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**Ocena wpływu wczesnego żywienia enteralnego
na przebieg ostrego zapalenia trzustki u dzieci**

**Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki medyczne**

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Abstract

“Assessment of the impact of early enteral nutrition on the course of acute pancreatitis in children”

Introduction and aims of the work

Acute pancreatitis (AP) is an acute inflammatory condition associated with premature activation of pancreatic proenzymes and varying degrees of local and systemic complications. Treatment of AP is based primarily on data from studies in adults. Because the disorder is often idiopathic, the treatment is largely supportive, symptoms-based, and aimed at preventing further complications. Nutrition is an integral part of AP treatment.

The first study aimed to present a summary of previously published research on the influence of the time of initiation of enteral nutrition in paediatric patients with mild and moderately severe AP on the course of the disease. The second study was aimed to assess the impact of introducing enteral nutrition in children during the first 48 hours of hospitalisation on the course of AP, with particular emphasis on the effects of very early (within 24 hours) introduction of nutrition, and the impact of nutrition on the concentration of inflammation-associated markers, including pro-inflammatory cytokines.

Methods

The first publication is a literature review conducted independently by two authors in April 2022, based on the PubMed (MEDLINE) and EMBASE (Ovid) databases. Full-text articles in English focused on patients up to 21 years of age and analysed the timing of nutritional initiation in children with mild and moderately severe AP, were included. In addition, studies cited in above-mentioned publications were also analysed.

The second publication is a randomised study conducted from January 2019 to September 2022 in three university hospitals in Poland. The study group consisted of children aged 1–18, diagnosed with mild and moderately severe AP. The patients were randomised according to a computer-generated list into two groups: group A received an oral nutrition within the first 24 hours of hospitalisation (very early), and group B between 24 and 72 hours from the beginning of hospitalisation (early nutrition). The nutrition was a specially prepared diet that was low in fats to the extent that was tolerable by the patient. In addition, patients

received adequate hydration and, if necessary, pain relief treatment. The primary endpoint was a measure of length of hospitalisation, measured in days. During the first three days of hospitalisation, blood samples were collected from patients, and the concentrations of pro-inflammatory cytokines were determined: tumour necrosis factor alpha (TNF α), interleukin 1-beta (IL-1 β), interleukin 6 (IL-6), and interleukin 8 (IL-8). Moreover, the concentration of C-reactive protein, the activity of amylase, lipase, alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transpeptidase were simultaneously determined, and the occurrence of symptoms (intensity of pain, vomiting, and nausea) was assessed.

Results

Four studies were included in the first publication: one randomised-control trial, one prospective study with retrospective chart review, and two retrospective chart reviews. A total of 394 paediatric patients were analysed for nutritional interventions. All four studies supported early enteral nutrition with a regular, normal-fat diet and indicated that there was no need to delay its introduction. Studies have demonstrated the safety of early enteral nutrition in children with mild and moderately severe AP. Moreover, early nutrition did not extend, and in some cases shortened, the length of patients' hospitalisation.

In the randomised trial 94 patients were recruited. The statistical analysis included 75 patients with mild pancreatitis – 42 in group A and 33 patients in group B. Both groups did not differ in terms of the length of hospitalisation ($p = 0.22$), symptoms of pancreatitis, or laboratory test results, except for the activity of aspartate aminotransferase on the first day of hospitalisation. Cytokines were determined in 64 children – 38 in group A and 26 in group B - and no statistically significant differences were found in their concentrations, except for IL-1 β concentration on the third day of hospitalisation ($p = 0.01$).

Conclusions

The literature review shows that enteral nutrition (optimally oral) can be introduced as early as possible, even within the first 24 hours of hospitalisation, in children with mild and moderately severe AP. Moreover, the introduction of a full-fat diet is a safe and well-tolerated intervention that can reduce pain and shorten the hospitalisation time.

The results of our study showed that the introduction of oral nutrition during the first 24 hours (very early) or after 24 hours (early) of hospitalisation onset has no effect on the length of hospitalisation, the concentration of pro-inflammatory cytokines, the activity of pancreatic enzymes and aminotransferases, or the occurrence of symptoms in children with mild AP. These results suggest that very early enteral nutrition is as safe as early enteral nutrition.