UDC 616.37-002-036.11-083.2 : 615.477.85
DOI: 10.24884/0042-4625-2021-180-6-56-61

PECULIARITIES OF NASOGASTRIC AND NASOJEJUNAL FEEDING DURING THE EARLY PERIOD OF ACUTE SEVERE PANCREATITIS

Oleg G. Sivkov[1]*, Aleksei O. Sivkov[2], Ivan B. Popov[2], Evgenii I. Zaitsev[2]

[1] Tyumen Cardiology Research Center, Tyumen, Russia
[2] Medical and Sanitary Unit "Neftyanik", Tyumen, Russia

Received 16.05.2021; accepted 09.03.2022

The OBJECTIVE of the study was to identify factors independently influencing intolerance to early enteral feeding via a nasogastric and nasojejunal tube in patients during the early phase of severe acute pancreatitis.

METHODS AND MATERIALS. An open, randomized, controlled, cohort study was carried out. Out of 64 patients with predictors of severe acute pancreatitis, a cohort with severe form was isolated, in which 16 patients received nasogastric and 15 patients – nasojejunal feeding. The enteral feeding intolerance criteria were: discharge via the nasogastric tube >500ml at a time or >500ml/day compared to total enteral feeding administered during 24 hours, intensified pain syndrome, abdominal distension, diarrhea, nausea and vomiting. Indicators featuring prognostic significance were identified using the logistic regression technique. The null hypothesis was rejected at $p<0.05$.

RESULTS. The presented findings demonstrate that a more severe multiple organ failure (SOFA – OR – 1.283, 95 % CI 1.029–1.6, p=0.027), the operative day (OR – 4.177, 95 % CI 1.542–11.313, p=0.005) increase while the nasojejunal route of nutrients delivery decreases (OR – 0.193, 95 % CI 0.08–0.4591, $p\leq0.001$) the incidence of large residual stomach volumes. Postpyloric feeding reduces the risk of developing pain syndrome (OR – 0.191, 95 % CI 0.088–0.413, $p\leq0.001$), abdominal distension (OR – 0.420, 95 % CI 0.203–0.870, p=0.002), nausea and vomiting (OR – 0.160, 95 % CI 0.069–0.375, $p\leq0.001$).

CONCLUSION. During severe acute pancreatitis, multiple organ dysfunction, the nasogastric route of enteral feeding delivery, and the fact of a surgery increase independently the risk of developing large residual stomach volumes. In case of severe acute pancreatitis, the nasogastric route of nutrients administration increases the development of such manifestations of enteral feeding intolerance as nausea, vomiting, pain intensification, and abdominal distension. In patients with severe acute pancreatitis, the nasoejunal route of administration of nutrients is preferable.

Keywords: *acute pancreatitis, artificial tube feeding, nasogastric and nasojejunal tubes, intolerance, residual volume stomach, nausea, vomiting, abdominal distention*

For citation: Sivkov O. G., Sivkov A. O., Popov I. B., Zaitsev E. I. Peculiarities of nasogastric and nasojejunal feeding during the early period of acute severe pancreatitis. *Grekov's Bulletin of Surgery*. 2021;180(6):56–61. (In Russ.). DOI: 10.24884/0042-4625-2021-180-6-56-61.

* **Corresponding author:** Oleg G. Sivkov, Tyumen Cardiology Research Center, 111, Melnikaite str., Tyumen, 625026, Russia. E-mail: sivkovog@mail.ru.

Introduction. Acute pancreatitis (AP) is the third most common acute surgical disorder of abdominal organs [1]. Most patients suffer from its mild form wherein oral feeding might be initiated almost immediately subject to its tolerance [2]. For patients suffering from severe acute pancreatitis (SAP), it is essential to provide timely and adequate nutritional support due to high catabolic activity resulting from local and systemic inflammation leading to a negative nitrogen balance [3].

Enteral feeding (EF) is assumed to help preventing bacterial translocation resulting from impaired barrier function of the intestinal mucosa and reduce the risk of infectious peripancreatic necrosis and severity of the systemic inflammatory response (SIR) [4, 5]. This is why quite a few studies have shown advantage of EF over parenteral feeding during SAP [6–10], which has finally changed the paradigm of the treatment of this disease [11]. EF can be administered via a nasogastral (NG) or a nasojejunal (NJ) tubes. The first work dedicated to safety of NG feeding during SAP was done 20 years ago [12]. In 2005, the first randomized controlled study was carried out, based on the findings of which it was

concluded that there is no difference between NG and NJ feeding in terms of mortality, tolerance, or the length of stay [13]. Subsequent studies supported the results obtained [14, 15]. Materials of these studies were summarized in meta-analyses that said that NG administration of nutrients in SAP patients is an effective method to improve their nutritional status [16–18]. However, there are still many outstanding questions today [19] concerning selection of the method of enteral feeding administration to SAP patients. There is no conclusive evidence of advantage, disadvantage, or equivalence of NG vs. NJ modes of enteral tube feeding during SAP [20], because analysis of the performed investigations found numerous methodological drawbacks, first of all, absence of a consensus criterion of SAP definition [21]. The relevance of our study is determined by the fact that most research papers had been completed before the AP classification was revised to identify, in addition to existent forms, the moderately severe form, such patients being previously classified as SAP, and lack of information about factors influencing feeding intolerance (FI) in SAP patients.

The **objective** was to identify factors that independently influence the intolerance of early enteral feeding via a nasogastric and nasojejunal tube in intensive care unit (ICU) patients at an early stage of SAP.

Methods and materials. An open, randomized, controlled, cohort study was carried out in the ICU of Medical and Sanitary Unit «Neftyanik» in Tyumen from November 2012 to October 2018. The inclusion criteria were: the AP diagnosis and presence of at least predictor of a severe illness. The exclusion criteria were: an age older than 80 years, terminal chronic diseases, pancreatogenic shock – lactate >4 mmol/L, the necessity to use adrenergic agonists to maintain average arterial blood pressure over 70 mm Hg. AP was diagnosed based on the characteristic clinical pattern supported by laboratory and instrumental tests [1]. As predictors associated with the development of severe AP, the following were used: C-reactive protein (CRP) >150 mg/L, severity according to Acute Physiology And Chronic Health Evaluation (APACHE) II >8, and SOFA score >2 [22]. The APACHE-II and SOFA scales were additionally used for dynamic assessment of severity of the status and multiple organ dysfunction during the observation period.The EF route was selected using the 'envelope' technique at a ratio of one to one. Later, out of 64 patients included in the study, a cohort of SAP patients was singled out. Of them, 16 patients received NG EF and 15 – a NJ tube inserted with the help of an endoscope. The EF formula was standard, isocaloric, enriched with dietary fiber (Nutricomp Standard Fiber, BBraun, Germany). Enteral feeding was initiated within the first 12–24 hrs. of admission to ICU. The observation period lasted for five days. In the NJ group, a nasogastral tube was inserted additionally. Regardless of the point of tube insertion, the feeding formula was administered continuously by dripping. In case of nasogastric feeding, gastric decompression was performed every 6 hrs. In the second group, gastric decompression was continuous. Feeding started at a rate of 15 ml/hrs that was increased by 15 ml/hrs each day. The prescribed volume of enteral feeding was 250 ml/day for the first day and increased by 250 ml/day each day depending on the subject to tolerance. If nausea, vomiting, increasing pain, instantaneous discharge via the nasogastric tube >500 ml/hr occurred, the rate was halved or the feeding was terminated unless the above symptoms resolved. After intolerance symptoms were reversed, the feeding rate was gradually increased to the previous rate. On all the patients who underwent surgery during the observation period, the following operation was performed: abdominal drainage via laparoscopic incision under total intravenous anesthesia with myoplegia and mechanical ventilation. Statistical processing of data was carried out with the help of SPSS – 22 software package. After the normality of distribution check using the Shapiro – Wilk test, the results were presented as the mean and mean root square deviation ($M\pm\sigma$) or the median and quartiles Me (Q25; Q75). Both parametric and non-parametric tests were used for comparison between the groups. Indices possessing the predictive power were identified with the help of logistic regression. The null hypothesis was rejected at $p<0.05$.

Results. The clinical and laboratory characteristics of the patients are given in *table 1*.

The formed groups of NG and NJ feeding were comparable in terms of age, the content of C-reactive protein during the first 48 hours, condition severity on the day of admission (*table 1*) and during the following five days (*table 2*). *Table 2* shows the percentage of patients who had this FI sign or other. A sign was assumed to be present if occurred at least once during the entire observation period. Pain syndrome, gastric residual volume (GRV), nausea and vomiting were statistically more frequent in the NG group while there was no statistically significant difference in other FI symptoms.

There was no statistically significant difference between the groups as regards the number of patients who were operated on (*table 2*); in most cases, surgery was performed on day three from admission to ICU (*table 3*).

Table 3 shows changes in the recorded parameters during five days. We can see from the table that the APACHE II and SOFA scores did not change statistically significantly during the entire observation period and displayed no statistically significant differences between the NG and NJ groups. GRV was found to occur statistically more frequently on day three due to patients who received nasogastric tube feeding. Pain syndrome that required to reduce the nutrient administration rate was statistically significantly more severe on days two, three, and four in the NG group. In the same group, nausea and vomiting statistically occurred more frequently on day one, three, and four, while abdominal distension – on day one. There were no statistically significant fluctuations of diarrhea in the groups. Logistic regression established the variables that independently influence the risk of FI (*table 4*). We can observe from the findings presented that a more severe multiple organ dysfunction, the day of surgery and the method of nutrients delivery have an impact on the incidence of large GRV. Pain syndrome occurs more frequently in case of NG feeding, while NJ feeding is associated with rarer abdominal distension, nausea and vomiting.

Discussion. One of the main factors preventing application of NG tube feeding in AP patients is the

Table 1

Clinical and laboratory characteristics of the patients included in the clinical study

Index	SAPa (n=31)	SAP nasogastric feeding (n=16)	SAP nasojejunal feeding (n=15)	P
Sex, m/f	21/10	11/5	10/5	
Age, years	41 (35.5; 57)	(44.62±12.75)	(47.2±13.17)	0.892[e]
Shapiro – Wilk test, p	0.032	0.146	0.122	
CRPb24, mg/L	(87.68±51.82)	(75.02±53.74)	(101.33±47.78)	0.373
Shapiro – Wilk test, p	0.334	0.315	0.144	
CRP48, mg/L	181 (159.5; 200)	(183.12±48.55)	175 (155; 203)	0.993[e]
Shapiro – Wilk test, p	0.011	0.298	0.043	
Operations, %	90.32	93.75	86.66	0.801[g]
APACHE-IIc, score (the first 24 hrs.)	(7.32±3.99)	(6.5±2.82)	(8.2±4.9)	0.498[f]
Shapiro – Wilk test, p	0.301	0.255	0.575	
SOFAd, score (the first 24 hrs.)	2 (1; 3)	1.5(1;2)	3 (1; 3.5)	0.356[e]
Shapiro – Wilk test, p	0.001	0.011	0.007	
MV >12 but <24hrs., patientsh	4	2	2	–

Note: [a] – SAP-severe acute pancreatitis; [b] – C-reactive protein; 24 – the first 24 hrs. of admission; 48 – the second day; [c] – Acute Physiology And Chronic Health Evaluation; [d] – Sepsis-related Organ Failure; [e] – Kruskal–Wallis test; [f] – ANOVA; [g] – Pearson's chi-squared test; [h] – mechanical ventilation not associated with anesthetic support that lasted for more than 12 hrs., but less than 24 hrs.

Table 2

The fraction of patients with feeding intolerance signs and the severity of the condition for the entire observation period with nasogastric and nasojejunal tube feeding for severe acute pancreatitis

Group	Surgeries, %	GRVa, %	Pain, %	Nausea, Vomiting, %	Distension, %	Diarrhea, %	Shapiro – Wilk Test, p	APACHE-IIb Score	Shapiro – Wilk Test, p	SOFAc Score
SAPd NGe	93.75	87.5*	93.75	87.5	75	6.25	0.037	9 (5;12)	<0.001	2(1;4)
SAP NJf	86.66	53.33	53.33	40	60	20	0.093	(9.05±4.83)	0.001	3(1;4)
p	0.505	0.036	0.015	0.006	0.372	0.333	–	0.526h	–	0.260h
SAP all patients	90.32	70.96	74.19	64.51	67.74	12.9	0.006	9 (6;12)	<0.001	2(1;4)

Note: [a] – gastric residual volume; [b] – Acute Physiology And Chronic Health Evaluation (for 5 days); [c] – Sequential Organ Failure Assessment (for 5 days); [d] – severe acute pancreatitis; [e] – nasogastric tube feeding; [f] – nasojejunal tube feeding; [g] – Pearson's chi-squared test; [h] – Mann – Whitney U test.

belief that it affects the pancreatic exocrine function because it is known that enteral feeding of any type stimulate pancreatic secretion in healthy humans [23, 24]. At present, there is convincing evidence that in AP patients, the rate of secretion of pancreatic enzymes into duodenum is not only considerably lower than in healthy humans, but is inversely proportional to AP severity [25]. The facts suggest that during AP, damaged acinar cells are not capable to respond properly to physiological stimuli in case of nasogastric tube feeding. Our study has discovered that the APACHE-II score render no influence on the incidence FI, which is in agreement with the recently published findings by U. Gungabissoon et al. [26]. The independent factors influencing high GRV among our SAP patients were progressing multiple organ dysfunction, which does not contradict the existent studies [27], the day of surgery, and feeding via a nasogastric tube. Intensification of pain syndrome, abdominal distension, nausea and vomiting were associated with NG feeding (*table 4*). FI incidence over the entire observation period of our study amounted to 23.87 %, but the percentage of patients who experienced a FI episode at least once was high (*table 2*). Our findings differ from existent ones where FI was observed only in 20 % of patients approximately. Such difference could be explained by the fact that in the known studies, not all clinical signs of FI were recorded, and in those papers, most patients had a moderately severe illness because multiple organ dysfunction occurred only in 4.3–23 % of patients. Besides, surgical activity equaled to 4.3–37.5 % in previously published papers vs. 90.3 % in our study. It is known that the surgery performed on abdominal organs may be a cause of FI [28, 29]. Finally, a semi-elemental formula was used for feeding in the existent studies [30], though the recent Cochrane review of 2015 did not find evidence supporting any one particular enteral formula [31]. The retrospective study of 2018 carried out in Japan demonstrated no clinical benefit of using an elemental formula compared to semi-elemental or polymer formula in AP patients [32]. In our study, we have proven that at an early stage of SAP some factors influence FI independently. The regularity we have identified is of particular relevance in patients

Table 3

The severity of the condition, multiple organ dysfunction, the fact of the operation and the clinical manifestations of feeding intolerance in the first 5 days of treatment in ICU with nasogastric and nasojejunal tube feeding for severe acute pancreatitis

Index	Type of Feeding		Day 1	Day 2	Day 3	Day 4	Day 5	p
APACHE-IIa	NGd	Score	(6.5±2.8)	(9.43±4.3)	(10.0±5.5)	(9.1±5.1)	(8.1±4.6)	0.236[f]
		Shapiro – Wilk Test, p	0.255	0.72	0.52	0.249	0.762	–
	NJe	Score	(8.2±4.9)	(10.9±4.2)	(12.3±5.3)	(8.8±4.9)	(8.1±4.6)	0.513[f]
		Shapiro – Wilk Test, p	0.575	0.126	0.987	0.868	0.126	–
	p		0.243[h]	0.362[h]	0.736[h]	0.886[h]	0.973[h]	–
	All	Score	(7.3±3.99)	(10.1±4.3)	(9.7±5.3)	(8.9±4.9)	(8.1±4.6)	0.12[f]
		Shapiro – Wilk Test, p	0.301	0.793	0.476	0.212	0.167	–
SOFAb	NG	Score	1.5 (1; 2)	3 (1; 5.5)	(3.5±2.8)	(1.9±1.9)	2 (0; 4)	0.423[g]
		Shapiro – Wilk Test, p	0.011	0.038	0.249	0.067	0.025	–
	NJ	Score	3 (1; 3.5)	(3.4±2.0)	3 (2; 5.5)	(2.7±2.1)	2 (0.5; 4.5)	0.579[g]
		Shapiro – Wilk Test, p	0.007	0.07	0.032	0.083	0.024	–
	p		0.154[i]	0.763[i]	0.952[i]	0.773[h]	0.904[i]	–
	All	Score	2 (1; 3)	3 (2; 4)	2 (2; 5)	2 (1; 4)	2 (0; 4)	0.119[g]
		Shapiro – Wilk Test, p	0.001	0.065	0.038	0.023	0.005	–
Surgery	NG	%	0	25	43.75	18.75	6.25	0.011[k]
	NJ	%	0	20	40	20	6.66	0.041[k]
	p		–	0.739[j]	0.833[j]	0.930[j]	1.0[k]	–
	All	%	0	22.5	41.9	19.35	6.45	0.001[k]
GRVc	NG	%	31.25	37.5	75	37.5	31.25	0.064[j]
	NJ	%	6.66	13.33	40	6.66	20	0.141[k]
	p		0.171[k]	0.124[j]	0.048[j]	0.083[k]	0.474[k]	–
	All	%	19.35	25.80	58.06	22.58	25.80	0.006[j]
Pain	NG	%	43.75	56.25	62.5	56.25	25	0.253[j]
	NJ	%	20	6.66	26.66	20	6.66	0.527[k]
	p		0.157[j]	0.006[k]	0.045[j]	0.038[j]	0.333[k]	–
	All	%	32.25	32.25	45.16	38.70	16.12	0.459[r]
Nausea, vomiting	NG	%	50	31.25	62.5	50	25	0.192[j]
	NJ	%	13.33	13.33	26.	0	6.66	0.286[k]
	p		0.029[j]	0.233[j]	0.045[j]	0.002[k]	0.333[k]	–
	All	%	32.25	22.58	45.16	25.80	16.12	0.561[j]
Abdominal distension	NG	%	43.75	37.5	50	37.5	18.75	0.443[j]
	NJ	%	6.66	20	46.66	26.66	6.66	0.043[k]
	p		0.037[k]	0.283[j]	0.853[j]	0.519[j]	0.6[k]	–
	All	%	25.8	29.03	48.38	32.25	12.9	0.362[j]
Diarrhea	NG	%	6.25	0	0	0	0	1.0
	NJ	%	0	0	6.66	13.33	6.66	0.792[k]
	p		1.0	–	0.484	0.226	0.484	–
	All	%	3.22k	0	3.22[k]	6.45[k]	3.22[k]	0.562[k]

Note: a – Acute Physiology And Chronic Health Evaluation, b – Sequential Organ Failure Assessment, c – gastric residual volume, d – nasogastric tube feeding; e –nasojejunal tube feeding, f – ANOVA, g – Kruskal–Wallis test, h – Student's t-test, i – Mann–Whitney U test, j – Pearson's chi-squared test, k – Fisher's exact test.

with SAP and stress hyperglycemia, in which there is a statistically significant increase in urinary nitrogen excretion [33], due to the possibility of personalized nutrition selection. In future, it is necessary to carry out a study to get an answer to the question whether the type of formula and form of the disease influence formation of FI in such patients and to continue looking for methods that can verify since when the enteral feeding can be initiated and what its volume should be [34, 35]. The current guidelines determine the priority of NJ feeding only when the risk of aspiration is high, GRV is high, or there is a pyloric block; in other cases, NG feeding should be performed [36]. Based on our findings, the NJ feeding has an advantage of the NG

Table 4

Predictive value of risk factors for feeding intolerance (logistic regression)

Dependent variables		Independent variables			
		APACHE II[a]	SOFA[b]	surgery	NG/NJc
GRV[d]	OR	1.115	1.283	4.177	0.193
	95 % CI	1.004–1.238	1.029–1.6	1.542–11.313	0.081–0.459
	p	0.08	0.027	0.005	<0.001
Pain	OR	1.029	1.03	2.115	0.191
	95 % CI	0.936–1.130	0.845–1.256	0.851–5.255	0.088–0.413
	p	0.557	0.769	0.107	<0.001
Nausea, vomiting	OR	1.017	1.16	1.840	0.160
	95 % CI	0.922–1.122	0.942–1.428	0.709–4.77	0.069–0.375
	p	0.737	0.162	0.21	<0.001
Abdominal distension	OR	1.037	1.088	1.435	0.420
	95 % CI	0.945–1.137	0.896–1.321	0.581–3.547	0.203–0.870
	p	0.446	0.397	0.434	0.002
Diarrhea	OR	0.058	1.171	1.215	4.811
	95 % CI	0.617–1.008	0.678–2.022	0.120–12.26	0.510–45.334
	p	0.789	0.571	0.869	0.170

Note: [a] – Acute Physiology And Chronic Health Evaluation; [b] – Sequential Organ Failure Assessment; [c] – nasogastric/nasojejunal tube feeding; [d] – gastric residual volume.

feeding during SAP thanks to reduction of non-fatal complications typical for NG feeding.

Conclusion. The fact of surgery, multiple organ dysfunction and nasogastric way of delivering nutrients independently rise the incidence of high gastric residual volumes during severe acute pancreatitis. The nasogastric way of nutrient administration during severe acute pancreatitis leads to a higher incidence of such manifestations of enteral feeding intolerance as nausea, vomiting, pain intensification, and abdominal distension. In patients suffering from severe acute pancreatitis, the nasojejunal way of nutrients administration is preferable.

Conflict of interest

The authors declare no conflict of interest.

Compliance with ethical principles

The authors confirm that they respect the rights of the people participated in the study, including obtaining informed consent when it is necessary, and the rules of treatment of animals when they are used in the study. Author Guidelines contains the detailed information.

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Information about authors:

Sivkov Oleg G., Cand. of Sci. (Med.), Chief of Anesthesiology and Intensive Care Service, Tyumen Cardiologic Scientific Center (Tyumen, Russia), ORCID: 0000-0002-7694-9293; **Sivkov Aleksei O.**, Physician of Anesthesiology and Intensive Care Unit, Medical and Sanitary Unit «Neftyanik» (Tyumen, Russia), ORCID: 0000-0003-3682-2789; **Popov Ivan B.**, Cand. of Sci. (Med.), General Director-Chief Physician, Medical and Sanitary Unit «Neftyanik» (Tyumen, Russia), ORCID: 0000-0002-2917-2709; **Zaitsev Evgenii Yu.**, Professor, Deputy General Director, Medical and Sanitary Unit «Neftyanik» (Tyumen, Russia), ORCID: 0000-0002-7685-1616.