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EDITORIAL

Are we jumping the gun with pharmaconutrition (immunonutrition) in gastrointestinal onoclogical surgery?

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Abstract

Over the last 20 years there has been considerable research into the use of immunonutrition, also referred to as pharmaconutrition, in the management of patients undergoing and recovering from elective gastrointestinal surgery for malignancy. In this group of patients, the use of pharmaconutrition seems to confer superior outcomes to standard nutrition formulations with regards to postoperative infective complications and length of hospital stay. It is therefore frequently recommended for use in elective gastrointestinal oncological surgical populations. However, it remains unclear whether the data supporting these recommendation is robust. Studies reporting improved outcomes with pharmaconutrition frequently compare this intervention with non-equivalent control groups, do not report on the actual nutritional provision received by study participants, overlook the potential impact of industry funding on the conduct of research and do not adopt a multi-disciplinary approach to the research undertaken. For these reasons, an urgent critical re-appraisal of the use and recommendations of pharmaconutrition in this group of patients is warranted to resolve some of the above mentioned issues.

Key words: Pharmaconutrition; Immunonutrition; Arginine; Gastrointestinal malignancy; Elective surgery

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INTRODUCTION

Nutrition is an important consideration in the management of patients undergoing and recovering from elective gastrointestinal surgery for malignancy. Malnutrition is highly prevalent in this group of patents due to the numerous predisposing factors such as cancer cachexia, dysphagia, small or large bowel obstruction, nausea, vomiting, diarrhoea and/or loss of appetite - all of which are often exacerbated by the effect of neo-adjuvant or adjuvant chemoradiotherapies[1]. Given that malnourished patients with gastrointestinal malignancies have been shown to experience a greater than two-fold increase in postoperative complications and require significantly longer hospital admissions than their well nourished counterparts[1], timely and appropriate nutritional intervention has the potential to positively influence postoperative surgical

outcomes in this patient group[2].

In surgical populations nutrition provides important substrates such as proteins and micronutrients for wound healing, as well as energy derived from lipids and carbohydrates to power the metabolic processes which facilitate recovery while preserving lean body tissue. In addition to this traditional view of nutrition, the last two decades has seen the development of the concept of providing supraphysiological doses of nutrients (primarily arginine, often in conjunction with omega-3 fatty acids, RNA, antioxidants and/or glutamine) to support the immune system in times of physiological stress[3]. This concept has been referred to as "immunonutrition", and more recently as "pharmaconutrition"[3].

PHARMACONUTRITION IN ELECTIVE SURGICAL ONCOLOGICAL PATIENTS

Much has been written about the use of pharmaconutrition in patients receiving elective surgery for gastrointestinal malignancies. In this group of patients when compared with conventional nutritional provision, pharmaconutrition has been reported to decrease postoperative infective complications and length of hospital stay, both of which have positive financial implications for the hospital and insurance companies[4-9]. While there have been concerns about increased mortality rates in a critically ill population, when feeding products containing high levels of arginine[6], no such effect is reported with the use of pharmaconutrition in elective surgical populations[4-9].

This general conclusion has recently gained support from six recent meta-analyses investigating the benefits of pharmaconutrition in elective gastrointestinal surgical patients, most of whom were oncology patients[5]. Given the increasing support for the benefits of pharmaconutrition, it is not surprising that many practice guidelines now incorporate the available evidence and recommend the use of these products in this population[10,11]. However, it remains unclear whether the current evidence underpinning the use pharmaconutrition in this patient group is sufficiently robust.

LIMITATIONS OF STUDIES INVESTIGATING PHARMACONUTRITION IN ELECTIVE GASTROINTESTINAL ONCOLOGICAL PATIENTS

While many trials and meta-analyses are now adopting CONSORT[12] and PRISMA[13] reporting guidelines, these were never designed to provide guidance on or evaluation of important considerations regarding a study's protocol. As a result, a well reported study or analysis may still contain fundamental flaws that can produce spurious results. For example, close examination of a large percentage of the papers that report investigations into the benefits of pharmaconutrition do not use equivalent control groups or control formulas. Pharmaconutrition has been studied in comparison to no nutritional intervention (nil by mouth)[14] or to control products that contain 50% to 80% less protein than the intervention product[15-20]. The effect of which may be to produce a benefit favouring the intervention product (i.e., pharmaconutrition group), independent of the immune-modulating components, due to a greater nitrogen provision. Pharmaconutrition has also been given as a preoperative supplement in addition to dietary intake, for which no equivalent product was provided to the control group[21-23]. The issue of non-equivalent control groups is a frequent concern in studies that are heavily funded by industry, and possibly representing a deliberate attempt to favour the product under investigation[24]. Given the high percentage of studies funded by companies that produce pharmaconutrition products, this issue warrants greater scrutiny than is currently evident in the literature on this topic.

Another issue of concern is the limited reporting of the actual volumes of pharmaconutrition or control formula received by patients randomised to each intervention. While most studies report the desired nutritional goals, few report the average volumes received by the patients in each group. Because of this, protocol violations or feed intolerance may go undetected, possibly resulting in inappropriate conclusions being drawn from results where significant differences in macronutrients are provided between groups, thus potentially providing greater clinical benefit to whichever intervention group receives nutrition closer to adequate or goal requirements.

Inspection of authorship of many of the papers investigating pharmaconutrition reveals a lack of multidisciplinary involvement, with surgical departments accounting for the large majority of authors. Given that nutrition is the particular area of expertise of dietitians and nutrition professionals, it would seem reasonable that multi-disciplinary involvement in a research topic so closely tied with nutritional provision should involve dietetic consultation both in the protocol development stages and throughout the trial. The multi-disciplinary collaboration with closer dietetic involvement would alleviate some of the issues outlined above and lead to a better design of randomised controlled trials in the future.

CONCLUSION

Pharmaconutrition represents an exciting paradigm shift in the way health professionals conceptualise nutrition and its potential to facilitate superior postoperative outcomes in elective surgical oncological patients is appealing. However, as in all evidence based practice, it remains important to critically appraise the available data. The increasing trend towards recommending pharmaconutrition may be premature, given that the concerns expressed above have received little mention in the literature, and no studies, to date, have adequately addressed them. It would behove health professionals to carefully re-examine the supporting literature before adopting pharmaconutrition as standard practice for patients receiving elective surgical

management of gastrointestinal malignancies.

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