TITLE

Letter to the Editor: Early Enteral Nutrition Within 24 h of Intestinal Surgery Versus Later Commencement of Feeding: A Systematic review and Meta-analysis

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SECTION OF THE JOURNAL

Letter to the Editor

SOURCES OF SUPPORT

None

Dear Dr Lewis, Andersen and Thomas:

It was with great interest that we read your most recent systematic review and meta-analysis addressing the important issue of early versus later commencement of enteral feeding in gastrointestinal surgery patients [1]. While your 2006 Cochrane review [2] has clear merit in that it expands on the number of studies and thus the power of your earlier analysis [3], we feel that the present study is essentially a duplication of your Cochrane effort, although with slightly different conclusions and adds nothing new to the literature.

While we concur with your overall conclusions about 'nil by mouth' conveying no benefit over early enteral feeding in terms of post-surgical outcomes in gastrointestinal surgery, there are several aspects of your analysis that in our opinion threaten to undermine your otherwise valid conclusions. Firstly, your inclusion of Helslin et al's [4] study utilising an immune-enhancing enteral feed product in 8% (n=97) of your pooled sample potentially confounds your results and limits the conclusions that can be made about benefits to postoperative infections conferred by early feeding, as immune-enhancing nutritional products may be independently associated with reduced risk of post operative complications and wound infections [5-8] in elective surgical oncology patients.

Secondly, a total of 10% (n=118) of your pooled sample are reported to have received nutrition distal to the anastomosis [4, 9-11]. Given that fear of anastomotic dehiscence has been purported as a primary reason for avoidance of early feeding, we feel that any meta-analysis attempting to refute these concerns regarding anastomotic dehiscence must include studies providing nutrition proximal to

anastomosis and not distal. It is therefore our expectation that studies where a substantial numbers of subjects are fed distal to the surgical site would be excluded. Failure to do so invalidates your ability to make comments on the benefit or harm posed by early feeding with regard to anastomotic breakdown.

Thirdly, as you have rightly stated, malnutrition is a common finding in patients undergoing elective gastrointestinal surgery [12, 13] and has been shown to be independently associated with poor outcomes such as delayed wound healing, development of postoperative complications and mortality in surgical patients [12-16]. For this reason we feel it is of vital importance that if early feeding be provided, it should be possible to consume a balanced, nutritionally complete intake within the early feeding period, if an adequate amount be consumed. Consequently we question the benefit of including studies that provide only clear fluids within 24-hours postoperatively[17] as it is impossible to meet nutritional requirements on this type of diet due to its absence of protein, lipids and many micronutrients[18].

Finally, we draw attention to a number of studies that appear to us to meet your inclusion criteria that have been omitted from your analysis. The study by Feo et al[19] was reported in your Cochrane review as being excluded as “both treatment groups were allowed liquid diet, therefore [there was] not control group to early feeding” [2]. The cited paper, however, clearly states liquid diet in the NBM group was only provided after passage of flatus[19], thereby meeting your inclusion criteria. Furthermore there are at least four eligible studies[20-24] we have located that do not appear to have been identified in your searches in which all or subgroups from the study population may provide additional numbers for your study.

From a statistical point of view we note that you report on both fixed and random effects models in the most recent paper[1], while only the former is reported in your earlier publications[2, 3]. In recent days, the relative appropriateness of of fixed versus random effect model has certainly received a considerable attention. The fixed effect meta-analysis assumes that there is one identical true treatment effect common to every study. However this is not the case in your meta-analysis (or in any meta-analysis). The random effects model of meta-analysis is an alternative approach to meta-analysis that does not assume that a common ('fixed') treatment effect exists. The random effects model assumes that the true treatment effects in the individual studies may be different from each other. That means there is no single number to estimate in the meta-analysis, but a distribution of numbers. The most common random effects model also assumes that these different true effects are normally distributed. Simply the random effect model allow for the possibility that population vary from study to study. The meta-analysis therefore estimates the *mean* and *standard deviation* of the different effects. As described above, there are several important differences among the interventions provided within the studies included in your meta-analysis that potentially impacts on treatment effects, and therefore a random effects model is likely the most appropriate model in this setting and fixed effect model should be discarded. However we were disappointed to see that the figures reported in your latest paper were solely that of the fixed effects model and not the random effects outcomes which further weakens your paper. An error in reporting the wound infection, under “Outcomes” subheading, of one out of 81 (not zero out of 16) in the control group along with the associated percentages may also be noted.

We agree that the mounting body of evidence showing no demonstrable harm from early enteral nutrition provision postoperatively justifies a large adequately powered clinical trial that in particular places a greater focus on linking nutritional intake to outcomes. This latter aspect has largely been omitted from investigations on this topic to date, to the detriment of our more informed understanding of this topic. In view of the absence of data in this area we find the closing comments of your (?latest paper) Cochrane review stating “patients only take a small proportion of required energy in the first few days post operation”[2] puzzling. We can only assume this comment is largely based on your clinical experience, which without the objective data to support it has no place in a Cochrane or any other similar publications [2, 3].

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