The use of pre- pro- and synbiotics in adult intensive care unit patients: systematic review

Watkinson P J, Barber V S, Dark P, Young J D

CRD summary
The authors concluded that use of prebiotics, probiotics or synbiotics in adult intensive care unit (ICU) patients did not lead to significant benefit in terms of rates of nosocomial infection or pneumonia, mortality or ICU stay. The conclusion reflected the available evidence, although potential limitations arising from the poor quality and variability of the studies made its reliability uncertain.

Authors' objectives
To assess the role of prebiotics, probiotics and synbiotics in patients admitted to adult intensive care units (ICUs).

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Clinical Trials and the UK National Research Register were searched with dates spanning 1966 to January 2006. Search terms were reported. The reference lists of included papers were searched for additional articles. Advice was sought from the UK ICU community to retrieve additional studies. The search was restricted to English-language articles.

Study selection
Randomised controlled trials (RCTs) of enteral prebiotics, probiotics and synbiotics (definitions detailed in the paper) compared to standard enteral feed alone in adult patients admitted to ICUs were eligible for inclusion. Included studies assessed a range of probiotics and synbiotics. Patients included ICU and high dependency unit (HDU) patients (abdominal surgery patients and patients undergoing liver surgery were mentioned specifically). The primary outcome was nosocomial (acquired in hospital) infection rates. Secondary outcomes included hospital mortality, ICU length of stay and pneumonia. Not all included studies reported all outcome measures.

One reviewer initially screened the titles and abstracts. Potentially eligible studies were independently screened for inclusion by two reviewers, with disagreements resolved through discussion.

Assessment of study quality
Each study was allocated a quality score from 0 (lowest) to 5 (highest) using the Jadad scale. Quality was assessed on the basis of allocation concealment, blinding, intention to treat analysis and power calculation. The process was carried out independently by two reviewers with disagreements resolved through discussion.

Data extraction
Two reviewers extracted the data on primary and secondary outcomes to calculate relative risk (RR) and 95% confidence intervals (CIs). Disagreements were resolved through discussion. Authors were contacted for additional information and unpublished data, where necessary.

Methods of synthesis
The studies were combined in a random-effects meta-analysis and pooled RRs with 95% CIs were calculated. Statistical heterogeneity was assessed using the $I^2$ statistic with a threshold for significant heterogeneity of 50 per cent.

Results of the review
Eight studies were included (n=999) in the meta-analysis. The sample size range was 17 to 330 (five studies contained less than 100 patients). In seven studies, allocation concealment was adequate and the overall mean Jadad score was 2.8 (range 1 to 5).

There were no statistically significant differences detected for nosocomial infections (five studies), pneumonia (four studies), mortality (eight studies) or ICU length of stay (three studies). Heterogeneity was present in the primary outcome analysis for nosocomial infection ($I^2=78.8\%$), but absent from the other analyses.
Authors' conclusions
The use of prebiotics, probiotics or synbiotics in adult ICU patients did not lead to significant benefit in terms of rates of nosocomial infection or pneumonia, mortality or ICU stay.

CRD commentary
The review addressed a clear question, with sufficiently well-stated inclusion criteria. Several sources were consulted to identify relevant studies, although the search was restricted to publications in English, meaning that language bias was a possibility. Some attempt was made to retrieve unpublished material, but there was no apparent assessment of publication bias. Appropriate methods were employed to minimise reviewer bias and error during the review process. An assessment of the methodological quality of the included studies was undertaken, and the quality of many of the included studies was poor. The methods used for synthesising the studies were appropriate in the presence of the high heterogeneity for the primary outcome. The diversity of patient groups was acknowledged by the authors as a limitation of the review. The authors’ conclusion reflected the available evidence, although limitations arising from the poor quality of heterogeneous data suggests that the reliability of this conclusion was uncertain.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that sufficiently powered and well-designed RCTs were required to detect clinically significant reductions in endpoints (for example infection rates) resulting from prebiotics, probiotics and synbiotics in adult ICU patients.

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