ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 12, Issue, 01, pp. 53386-53390, January, 2022
https://doi.org/10.37118/ijdr.23769.01.2022

RESEARCH ARTICLE OPEN ACCESS

NUTRITIONAL IMMUMOMODULATORY THERAPY IN PATIENTS WITH GASTRIC NEOPLASMS: AN INTEGRATIVE REVIEW

Bruno Vasconcelos Rodrigues[1]*, Edilayne Gomes Boto [2]and Janssen Loiola Melo Vasconcelos[3]

[1]Federal University of Ceará (UFC), Sobral-Ceará, [2]North Regional Hospital (HRN), Sobral-Ceará, [3]Federal University of Ceará (UFC), Sobral-Ceará

ARTICLE INFO

Article History:
Received 27th October, 2021
Received in revised form
11th November, 2021
Accepted 26th December, 2021
Published online 30th January, 2022

Key Words:

Immunonutrition. Enteral Nutrition. Gastric Carcinoma. Nutritional Therapy.

Corresponding author:
Bruno Vasconcelos Rodrigues

ABSTRACT

This work consists of an integrative, exploratory-descriptive review, which aims to review the available evidence on the role of immunonutrition in the treatment of patients with surgical gastric cancer, being carried out through a retrospective survey of studies that raised data on immunonutrition and its attributions in patients with gastric cancer. The results of this study reveal that the use of immunomodulatory nutrients in people with gastric cancer undergoing gastrectomy showed beneficial effects, being able to positively modulate immunological, metabolic and inflammatory processes, contributing to the acceleration of the recovery process. However, there are still no conclusive results regarding its relationship with survival in the short, medium and long term. Bringing as conclusive precepts the importance of specific methodological tools in order to understand and confirm the properties of the studied compounds and their properties.

Citation: ***Bruno Vasconcelos Rodrigues, Edilayne Gomes Boto and Janssen Loiola Melo Vasconcelos.*** "Nutritional immumomodulatory therapy in patients with gastric neoplasms: an integrative review*", International Journal of Development Research*, 12, (01), 53386-53390.

INTRODUCTION

Gastric carcinoma is one of the main types of malignant neoplasms detected worldwide, with an important incidence and mortality, being even more prevalent in less developed countries. As one of the types of cancer with an incidence, the World Health Organization (WHO) highlights that in 2030 the number of cases will increase to 21.7 million and the number of deaths to 13 million (WHO, 2021). As this is a clinical condition that has its multifactorial genesis, numerous studies are being developed to assist in the treatment and improve the quality of life of this group. It is noteworthy that with technological advances, several treatment modalities are indicated, and the therapy adopted will be closely related to the stage of the disease, clinical and nutritional status of the individual (GONÇALVES, et al., 2020). Thus, based on the predictive factor of nutritional status as one of the primordial points in the recovery process and assertive choice of treatment, some theoretical assumptions highlight immunomodulatory nutritional therapy consisting of omega-3 fatty acids, arginine and nucleotides, as a supporting therapy , providing promising results, since they are able to act on the immune system, providing a reduction in infection rates, fewer postoperative complications and a reduction in the hospital stay (WEIMANN, et al., 2017). In this perspective, this study was designed to review the available evidence on the role of immunonutrition in the treatment of patients with surgical gastric cancer.

METHODOLOGY

This is an exploratory-descriptive integrative review, guided by the following guiding premise: what are the main actions that immunomodulatory nutritional therapy exerts on the clinical outcomes of patients with gastric neoplasia undergoing surgical procedures?. The present study was carried out through a retrospective bibliographic research, where the relevance of the topic was considered from indexed articles, all written in English, Spanish and/or Portuguese, published from the year 2015 to 2020, which studied and/or raised data on immunonutrition and its attributions in patients with gastric neoplasia. The articles were searched in the database of the VHL (Virtual Health Library), SCIELO (Scientific Electronic Library Online), MEDLINE (International Literature on Health Sciences), LILACS (Latin American and Caribbean Literature on Health Sciences) and PubMed. For this, we used search descriptors in English such as the words: "nutrition" AND "surgery" AND "gastrointestinal neoplasms" AND "arginine" AND "fatty acids, omega-3". All selected articles were available in full. The steps for the construction of the integrative review were used as a data search strategy, following the organization proposed by Mendes, Silveira and Galvão (2008). We considered as exclusion criteria the articles that were not categorized according to the year of publication, study in annals and those that did not address the topic under study.

RESULTS AND DISCUSSION

In a search carried out in the health sciences databases, 83 comparative studies were initially found, including clinical trials, cohorts and reviews in general. Among these, 12 articles were selected for bringing specific and essential data related to the topic in question, in addition to meeting the methodological criteria described.

After carrying out the analyzes in the published editions, a significant number of articles of international scope on the subject were observed, 9 in English and 3 in Portuguese. In addition, it is noteworthy that no publication in the Spanish language was elucidated during the search. Given the low number of national articles, important questions about scientific production in the Brazilian territory are addressed. In general, through the data searches, it can be noted that there is great scientific concern about

Table 1.

SYNOPTIC TABLE ARTICLE TITLE	AUTHORS	YEAR	OBJECTIVE	METHODOLOGY	CONCLUSION
Immunonutrition Support for Patients Undergoing Surgery for Gastrointestinal Malignancy: Preoperative, Postoperative, or Perioperative? A Bayesian Network Meta-Analysis of Randomized Controlled Trials	SONG, et al.	2015	Conduct a meta-analysis evaluating the impacts and differences of immunomodulatory enteral nutrition (EIN) compared to standard enteral nutrition (EN) in order to establish the optimal immunonutrition regimen	Meta-analysis protocols (PRISMA-P) and the Cochrane Manual for Systematic Reviews of Interventions were used to guide this study. As a combination of descriptors, the ones to guide the research were used.	The EIN support method is superior to standard EN, and the perioperative EIN regimen is the ideal treatment option for patients undergoing surgery for gastrointestinal cancer due to the low incidence of postoperative infectious and non-infectious complications and shorter postoperative hospital stay. operative.
Cost-effectiveness of perioperative immunonutrition in gastrointestinal oncologic surgery: a systematic review	REIS, *et al.*	2016	Assess immunonutrition in cancer patients undergoing digestive tract surgery and its cost-effectiveness	This is a systematic literature review based on PubMed, Lilacs and SciELO databases. The search was performed with a combination of descriptors in English and Portuguese related to the review topic:	The studies analyzed explained an important reduction in postoperative complications in patients who received immunonutrition, reducing infections and hospitalizations. Also pointing out that the group that received the supplement had a significant reduction in the period of hospitalization compared to the group that did not receive the supplement, translating its effectiveness in also reducing hospital costs
Systematic review with network meta-analysis: comparative efficacy of different enteral immunonutrition formulas in patients underwent gastrectomy	SONG, et al.,	2017	To analyze the comparative efficacies of different immunonutrition enteral nutrition formulas for the support of gastric cancer patients undergoing gastrectomy	This is a direct and network meta-analysis for randomized clinical trials comparing EIN formulas with each other or standard enteral nutrition (SEN) in reducing infectious and non-infectious complications, and length of hospital stay, until January 2016.	EIN is an effective nutritional support regimen to promote the recovery of GC patients undergoing gastrectomy, minimizing postoperative complications and decreasing hospital stay
Effects of omega-3 fatty acids on patients undergoing surgery for gastrointestinal malignancy: a systematic review and meta-analysis	YU, *et al.*	2017	The aim of this systematic review is to assess the potential role of n-3 PUFAs in the outcome of patients with gastrointestinal cancer after surgery	The following databases were used for the research: PubMed, EMBASE, the Cochrane Library, CNKI, Wanfang and VIP databases, using common keywords related to n-3 PUFAs and GI cancer.	The study has important limitations. Intake of n-3 PUFAs varies considerably within countries, and this may explain the heterogeneity across studies. However, we confirm that the addition of n-3 fatty acids improved immune function and reduced the level of inflammation in patients with postoperative gastrointestinal cancer. Therefore, more larger studies are needed, these fatty acids should be widely used in the clinic.
Enteral immunonutrition versus enteral nutrition for gastric cancer patients undergoing a total gastrectomy: a systematic review and meta-analysis	CHENG, *et al.*,	2018	Evaluate the impact of immunonutrition in patients with gastric cancer, based on biochemical, immunological and clinical outcomes.	Four electronic databases (Medline, EMBASE, Scopus and Cochrane library) were used. Heterogeneity was assessed by Cochrane Q and I 2 statistic combined with the corresponding P value. The analysis was performed with RevMan 5.3	Immunonutrition improves cellular immunity, modulates the inflammatory reaction and reduces postoperative complications in GC patients undergoing radical gastrointestinal surgery. In addition, clinical outcomes such as systemic inflammatory response syndrome (SIRS) and postoperative complications were significantly reduced in the EIN group
Effects of the use of immunomodulating formulas in surgical patients with cancer of the gastrointestinal tract	CARMO E FORTES	2019	To investigate the effects of using immunomodulating formulas on clinical outcomes and rates of perioperative and hospital complications in surgical patients with cancer of the gastrointestinal tract	This is an integrative review in which descriptors in indexed databases were used.	The studies analyzed emphasize the importance of using immunomodulating formulas for surgical and oncological patients, in specific periods (especially throughout the perioperative period), due to their beneficial effects on the nutritional status and immunity
Effects of nutritional interventions on nutritional status in patients with gastric cancer: A systematic review and meta-analysis of randomized controlled trials	RINNINELL A, *et al.*,	2020	Evaluate the effects of these nutritional interventions on the nutritional status of patients with GC undergoing gastrectomy and/or chemotherapy	This is a systematic review of the literature carried out in the Pubmed, Web of Science and Scopus databases.	The analysis showed promising results of nutritional supplement interventions on immunonutrition and nutritional status, based on optimal provision of nutritional support in gastric cancer. However, its correlation with nutritional status is not yet clear, indicating the need for further studies.

this topic, having seen the prevalence and incidence of cases of gastric cancer on a worldwide scale and its impact on public health and quality of life of the population. According to the synoptic view, it is possible to see that the researches carried out comprise some methodological classes, such as: Literature Reviews (7 studies) and Clinical essays (5 studies). Of the selected studies, all presented important data suggesting the potential effect of nutritional therapy added with immunomodulator in the mitigation of postoperative complications, demonstrating that its use throughout the perioperative period was able to reduce the inflammatory level caused by the endocrine, metabolic and immunologic of surgical trauma.

In addition, it is noteworthy that the studies analyzed indicate that immunomodulatory enteral nutrition, when compared to standard enteral nutrition formulas, demonstrate immunological benefits that impact on the low incidence of infectious and non-infectious postoperative complications and shorter hospital stay, reducing associated costs. Also based on the findings, as promising clinical outcomes, an important reduction in events associated with systemic inflammatory response syndrome (SIRS) and postoperative complications in the groups that received immunonutrition is cited. However, the relationship with nutritional status is not yet clearly defined in the literature, requiring further research in the area.

Table 2. Researches that address in vivo clinical trials, between the years 2015 and 2020

SYNOPTIC TABLE					
ARTICLE TITLE	**ARTICLE TITLE**	**ARTICLE TITLE**	**ARTICLE TITLE**	**ARTICLE TITLE**	**ARTICLE TITLE**
Nutrition and Immune-Modulatory Intervention in Surgical Patients With Gastric Cancer	RODRIGUES, et al.,	2017	Evaluate the effect of an immunomodulatory diet in patients with gastric cancer and identified the parameters associated with postoperative results	This is a prospective observational intervention study in patients with GC at the Cancer Hospital of the Instituto Nacional do Câncer (INCA, Rio de Janeiro, Brazil). Inclusion criteria were as follows: patients with previously untreated CG with exclusive surgical indication who were referred from the surgical clinic to the nutrition clinic, including women and men aged between 20 and 75 years. Patients were referred to the nutrition clinic for nutritional counseling and adjuvant immunonutrition supplementation	The high-protein/caloric supplementation and the immunomodulating diet, with the regular diet, were able to maintain the nutrition and the immune status of patients with Gastric Cancer in the pre- and postoperative periods, even when the disease was in advanced stages. This suggests that, under such conditions, supplements positively affect nutritional status, providing enough nutrients to meet nutritional needs.
The Impact of Postoperative Enteral Immunonutrition on Postoperative Complications and Survival in Gastric Cancer Patients - Randomized Clinical Trial	SCISLO, *et al*.,	2018	Evaluate the impact of postoperative immunomodulatory enteral nutrition on postoperative complications and survival of patients with gastric cancer	This is a clinical, prospective and randomized study. A group of 98 patients with gastric cancer was randomly assigned to post-operative immunomodulatory enteral nutrition or standard enteral nutrition. Postoperative complications, mortality, 6 months and 1 year survival were analyzed	Postoperative immunomodulatory enteral nutrition can reduce respiratory complications and postoperative mortality compared to standard enteral nutrition. Despite this effect, it did not improve the 6-month and 1-year survival in the immunomodulation group.
Combination of arginine, glutamine, and omega-3 fatty acid supplements for perioperative enteral nutrition in surgical patients with gastric adenocarcinoma or gastrointestinal stromal tumor (GIST): A prospective, randomized, double-blind study	MA, *et al.*	2018	Evaluate the effectiveness of immunomodulatory nutritional therapy in patients with gastrointestinal neoplasia and gastric adenocarcinoma undergoing surgery	This is a prospective, randomized, double-blind study that recruited patients with gastric adenocarcinoma or gastric GIST undergoing elective curative surgery. These patients were randomly assigned to the study group, receiving EN enriched with immunomodulatory nutrients, or the control group, receiving standard EN from 3 days before surgery until day 14 postoperatively or discharge. Laboratory and inflammatory parameters were evaluated preoperatively on the 14th postoperative day or at discharge.	The effects of EN enriched with immunomodulatory nutrients on laboratory parameters were comparable to the standard formula. EN enriched with immunomodulatory nutrients had no significant anti-inflammatory effect in patients undergoing elective surgery for gastric cancer and resulted in mild inflammation, as a small population study in the short-term perioperative use of EN enriched with immunomodulatory nutrients with some limitations mentioned above, which may be a part of the causes
Effect of Enteral Immunonutrition on Immune, Inflammatory Markers and Nutritional Status in Gastric Cancer Patients Undergoing Gastrectomy: A Randomized Double-Blinded Controlled Trial	LI, *et al*.,	2020	Evaluate the effect of immunomodulatory enteral nutrition on immune function, response to inflammation and nutritional status when compared to standard enteral nutrition	A total of 124 patients with gastric cancer after gastrectomy were randomized to receive either immunomodulatory enteral nutrition at the beginning of the 5-day postoperative period (formula enriched with arginine, glutamine, omega-3 fatty acids and nucleotide) or standard enteral nutrition	Early postoperative immunomodulatory enteral nutrition significantly improves immune function and inflammatory response in gastric cancer patients undergoing gastrectomy
Postoperative complication rate and survival of patients with gastric cancer undergoing immunonutrition: A retrospective study	CLAUDINO, *et al*.,	2020	Evaluate the effect of preoperative immunonutrition on the rate of postoperative complications and survival of patients with gastric cancer	A retrospective cohort was constituted after data collection from hospitalized patients with gastric cancer. Postoperative complications classified according to the Clavien-Dindo classification system, length of hospital stay, readmissions, and 6-month, 1-year, and 5-year survival rates were analyzed.	Preoperative immunonutrition in patients with gastric cancer did not reduce postoperative complications or length of hospital stay. More studies are needed to confirm the benefit of immunonutrition supplementation for overall survival when combined with other protective factors

Corroborating the above findings, Niu et al. (2021) inferred that immunonutrition significantly reduced the white blood cell count and the level of C-reactive protein in patients, as well as the risk of surgical site infection when compared to patients who received standard nutrition. It is noteworthy that hospital stay was especially shorter in patients who received immunonutrition after surgical resection of gastric cancer. Assessing the effects of an immunomodulatory diet associated with the consumption of caloric-protein nutritional supplements, Rodrigues et al. (2017) elucidated, in their prospective clinical trial, that such measures during the perioperative period brought promising results in the immune response in patients who required procedures invasive surgical procedures such as gastrectomy, being able to exert a significant improvement in the adaptive and immunological response to metabolic and surgical trauma. Corroborating, Li et al. (2020), evaluated the application of a standard enteral formula versus an enteral formula with immunonutrients (arginine, nucleotide and omega-3), where it was possible to infer, after clinical analysis, that the immunomodulatory therapy, when instituted early, significantly improves the immune and inflammatory response, favoring a significant reduction in future complications resulting from surgical trauma and the catabolic effect that gastric carcinoma triggers.

However, Claudino et al. (2020), when investigating the impacts that immunonutrition is capable of having in reducing the length of hospital stay, readmission rates and survival, they found some promising data regarding the reduction in hospital stay, this fact is associated with a reduction in postoperative complications. However, when readmission and survival rates were evaluated, these presented inconsistent data expressing the need for additional studies for better elucidation. This fact is reaffirmed in the research carried out by Scislo et al. (2018) and Ma et al. (2018), that although the anti-inflammatory effect that immunomodulation offers to patients is expressive, in the long term its effects are still limited, demonstrating the importance of accurately assess which associated factors may justify such assumptions. According to Cui, Liao and Zhao (2020), when the first proposals on immunonutrition were dated approximately 20 years ago, its effect on immune function was still controversial. This fact is perpetuated today, and this questioning may be associated with the heterogeneity of the methodological designs of the studies, as several high-quality meta-analyses validate the benefit conferred by immunonutrients in different fields and surgical treatments. It is necessary to adopt more complex studies with well-defined methodologies in order to elucidate the properties of these nutrients in human health.

REFERENCES

CARMO, S.G.; FORTES, RC Effects of the use of immunomodulatory formulas in surgical patients with cancer of the gastrointestinal tract, Revisa (online), v.8, n.1, p.96-111, 2019. Available at: <Error! Hyperlink reference not valid.> Accessed on 23/08/2021

CHENG, Y.; ZHANG, J.; ZHANG, L.; WU, J.; ZHAN, Z. Enteral immunonutrition versus enteral nutrition for gastric cancer patients undergoing a total gastrectomy: a systematic review and meta-analysis. BMC Gastroenterol, n.18, v.1, 2018. Available at: <https://pubmed-ncbi-nlm-nih.ez11.periodicos.capes.gov.br/29338698/> . Accessed on: 04/09/2021

CLAUDINO, M.M.; LOPES, J.R.; RODRIGUES, V.D.; PINHO, N.P.; MARTUCCI, R.B. Postoperative complication rate and survival of patients with immunonutrition: A retrospective study. Nutrition, v.70, 2020. Available at: <https://pubmed-ncbi-nlm-nih.ez11.periodicos.capes.gov.br/31739174/>. Accessed on 04/09/2021.

CUI, M.; LIAO, Q.; ZHAO, Y. Enteral Immunonutrition Promotes Immune and Inflammatory Recovery after Surgery for Gastric Cancer. Journal of Investigative Surgery, v.33, 2020. Available at: <https://www.tandfonline.com/doi/full/10.1080/08941939.2019.1583295>. Accessed on: 05/09/2021.

GONÇALVES, F.S.; SARGES, R.M.; RAMOS, M.A.; SOUZA, M.J.C.; NEMER, CR.B.; MENEZES, R.A.O. Clinical epidemiological profile of gastric cancer: integrative review, Pubsaude, v.3, 2020. Available at: <https://pubsaude.com.br/revista/perfil-clinico-epidemiologico-do-cancer-gastrico-revisao-integrativa/ .> Accessed on: 09/21/2021

LI, K.; XU, Y.; HU, Y.; LIU, Y.; CHEN, X.; ZHOU, Y. Effect of Enteral Immunonutrition on Immune, Inflammatory Markers and Nutritional Status in Gastric Cancer Patients Undergoing Gastrectomy: A Randomized Double-Blinded Controlled Trial. Journal of Investigative Surgery, v.33, 2020. Available at: <https://www.tandfonline.com/doi/full/10.1080/08941939.2019.1569736 >. Accessed on: 04/09/2021

MA, C.; TSAI, H.; SU, W.; SUN, L.; SHIH, Y.; WANG, J. Combination of arginine, glutamine, and omega-3 fatty acid supplements for perioperative enteral nutrition in surgical patients with gastric adenocarcinoma or gastrointestinal stromal tumor (GIST): A prospective, randomized, double-blind study, J Postgrad Med, v.64, n.3, p. 155-163, 2018. Available at: < https://pesquisa.bvsalud.org/portal/resource/pt/mdl-29848836>. Accessed on: 23/08/2021

MENDES, K. D. S; SILVEIRA, R. C. C. P.; GALVÃO, C. M. Integrative review: research method for incorporating evidence in health and nursing. Text Context Nursing, Florianópolis, v. 17, no. 4, p.758-64, 2008.

NIU, J.W.; ZHOU, L.; LIU, Z.Z.; PEI, D.P.; FAN, W.Q.; NING.N. A Systematic Review and meta-analysis of the effects os perioperative immunonutrition in gastrointestinal câncer patientes. Nutr cancer, v.73, n.2, p.252-261, 2021. Available at: <https://www.tandfonline.com/doi/abs/10.1080/01635581.2020.1749291?journalCode=hnuc20>. Accessed on: 12/09/2021

REIS, A.M.; KABKE, G.B.; FRUCHTENICHT, A.V.G.; BARREIRO, T.D.; MOREIRA, L.F. Cost-effectiveness of perioperative immunonutrition in gastrointestinal oncologic surgery: a systematic review, ABCD Brazilian files of digestive surgery, n.29, v.2, p.121-125, São Paulo, 2016. Available at: https://www.scielo.br/j/abcd/a/KFS5dXJTmvZH4JZt9Nzy57H/?lang=pt&format=pdf. Accessed on 21/08/2021

RINNINELLA, E.; CINTONI, M.; RAOUL, P.; POZZO, C.; STRIPPOLI, A.; BRIA, E.; TORTORA, G.; GASBARRINI, A.; MELE, M.C. Effects of nutritional interventions on nutritional status in patients with gastric cancer: A systematic review and meta-analysis of randomized controlled trials. Clin Nutr ESPEN, v.38, p. 28-42, 2020.

RODRIGUES, V.D.; PINHO, N.B.; ABDELHAY, E.; VIOLA, J.P.D.; CORREIA, M.I.; MARTUCCI, R.B. Nutrition and Immune-Modulatory Intervention in Surgical Patients With Gastric Cancer. Nutr Clin Pract, n.32, p. 122-129, 2017.

SCISLO, L.; PACH, R.; NOWAK, A.; WALEWSKA, E.; GADEK, M.; BRANDT, P.; PUTO, G.; SZCZEPANIK, A.M. KULIG, J. The Impact of Postoperative Enteral Immunonutrition on Postoperative Complications and Survival in Gastric Cancer Patients - Randomized Clinical Trial. Nutr Cancer, v.70, p. 453-459, 2018.

SONG, G.; M.; TIAN, X.; ZHANG, L.; OU, Y.; YI, L.; SHUAI, T.; ZHOU, J.; ZENG, Z.; YANG, H. Immunonutrition Support for Patients Undergoing Surgery for Gastrointestinal Malignancy: Preoperative, Postoperative, or Perioperative? A Bayesian Network Meta-Analysis of Randomized Controlled Trials, Medicine (Baltimore), v.94, n.29, July, 2015.

SONG, G.M.; LIU, X.L.; BIAN, W.; WU, J.; DENG, Y.H.; ZHANG, H.; TIAN, X. Systematic review with network meta-analysis: comparative efficacy of different enteral immunonutrition formulas in patients underwent gastrectomy. Oncotarget, v.8, 2017. Available at: <https://www.oncotarget.com/article/15580/text/>. Accessed on 04/09/2021

WEIMANN, A.; BRAGA, M.; CARLI, F.; HIGASHIGUCHI, T.; HUBNER, M.; KLEK, S.; LAVIANO, A.; LJUNGQVIST, O.; LOBO, D.N.; MARTINDALE, R.; WAITZBERG, D.L.; BISCHOFF, S.C.; SINGER, P. ESPEN guideline: Clinical nutrition in surgery. Clinical nutrition, v.36, p. 623-650, 2017. Available at: < https://www.espen.org/files/ESPEN-guideline_Clinical-nutrition-in-surgery.pdf>. Accessed on: 20/09/2021.

WORLD HEALTH ORGANIZATION, 2021. Cancer. Available at: https://www.who.int/news-room/fact-sheets/detail/cancer>. Accessed on: 11/08/2021

YU, J.; LIU, L.; ZHANG, Y.; WEI, J.; YANG, F. Effects of omega-3 fatty acids on patients undergoing surgery for gastrointestinal malignancy: a systematic review and meta-analysis, BMC Cancer, v.17, n. 271, 2017.

****