Clinical Nutrition xxx (2014) 1–9

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Meta-analyses

Parenteral immunonutrition in patients with acute pancreatitis: A systematic review and meta-analysis

Tina Jafari [a, *], Awat Feizi [b], Gholamreza Askari [a], Aziz A. Fallah [c]

[a] Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
[b] Department of Epidemiology and Biostatistics, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran
[c] Department of Food Hygiene and Quality Control, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord 34141, Iran

ARTICLE INFO

Article history:
Received 11 August 2013
Accepted 15 May 2014

Keywords:
Acute pancreatitis
Parenteral immunonutrition
Glutamine
Omega-3 fatty acids
Randomized controlled trials
Meta-analysis

SUMMARY

Background & aims: Acute pancreatitis is a systemic immunoinflammatory response to auto-digestion of the pancrease and peri-pancreatic organs. Patients with acute pancreatitis can rapidly develop nutritional deficiency; hence nutritional support is important and critical. Sometimes parenteral nutrition (PN) is inevitable in acute pancreatitis. Due to immunosuppressive and inflammatory nature of the disease, it seems that immunonutrients like glutamine and omega-3 fatty acids (ω-3 FAs) added to parenteral formulas may improve the conditions. We conducted a meta-analysis to evaluate the effects of parenteral immunonutrition on clinical outcomes (infectious complications, length of hospital stay (LOS) and mortality) in patients with acute pancreatitis.

Methods: A computerized literature search on four databases (PubMed, Cochrane, ISI Web of Science, and Iran Medex) was performed to find all the randomized controlled trials (RCTs) assessed the effects of parenteral immunonutrition in acute pancreatitis. Necessary data were extracted and quality assessment of RCTs was performed with consensus in the study team. Fixed effects model was used to conduct the meta-analysis.

Results: One hundred and ninety four references were found via our search in which 7 articles matched our criteria for enrolling the meta-analysis. Parenteral immunonutrition significantly reduced the risk of infectious complications (RR = 0.59; 95% CI, 0.39–0.88; $p \leq 0.05$) and mortality (RR = 0.26; 95% CI, 0.11–0.59; $p \leq 0.001$). LOS was also shorter in patients who received immunonutrition (MD = −2.93 days; 95% CI, −4.70 to −1.15; $p \leq 0.001$).

Conclusion: Immunonutrients like glutamine and ω-3 FAs added to parenteral formulas can improve prognoses in patients with acute pancreatitis.

1. Introduction

Acute pancreatitis is a systemic immunoinflammatory response to auto-digestion of the pancrease and peri-pancreatic organs. Gallstone and alcohol abuse (usually in men) are the most important causes of acute pancreatitis. The disease is revealed clinically in different patterns ranging from mild forms to severe necrosis of the gland [1].

Patients with acute pancreatitis can rapidly develop nutritional deficiencies due to organs dysfunctions and systemic inflammation; hence nutritional support is very important and even would be critical if the patients had been in malnourished situation before attack [2]. The main predictors of the patients outcomes are: (*i*) severity of the disease, and (*ii*) nutritional status of the patients [3]. There is no specific treatment for acute pancreatitis. In most mild to moderate cases, condition of patients improves spontaneously in a week. During this time, monitoring and supportive treatments such as endoscopic retrograde cholangiopancreatography (ERCP; only in gallstone pancreatitis), intravenous rehydration, and oxygenation may ameliorate the condition [2,4]. Patients with severe acute pancreatitis require more intensive care. Nutritional support is more important and critical due to the significant risk of malnutrition in such patients [5].

Abbreviations: CI, confidence interval; EN, enteral nutrition; ICU, intensive care unit; IMDs, Immunomodulating diets; LOS, length of stay in hospital; MD, mean difference; ω-3 FAs, Omega-3 fatty acids; RCT, randomized controlled trial; RR, relative risk; PN, parenteral nutrition; SE, standard error.

* Corresponding author. Tel./fax: +98 311 7922776.
E-mail address: tinajafari15@yahoo.com (T. Jafari).

http://dx.doi.org/10.1016/j.clnu.2014.05.008

Please cite this article in press as: Jafari T, et al., Parenteral immunonutrition in patients with acute pancreatitis: A systematic review and meta-analysis, Clinical Nutrition (2014), http://dx.doi.org/10.1016/j.clnu.2014.05.008

Until the late 1990s, it was believed that the best way to control the condition of patients with acute pancreatitis is gut rest with or without parenteral nutrition (PN) [5]. Recently, the body of evidence has been increased regarding the use of enteral nutrition (EN) in acute pancreatitis because gut is working [6]. According to the International Consensus Guidelines for Nutrition Therapy in Pancreatitis-2012, EN is preferred over PN in patients with acute pancreatitis. The committee has stated that PN must be restricted to situations in which EN is contraindicated or not feasible (for example when it is difficult to install the feeding tube correctly or when the patients cannot tolerate EN), or as a supplementary therapy when EN cannot provide full nutritional support [7]. In addition to the severity of pancreatitis and presence or absence of necrosis or pseudocysts, conditions like ileus or colonic perforation enforce us to choose PN [8,9].

Owing to immunosuppressive and hyper inflammatory nature of acute pancreatitis, the immune-enhanced products can be useful to improve the immune responses and modulation of inflammation if these products are used enterally or parenterally [6,10,11]. Immunomodulating diets (IMDs) contain immunonutrients such as glutamine or omega-3 fatty acids (ω-3 FAs) that have demonstrated beneficial effects on immune system in experimental models [12]. Glutamine improves lymphocyte functions and contributes to antioxidative defenses. It can also support the intestinal integrity and decrease bacterial translocation; hence reduce systemic inflammatory responses and sepsis, which are important in critical illnesses such as acute pancreatitis [13]. Omega-3 fatty acids may ameliorate the condition of critically ill patients by modulating the production of inflammatory eicosanoids and cytokines; therefore, improve several physiological functions such as immune response, cell proliferation, blood clotting, and inflammation [14]. No adverse effects of the use of ω-3 FAs in parenteral formulas have been reported, but there are few studies in this subject to make a strong deduction. However, there are some evidences asserting that high dosages of ω-3 FAs (≥5 g/d) may increase glucose level, bleeding time, and production of low-density-lipoprotein cholesterol [15,16].

Several meta-analyses failed to produce convincing evidence on the beneficial effects of immunomodulating parenteral nutrition in clinical outcomes of critically ill patients [17–20]. It is important to note that the clinical response depends on the parenteral formula, illness background and severity [5]. Previous meta-analyses grouped different immunomodulating formulas and different types of patients together [18–20]. It may lead to heterogeneity and perhaps masking treatment effects [21]. Therefore, this study aims to evaluate the clinical outcomes of immunoparenteral vs. standard parenteral nutrition in patients with acute pancreatitis by quantitative review of randomized controlled trials (RCTs) published in this field.

2. Materials and methods

2.1. Literature search and selection

The project was registered in PROSPERO, international prospective register of systematic reviews with the registration number: CRD 42013004746. We followed PRISMA criteria to conduct the systematic review and also to report the results of meta-analysis of RCTs [22]. The method and eligibility criteria were documented as a protocol submitted to PROSPERO that was available at the mentioned database. A computerized literature search on four databases (PubMed, Cochrane register of control trials, ISI Web of Science, and Iran Medex) was performed. After achieving consensus within study team on search strategy, RCTs published until June 2013 were identified.

The search strategy for PubMed was: ("acute pancreatitis"[tiab] OR "pancreatitis"[tiab] OR "acute necrotizing pancreatitis"[tiab]) AND ("nutritional support"[tiab] OR" dietary supplementation"[tiab] OR "parenteral nutrition"[tiab] OR "total parenteral nutrition"[tiab] OR "parenteal nutrition solutions"[tiab] OR "immunonutrition"[tiab]) AND ("Fatty Acids, Omega-3"[Mesh] OR "Fish oil"[tiab] OR "glutamine"[tiab] OR "glutamine dipeptides"[tiab] OR "L-glutamine"[tiab] OR "glutamine supplementation"[tiab]). We decided to search other databases with the key words: "parenteral nutrition" AND "acute pancreatitis". Three authors evaluated the total identified articles separately through study of the titles, abstracts, and if necessary, full texts. An additional search was done on the references of the probable related literature to avoid missing articles. The eligibility criteria for articles to be selected were parallel-group RCTs in which a parenteral immunonutrition solution was compared with standard form in patients with acute pancreatitis.

2.2. Inclusion and exclusion criteria

Among the articles with the subject of parenteral nutrition in acute pancreatitis, we selected those consistent with the inclusion and exclusion criteria:

Inclusion criteria:

- RCTs which used parenteral immunonutrition containing glutamine or glutamine dipeptide and compared its effects with standard parenteral nutrition on clinical outcomes of patients with acute pancreatitis.
- RCTs which used parenteral immunonutrition containing ω-3 FAs or fish oil and compared its effects with standard parenteral nutrition on clinical outcomes of patients with acute pancreatitis.
- Both parenteral immunonutrition solution and standard form had to be iso-caloric and also iso-nitrogenus.
- Patients involved were females or males aged 16 or over, with acute pancreatitis whom needed PN therapy, and the parenteral feeding had begun within 72 h after admittance to ICU.
- RCTs that had our desirable clinical outcomes (infectious complications, mortality rate, or LOS).

Trials were included regardless of glutamine or ω-3 FAs doses, and patients could receive additional fluid and electrolytes via supplementation therapy.

Exclusion criteria:

- RCTs evaluated EN, or compared EN with PN.
- RCTs evaluated parenteral immunonutrition in any other condition except acute pancreatitis or gathered all critically illnesses together.

2.3. Quality assessment

Two authors independently assessed the quality of selected articles using modified Jadad score [23]. Intention-to-treat and use of blinded endpoints were added according to Bollhalder et al. [20], with a minor modification in scoring. Each question scored 1 for "Yes", and 0 for "No" answer, thus our new scoring was ranged from 0 to 7. The quality score was not used to exclude the articles; it was used to explain the probable heterogeneity of the results and to achieve a more logical deduction. Final scores were discussed within the study team to consent about doubtful points.

The quality of the evidence for each outcome was assessed according to Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group using GRADE pro software version 3.6. The criteria assessed in each study were consistency and precision of data, directness, the study design and potential

Please cite this article in press as: Jafari T, et al., Parenteral immunonutrition in patients with acute pancreatitis: A systematic review and meta-analysis, Clinical Nutrition (2014), http://dx.doi.org/10.1016/j.clnu.2014.05.008