Proceedings of the Nutrition Society (2009), **68 (OCE1)**, E4 doi:10.1017/S0029665109001451

OCE Malnutrition Matters, Joint BAPEN and Nutrition Society Meeting, 4–5 November 2008, Harrogate

Safety of probiotics in patients receiving enteral or parenteral nutrition: a systematic review of trials and case reports

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Probiotics are generally considered to be safe for consumption by healthy human individuals. However, they are increasingly being used for patients receiving nutritional support for the prevention of diarrhoea in enteral nutrition or for the prevention of infection in patients receiving enteral or parenteral nutrition on the intensive care unit[1]. The safety of probiotics in these patients cannot be assumed due to both the patient's underlying clinical condition and altered route of probiotic delivery that may allow increased gastrointestinal survival due to higher gastric pH in nasogastric feeding or total bypass of gastric acid in nasojejunal feeding. Therefore, the aim of the present study was to systematically review the evidence for the safety of probiotics in patients receiving enteral or parenteral nutrition.

A systematic review was conducted in line with Cochrane guidelines for conducting systematic reviews of interventions. Extensive keyword searching of six electronic databases was conducted, together with hand-searching of relevant journals for conference abstracts (including American Society for Parenteral and Enteral Nutrition, British Association for Parenteral and Enteral Nutrition, European Society for Parenteral and Enteral Nutrition) and reference lists of included papers and relevant reviews. Key opinion leaders (n 68) were contacted in order to retrieve unpublished data or citations that may not have been identified elsewhere. Inclusion criteria were English-language clinical trials or case reports of the enteral administration of probiotics to neonatal, paediatric or adult patients receiving either enteral or parenteral nutrition.

In total forty-one clinical trials fulfilled the inclusion criteria, detailing the enteral administration of probiotics to more than 3000 patients receiving enteral or parenteral nutrition. However, only one of these trials specifically investigated the safety of probiotics through prospective routine screening to detect the presence of an infection that was microbiologically attributable to the probiotic administered. That study used *Lactobacillus caseii* Shirota in twenty-eight paediatric patients and did not detect its presence in serum, urine or on skin and did not detect any adverse effects resulting from probiotic administration[2]. The remaining forty trials investigated the efficacy of the probiotic in reducing adverse events (e.g. diarrhoea, nosocomial infections, necrotizing enterocolitis) but did not specifically screen for infections arising as a result of the probiotic itself. Of these, one trial in patients with severe acute pancreatitis reported an increased risk of mortality (relative risk 2.53; $P=0.01$) and ischaemic bowel (0% control, 6% intervention; $P=0.004$) in patients receiving a novel probiotic preparation delivered nasojejunally[3]. Ten case reports detailing adverse events occurring in twenty-one patients receiving enteral or parenteral nutrition who had received probiotics via enteral administration were also identified.

In general, lactobacilli and bifidobacteria probiotics appear to be safe in patients receiving enteral or parenteral nutrition. Although statistical aggregation of the clinical trials and case reports is not possible, it would appear that probiotics should be used cautiously in patients receiving enteral or parenteral nutrition who are immuno-compromised, have congenital heart disease, have central venous catheters *in situ*, are likely to have increased gastrointestinal permeability or in whom the probiotic is being delivered nasojejunally. However, making generalized conclusions is impeded because of the diversity of patient groups investigated and the probiotic strains, doses and routes of administration used in the trials.

1. Whelan K (2007) *Proc Nutr Soc* **66**, 299–306.
2. Srinivasan R, Meyer R, Padmanabhan R *et al*. (2006) *J Pediatr Gastroenterol Nutr* **42**, 171–173.
3. Besselink M, Santvoort H, Buskens E *et al*. (2008) *Lancet* **371**, 651–659.