutrition, %	63.63	42.42	54.54	48.48	42.42	30.30	0.001	4 (2; 6)	0.001	1 (0; 2)

Notes: a — gastric residual volume; b — Acute Physiology And Chronic Health Evaluation (for 5 days); c — SOFA — Sequential Organ Failure Assessment (for 5 days); d — moderately severe acute pancreatitis; e — nasogastric; f — nasojejunal; g — Pearson's chi-square test; h — Mann-Whitney U test

Table 3

The severity of the condition, multiple organ dysfunction, the fact of the operation and the clinical manifestations of food intolerance in the first 5 days of treatment in the intensive care unit

Parameter	Group	1-st day	2-nd day	3-d day	4-th day	5-th day	p
APACHE IIa, points	d nutrition	4 (3; 5)	4.81±3.25	4.88±3.55	4.11±3.01	4 (0; 6)	0.634f
	Shapiro–Wilk's test, p	0.008	0.433	0.364	0.153	0.022	–
	e nutrition	4 (3; 7.5)	7.25±3.83	5.37±2.52	4.25±2.46	4.52 (2; 5)	0.968f
	Shapiro–Wilk's test, p	0.022	0.141	0.931	0.411	0.024	–
	p=	0.495g	0.065h	0.651h	0,891h	0.631g	–
	NG and NJ nutrition	4(3;8)	6.03±3.69	5.12±3.05	4 (2; 6)	4 (2; 5)	0.193f
	Shapiro–Wilk's test, p	0.001	0.097	0.261	0.043	0.007	–
SOFAb, points	NG nutrition	2 (1; 2)	2 (0; 2)	2 (0; 4)	1 (0; 1)	0 (0; 1)	0.041f
	Shapiro–Wilk's test, p	0.024	0.013	0.02	0.001	0.001	
	NJ nutrition	1.5 (1; 2)	1 (0; 2)	0 (0; 1)	0 (0; 0,5)	0 (0; 0)	0.317f
	Shapiro–Wilk's test, p	0.027	0.003	0.001	0.001	0.001	
	p=	0.90g	0.382g	0.034g	0.157g	0.217g	
	NG and NJ nutrition	2 (1; 2)	1 (0; 2)	0.5 (0; 2)	2 (0; 1)	0 (0; 1)	0.027f
	Shapiro–Wilk's test, p	0.001	0.001	0.001	0.001	0.001	
Surgeries, %	NG nutrition	0	23.52941	29.41176	17.64706	0	0,020i
	NJ nutrition	0	25	12.5	12.5	6.25	0.290i
	p=	–	0.765j	0.312j	0.790j	0.455i	
	NG and NJ nutrition	0	23.5	20.5	14.7	2.9i	0.002i
GRV, %	NG nutrition	5.88	35.29	35.29	5.88	5.88	0.016i
	NJ nutrition	6.25	18.75	18.75	6.25	0	0.334
	p=	1.0i	0.394j	0.392j	1.0i	1.0i	
	NG and NJ nutrition	5.88	26.47	26.47	2.94	2.94	0.003i
Pain syndrome, %	NG nutrition	35.29	17.64	41.17	11.76	23.52	0.260i
	NJ nutrition	25	0	25	0	6,25	0,025i
	p=	0.24	0.233i	0.458	0.486i	0.346i	
	NG and NJ nutrition	30.3	9.09	33.33	6.06	15.15	0.568i
Nausea, vomiting, %	NG nutrition	23.52	23.52	35.29	23.529	11.76	0.624
	NJ nutrition	12.5	12.5	18.75	0	6.25	0.622i
	p=	0.1j	0.510j	0.101j	0.108i	1.0i	
	NG and NJ nutrition	18.18	18.18	27.27	12.12	9.09	0.990i
Bloating, %	NG nutrition	29.41	11.76	11.76	5.88	5.88	0.228i
	NJ nutrition	12.5	18.75	18.75	0	12.5	0.489i
	p=	0.312j	0.478	0.790	1.0i	1.0i	
	NG and NJ nutrition	21.21	15.15j	15.15j	3.03	9.09	0.762
Diarrhea, %	NG nutrition	5.88	0	0	5.88	5.88	1.0
	NJ nutrition	18.75	0	6.25	12.5	18.75	0.445i
	p=	0.308i	–	0.455i	0.578i	0.308i	
	NG and NJ nutrition	12.12	0	3.03	9.09	12.12	0.794i

Notes: GRV — gastric residual volume; a — Acute Physiology And Chronic Health Evaluation; b — Sequential Organ Failure Assessment; c — gastric residual volume; d — nasogastric; e — nasojejunal; f — the Kruskal-Wallis test; g — Mann-Whitney U test; h — Student's t-test; i — Fisher's exact test; j — Pearson's chi-square test

Table 2 shows the percentage of patients who experienced one of the symptoms of ENI. It was found that pain syndrome and high GRVs were statistically more often recorded in patients with NG nutrition. No statistically significant differences were found for other ENI criteria. Table 3 shows the dynamics of the recorded parameters during the first 5 days of observation in the ICU.

The APACHE II score for all 5 days had no statistically significant differences between the groups with NG and NJ nutrition (see Table 3). The SOFA score on the 3rd day was statistically significantly higher in the NG group. We found that a high GRV was statistically significantly more common on the 2nd and 3rd days in patients who received NG nutrition. In the group of patients with postpyloric nutrition, pain syndrome was statistically significantly more common on the 1st and 3rd days. Bloating and diarrhea had no statistically significant fluctuations over the entire observation period.

Using the method of logistic regression, variables were identified that independently affect the risk of developing ENI (Table 4). From the presented results, it can be seen that the value of the SOFA score affects the incidence of high GRV. Pain syndrome is less common on the day of surgery (drainage of the abdominal cavity via laparoscopic access) and in the postpyloric variant of EN. In addition, NJ nutrition is less likely to cause nausea and vomiting, but more often diarrhea.

Table 4

Prognostic significance of risk factors for the development of nutrition intolerance (logistic regression) in patients with moderately severe acute pancreatitis

Dependent variables		Independent variables			
		APACHE IIa	SOFAb	Surgery	c nutrition
GRV	OR	1.145	1.337	0.355	0.432
	95% CI	0.996–1.317	1.001–1.787	0.076–1.667	0.167–1.119
	p	0.057	0.049	0.189	0.084
Pain	OR	0.99	1.237	0.103	0.258
	95% CI	0.878–1.117	0.939–1.630	0.012–0.882	0.110–0.606
	p	0.876	0.130	0.038	0.002
Nausea, vomiting	OR	0.993	1.251	0.513	0.168
	95% CI	0.874–1.128	0.944–1.659	0.126–2.09	0.06–0.473
	p	0.912	0.119	0.351	0.001
Bloating	OR	1.032	1.211	0.414	0.777
	95% CI	0.899–1.185	0.898–1.633	0.083–2.069	0.314–1.919
	p	0.653	0.209	0.283	0.584
Diarrhea	OR	0.857	1.22	2.063	6.411
	95% CI	0.694–1.058	0.747–1.992	0.371–11.476	1.274–32.262
	p	0.15	0.427	0.408	0.024

Notes: ДИ — confidence interval; ООЖ — gastric residual volume; ОШ — odds ratio; a — Acute Physiology and Chronic Health Evaluation; b —Sequential Organ Failure Assessment; c — nasogastric/nasojejunal; d — gastric residual volume

DISCUSSION

The development of AP may be accompanied by impairment in intestinal motor, secretory, digestive, barrier functions which are combined into the concept of "acute gastrointestinal injury". These changes can cause ENI syndrome. In our study, it was shown that the severity of the condition (APACHE II score) does not affect the incidence of ENI directly. Similar results were obtained in a recent study by U. Gungabissoon et al. [16].

However, the severity of MOD, assessed using the SOFA scale, independently affects the incidence of high GRV [17]. The regularity obtained in our study - a decrease in pain on the day of surgery (drainage of the abdominal cavity via laparoscopic access) is most likely associated with low-traumatic access, post-anesthesia analgesia and the planned prescription of analgesics. Diarrhea is one of the common clinical symptoms of EEN intolerance [18]. In our study, it was detected in 30.3% of patients. The results obtained are consistent with

existing studies in which the incidence of diarrhea in critically ill patients is in the range of 14.7–38.9% [19, 20]. In our study, diarrhea occurred in 17.64% of NG route patients, and in 43.75% of NJ route patients, which does not contradict the findings in already published works, where in critically ill patients receiving postpyloric nutrition, diarrhea was more common than in case of NG nutrition [21]. In our study, the initial rate of feeding was 15 ml/h, and then every subsequent day it was increased by 15 ml/h. The required volume of enteral nutrition for the first day was 250 ml/day, and every subsequent day it was increased by 250 ml/day depending on tolerance. NJ tube feeding was found to be less likely to cause nausea and vomiting, but more likely to cause diarrhea, compared to NG enteral feeding.

It is known that optimal nutritional support during the first week of ICU stay is associated with better treatment outcomes [22, 23]. However, a recently published meta-analysis noted that there is ongoing debate about the exact timing, dose, and composition of nutritional support formulas [24]. The optimal nutrition strategy for critically ill patients has not yet been found [25, 26], which determines the search for methods capable of verifying from what moment enteral nutrition can be started and how much of it can be absorbed [27, 28]. Considering that at the moment for patients with AP there are no clear recommendations on the time of nutrition initiation, its optimal composition and target for energy and protein, we recommend starting EEN via NG route due to ease of execution, despite the fact that in this case ENI develops more often.

Our recommendations are consistent with the study that noted that in less severe patients there is no difference between NG and NJ EEN, as there was no statistically significant difference between the groups in daily energy intake, protein intake, complications, length of ICU stay, and nitrogen balance [29].

CONCLUSIONS

1. The route of nutrient delivery, abdominal drainage via laparoscopic access, and multiple organ dysfunction in the early period of moderately severe acute pancreatitis are the factors that independently affect the development of enteral nutrition intolerance.
2. Progression of multiple organ dysfunction increases the incidence of high gastric residual volumes.
3. Abdominal drainage via laparoscopic access reduces the severity of pain, but nutrition via a nasogastric tube, on the contrary, can increase pain.
4. In case of nasojejunal administration of nutrients, nausea and vomiting are less common, but diarrhea is more common.
5. In patients with moderately severe acute pancreatitis, the nasogastric route of nutrient administration is more preferable due to the ease of its initiation.
6. If symptoms of nasogastric feeding intolerance persist, it is necessary to switch to postpyloric administration of nutrients via nasojejunal tube installed using fibrogastroduodenoscopy to a depth of 30–50 cm distal to the ligament of Treitz.

Nasogastric administration of the nutrient mixture is effective only if the evacuation function of the stomach is preserved. The administration of a nutrient mixture into the small intestine should be regulated, first of all, taking into account the overall absorptive capacity of the jejunum.

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