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Review

Probiotics and synbiotics for the prevention of postoperative infections following abdominal surgery: a systematic review and meta-analysis of randomized controlled trials

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SUMMARY

Background: Postoperative infections, particularly surgical site infections (SSIs), cause significant morbidity and mortality. Probiotics or synbiotics are a potential prevention strategy.

Aim: To evaluate the efficacy of probiotics/synbiotics for reducing postoperative infection risk following abdominal surgery.

Methods: We searched AMED, Central, CINAHL, Embase, Medline, and grey literature for randomized controlled trials of elective abdominal surgery patients administered probiotics or synbiotics compared to placebo or standard care. Primary outcome was SSIs. Secondary outcomes were adverse events, respiratory tract infections (RTIs), urinary tract infections (UTIs), combined infections, length of hospital stay, and mortality. Using random-effects meta-analyses, we estimated the relative risk (RR) or mean difference (MD) and 95% confidence interval (CI). Tests were performed for heterogeneity, subgroup and sensitivity analyses were conducted, and the overall evidence quality was graded.

Findings: We identified 20 trials ($N = 1374$ participants) reporting postoperative infections. Probiotics/synbiotics reduced SSIs (RR: 0.63; 95% CI: 0.41–0.98; $N = 15$ studies), UTIs (RR: 0.29; 95% CI: 0.15–0.57; $N = 11$), and combined infections (RR: 0.49; 95% CI: 0.35–0.70; $N = 18$). There was no difference between groups for adverse events (RR: 0.89; 95% CI: 0.61–1.30; $N = 6$), RTIs (RR: 0.60; 95% CI: 0.36–1.00; $N = 14$), length of stay (MD: −1.19; 95% CI: −2.94 to 0.56; $N = 12$), or mortality (RR: 1.20; 95% CI: 0.58–2.48; $N = 15$).

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Conclusion: Our review suggests that probiotics/synbiotics reduce SSIs and UTIs from abdominal surgeries compared to placebo or standard of care, without evidence of safety risk. Overall study quality was low, owing mostly to imprecision (few patients and events, or wide CIs); thus larger multi-centered trials are needed to further assess the certainty in this estimate.

Introduction

Patients undergoing surgery are at high risk of hospital-acquired infections (HAIs); surgical site infections (SSIs) are the most frequent HAI in the surgical population, with the highest rates (2–20%) for abdominal surgeries.[1,2] Patients with SSIs have up to twice the mortality risk, an increased length of hospital stay (LOS), and require resources costing the healthcare system about US$25,000 per case.[2–4]

A promising novel infection prevention strategy is the administration of probiotics, which are live microbial preparations that may confer a positive benefit to the host when taken in sufficient amounts.[5] Probiotics could be used in combination with prebiotics, known as synbiotics. Prebiotics are non-digestible fibres that stimulate bacterial growth, and are thought to improve the effects of probiotics.[6] There has been a growing interest in using these agents for preventing SSIs, as well as other frequently occurring HAIs, including respiratory tract infections (RTIs), and urinary tract infections (UTIs).[7–9] A recent survey of consultant gastroenterologists and surgeons practising in the UK showed that many of those surveyed (123/177) already recommend or prescribe probiotics to their patients for these and other conditions.[10] However, whereas numerous studies show that probiotics are safe, there have been case reports of bacteraemia or fungaemia, though these are rare and usually among immunocompromised patients or those with underlying comorbidities.[11,12] If probiotics/synbiotics are effective and safe, their low cost and ease of administration would make them a useful SSI prevention strategy.

Three systematic reviews on probiotics/synbiotics for preventing infections in abdominal surgery patients have been published to date, but none quantified adverse events, nor formally assessed risk of bias, and only two had independent and duplicate study selection.[13–15] Furthermore, seven additional trials have been published since the most recent review.[15] Using advanced evidence synthesis methods, we conducted a systematic review to assess both the efficacy and safety of probiotics and synbiotics for the prevention of postoperative infections in patients undergoing elective abdominal surgery.[16,17]

Methods

Literature search

Five primary databases were searched up to February 2014: AMED (1985–), Central (1995–), CINAHL (1981–), Embase (1974–), and Medline (1946–). We used subject terms, keywords, and a randomized controlled trial (RCT) filter, developed with a librarian (L.B.) and validated with the Cochrane Collaboration filter.[18] A detailed search strategy is presented in Supplementary Table I. There were no language restrictions. Additionally, we searched biographies of included studies, the metaRegister of Controlled Trials, and conference proceedings from 2000 to 2014 from the American Society of Colon and Rectal Surgeons (ASCRS), International Hepato-Pancreato-Biliary Association (IHPBA), British Society of Gastroenterology (BSG), and World Transplant Congress (WTC).

Study selection and data extraction

We included RCTs of participants (any age) who had elective abdominal surgery (any type, for any indication), who were administered probiotics or synbiotics (any species, any strain, any dose, before and/or after surgery), compared to participants given standard care or placebo, and who reported on postoperative infections. Based on a recent systematic review, we accepted the use of prebiotics alone as placebo because no evidence exists demonstrating a direct link between prebiotics and the incidence of infections.[19]

Titles and abstracts of articles were screened by two reviewers (L.L., K.Q.) independently. Studies deemed potentially eligible proceeded to independent and duplicate full-text review. At both stages, disagreement was resolved by consensus or discussion with a third party (B.C.J., D.M.). Inter-rater agreement was calculated using the weighted kappa coefficient.[20] Data were extracted by reviewers (L.L., K.Q.) independently, using standardized, pilot-tested forms.

Outcomes

The primary outcome was SSI, and our secondary outcomes were adverse events, RTI, UTI, a composite of all types of infection (hereafter referred to as combined infections), LOS, and mortality. SSIs were accepted when defined as wound or superficial incisional infection, deep incisional infection, or organ/space infection.[21] Surgery may result in numerous complications; thus we considered any definitions of adverse events as reported in the original articles. We accepted the author's definitions of RTIs, UTIs, and all infections. If information was missing or unclear, we attempted to contact the authors.

Assessment of risk of bias

Two reviewers independently assessed the risk of bias using standardized instructions based on the Cochrane Handbook (L.L., K.Q.).[22] Surgical site infections, adverse events, RTIs, UTIs and combined infections were considered subjective outcomes, unless defined objectively (e.g. radiograph, cultures).[23] LOS and mortality were considered objective outcomes. If blinding and allocation concealment was inadequate, subjective outcomes were considered at high risk of bias,