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Nutrition in acute pancreatitis: a review

Review Article

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Abstract: We perform an update about nutritional measures that have been adopted in patients with acute pancreatitis (AP). The nutritional support is an essential part of treatment in AP. When the AP is mild or moderate, there is no doubt that is not necessary to use an artificial nutritional support, and it is recommended that oral nutritional support should begin as soon as possible. If the AP is severe, the best way to provide nutritional support is through enteral nutritional (EN) because it reduces infection, length of hospitalization and mortality rate. Parenteral nutrition (PN) should be used only when EN is Impossible. However, there is no scientific evidence for recommending the most optimal route necessary to administer this type of nutritional support; we seek to uncover whether this is by gastric or jejunal route and the proper formula to use. There is an international agreement that the nutritional support should begin quickly, within the first 24 and 72 hours of hospitalization. As conclusion, more research needs to be done concerning nutritional support in AP, and many questions are not been answered yet.

Keywords: *Pancreatitis • Nutrition • Enteral • Parenteral • Review*

Acute pancreatitis (AP) remains a significant problem, with evidence to suggest a global trend toward an increasing incidence of disease [1]. It can be potentially dangerous, but in approximately 80% of the patients who suffer from mild pancreatitis only need to undergo a treatment that includes a short period of fasting, intravenous hydration and intake of analgesics [2,3]. The remaining 20% of the people who have pancreatitis have a more complicated recovery and there is a mortality rate between 8 and 39% [2]. Severe AP presents a syndrome that has a systemic inflammatory response, high protein catabolism and hypermetabolism, which lead to a rapid consumption, making it possible for 30% of patients to present serious malnutrition [4,5]. For this reason, there have been studies based on the nutrition support of these patients because it is an essential part of the management of this disease.

Since 1987 Sax et al, published a study that showed that parenteral nutrition (PN) added to traditional treatment with fluid therapy and analgesia did not decrease the number of deaths, infective complications or length of hospitalization [6]. Therefore, it has been put into question the need for nutritional support in severe AP. Petrov (2008), published a meta-analysis that reviewed articles that compared the results obtained on AP depending on the nutritional support used: enteral nutrition (EN), PN and lack of nutritional support. Three clinical trials were found, in which 113 patients were included to compare the difference between PN and the absence of nutrition support. It was demonstrated that PN decreased the mortality rate, but the risk of infection was not reduced [7]. Based on these and other studies, different scientific societies agree that nutritional support should be initiated only in severe cases; this meaning it should only begin for those who are not going to be able to start an oral diet within 5-7 days [8-11]. The exception to this issue is the patients who are admitted with malnourishment, who require and artificial nutritional support from the beginning of the recovery process.

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Oral refeeding with a soft diet in patients with mild AP can be considered safe and can result in shorter length of hospitalization [12,13]. Petrov et al, in a study published in January 2013, compared the results from initiating nutritional support in gastric cavity with semi elemental EN vs. conventional treatment without nutritional support in seventeen patients with mild to moderate AP. The results show improvement in the group of patients who received EN in terms of pain, oral tolerance and the intake of opiates, but no decrease in the average hospitalization period [14]. These results show that the ideal treatment of mild-moderate pancreatitis has yet to be defined, and that the subject has to continue to be investigated.

1. Severe AP

When talking about severe AP, there is no doubt that the nutritional support is an important part of the treatment, yet there is still a debate on which is the best treatment and way to administer nutritional support, when to begin, which is the ideal nutritional formula and if there are any specific nutrients that can positively intervene in evolution this severe diagnosis.

Concerning the administration of the nutritional support, it is agreed that EN should be initiated and replaced with PN only when EN is impossible [15,16]. This began to take place in 2003 when Al-Omran [17] published his first meta-analysis in which EN vs PN were compared in patients who suffer an AP. In this meta-analysis, it was observed that there was a trend that showed a reduction of adverse outcomes using EN, but the results were not conclusive. Shortly after, in 2004, Marik et al published a meta-analysis in which, also, EN vs PN were compared. In this meta-analysis, six studies were reviewed and a total of two hundred and sixty three patients were included [18]. The data showed significant differences in favor of using EN, although these conclusions were debatable (in one of the trials, not all patients were diagnosed with severe AP and not all of the clinical trials were up to par, according to Jadad's standards). In two following meta-analysis these conclusions proved to be correct [19,20]. In the latest meta-analysis published by Heming in 2012 [21], six studies were reviewed comparing EN vs PN and it becomes clear that nutritional support with EN decreases pancreatic complications (infections, abscesses and necrosis), mortality rate and multi-organ failure. Concerning infective complications with a non-pancreatic origin, including pneumonia, urinary tract infection and catheter infection, there were not significant differences. Regarding non-infection-related complications, the results are poorer when using EN, but in this case, the studies do not pass the test for heterogeneity. It is so important to maintain the enteral feed that the American Society of Parenteral and Enteral Nutrition (ASPEN) recommend trying different strategies to improve the tolerance. In other way, it is known the importance of glycemic control in-patients, and it is more easily when EN is administered instead of PN [22]. However, a recent study shows that there is an overuse of PN (total of peripheral) and underutilization of jejunal feedings in the management of AP [23].

The position whereby EN should be administered has also been a subject of interesting studies. To achieve this purpose, semi-elemental formulas were used through nasojejunal tubes past the ligament of Treitz. However, some studies have shown that the stimulation of the exocrine pancreatic secretion in patients with AP is much lower than that in healthy individuals [24]. Consistent with this data, Eatock published a paper in 2000 where the possibility of nasogastric feeding was introduced. Patients were randomly selected to receive either nasogastric or nasojejunal feeding and no significant differences were found in terms of length of hospitalization, mortality, need for intensive care, pain relief or the need for analgesics [25]. The major limitation of this study was that the position of the tube was not properly tested and therefore, the results could be put into question. However, the results have been confirmed in a later trial by Eatock in 2005 [26]. At least other two subsequent systematic reviews are published, in which there are no differences between the two options [27,28]. Nonetheless, it is recommended that randomized trials continue to clarify this aspect.

Regarding when to initiate nutritional support, the views are not as consistent, although the majority of the authors prefer to initiate nutritional support quickly, usually within 24-48 hours after admission and initial resuscitation support [8,10,29]. No accurate clinical trials have been found comparing different times to begin EN in severe AP. Currently there is clinical trial that began in 2011 (PYTHON), that is scheduled to last for approximately three years, in which it intends to compare the early onset within the first 24 hours of admission to a later initiation of nutritional support after 72-96 hours since admission [30]. Until the results are obtained, we should take in to account the information found in previous studies, in which the beginning of the EN occurs within the first 24-72 hours after hospitalization (there are very few that contain a later initiation of nutritional support).

Finally, the last question concerning nutritional support in AP is what formula is preferred and whether there nutrients that provide additional benefits. The recommendation of the European Society Parenteral

Enteral Nutrition (ESPEN) is that peptide formulas can be used safely (grade A), although polymers formulas can be used if they will be tolerated (grade C) [11]. Tiengou et al published an essay in 2006 that associated the decrease in hospitalization time with the use of peptide formulas for nutritional support with EN, but the trial included only nineteen patients (there were thirty in total, but eleven had a mild to moderate evolution) [31]. Only one meta-analysis has been found in which the objective was to compare the safety and tolerance of EN formulas in severe AP. It concludes that the use of a peptide vs polymeric formulas does not improve the feeding tolerance in patients (relative risk (RR) 0.62, confidence interval of 95 percent (CI) 0.10 to 3.97, p=0.611) and no differences were found in the risk of infectious complications or mortality [32].

With advances in nutritional support, it has been proved that the addition of certain nutrients can benefit the course of the disease, for example, using glutamine in PN in a critically ill patient [33,34]. As mentioned above, patients who suffer severe AP could be categorized as critically ill and this is the reason why the ESPEN recommended glutamine supplementation in PN, if it will be necessary for the treatment of severe AP (grade A) [35]. There are three randomized clinical trials that included eighty two patients that compare the results between using glutamine or not in PN (fourty and fourty two patients respectively) [36-38]. Most of the patients had mild pancreatitis and the overall mortality rate was 4.8%. These trials have small differences in their design and in the interpretation of the data collected, but the effect of contribution of glutamine still comes out positive: overall decrease in possible complications (RR 0.68, 95% CI 0.42-1.09, p=0.11) and in two of these studies a decreased in the hospitalization period was also found. However, there is no data on the optimal dose, and therefore, the recommendation is similar to those of critically ill patients: > 0.20 g/kg/day of L-glutamine or > 0.30 g/kg/day of Ala-Glutamine.

Also, the EN has been enriched with other nutrients with irregular results. On the one hand, it has been tried enrich fiber, both soluble and insoluble. For now, it is not recommended that critically ill patients intake insoluble fiber, and for this reason it is not recommended in the early stages of severe AP. However, Karakan T et al published a trial in which 1.5 g per 100 ml of insoluble fiber was added in to the EN for thirty patients and there were significant differences in the rate of infection and hospitalization in favor of the use of EN with fiber [39]. Nevertheless, there is very little information available on this subject that has made any impact or changes. On the other hand, it seems that probiotics can prevent infectious complications, which reduces bowel bacterial overgrowth, restoring the gastrointestinal barrier and modulating the immune response [40,41]. For these reasons, it is considered that it could be useful in the treatment of AP. When in 2002 Olah, combined oat fiber (prebiotic) and probiotics (Lactobacillus plantarum), a reduction of septic complications was found (4,5 vs 30% in the control group) [39]. Five years later, this results were confirmed, creating expectations in the scientific community [42]. However, Besselink et al published a multicenter randomized trial that included two hundred and ninety six patients with a severe AP. They were randomly chosen to receive a probiotic (Lactobacilli sp and Bifidobacteria sp) or enterally administered placebo [43]. There was no difference in the rate of infectious complications, but in the probiotic group, the incidence of multiple organ failure (MOF) was significantly higher (22% in case of probiotics vs 10% in the control group; p=0.01) and mortality was higher too (16% vs. 6% p=0.01). Nine patients in the probiotics group developed bowel ischemia and none in the placebo group. Studies show that MOF occurs between hospitalization and randomization, and MOF post randomization is only 12% vs 8%, which is not very significant. This may consist of the need for vasopressors, which could facilitate the development of intestinal ischemia. Later, in Petrov's review from 2009, it was concluded that enteral probiotic supplementation does not improve clinical outcomes and does not recommend its use [32]. In the last meta-analysis on this topic, Zhang MM et al reviewed fourty eight articles, of which only seven met the quality criteria necessary. In these studies, five hundred and fifty nine patients were randomized to one of three groups: the use of prebiotics, probiotics or symbiotics. The results were similar in the three groups, and even the use of pre-, pro- or symbiotics was associated with shorter hospitalization (OR -3.87, 95% CI -6.20 to -1.54, p=0.001), when classified by the severity of pancreatitis of each patient, the results were similar. Therefore, the conclusion was that the use of pre-, pro- or symbiotics shows no influence on the outcome of patients with AP and as a result, there is no evidence to recommend its use [44].

Other nutrients which has been attempted to modulate the inflammatory response in AP are fatty acids and different antioxidants. By using omega-3 acids, it is attempted to modify the inflammatory cascade that acts upon eicosanoid production and cytokine release. Laszity et al published a clinical trial in 2005 which compares standar EN (fourteen patients) vs EN with 1.95 g of linoleic acid enriched with 3.3 g of free n-3 polyunsaturated fatty acids (PUFAs), containing 1.66 g of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and 1.18 g of 1 IU/g of vitamin E (fourteen patients) [45].

The sample included patients with moderate and severe AP according to Atlanta's criteria. Benefits were found in terms of reduced hospital stay and the number of days of nutritional support, but not in terms of MOF, cholangitis, sepsis, pseudocyst or mortality. It is recommended that further investigations have been done on the optimal inmunocomposition in EN on patients with AP. The following year Pearce et al, published another trial comparing standard EN (sixteen patients) with EN supplemented with arginine, glutamine, PUFAs and tributyrin, vitamin C, E and beta-carotene and micronutrients such as zinc, selenium and chromium (fifteen patients). A significant increase was found in C reactive protein in the supplementation group compared with the control group, but there were no statistically significant differences in terms of hospitalization period, need for surgery or death [46].

2. Conclusions

The nutritional support is an essential part of treatment in AP. When the AP is mild or moderate, there is no dispute on whether is it necessary to use an artificial nutritional support, and it is recommended that oral intake should begin as soon as possible.

However, if the AP is severe, the best way to provide nutritional support is EN because of the fact that it reduces infective complications, length of hospital stay and mortality rate. Although there is no existing scientific evidence that recommends the correct nutritional support (gastric or jejunal feeding and the type of formula to use), more and more studies suggest that it is safe the infusion of a polymeric formula in the gastric cavity. However, there is a homogenous agreement that the nutritional support should begin quickly, within the first 24 and 72 hours of hospitalization. PN should be used when the use of EN is impossible, in which case, the PN would need to be supplemented with glutamine. There is no conclusive data that recommends the use of other nutrients or probiotics.

In conclusion, much research should be done concerning nutritional support in severe AP to resolve the pending issues.

Conflict of interest statement

Authors state no conflict of interest.

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