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Meta-analyses

Yogurt for treating acute gastroenteritis in children: Systematic review and meta-analysis

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SUMMARY

Background: In May 2014, the updated guidelines for the management of acute gastroenteritis (AGE) were published. The use of yogurt in the nutritional management of AGE was not addressed, although it is frequently used in many countries for this purpose. We aimed to systematically evaluate the efficacy of yogurt consumption for the management of AGE in children.
Design: In this systematic review, a number of databases, including MEDLINE, EMBASE, and the Cochrane Library, with no language restrictions, were searched up to July 2014 for randomized controlled trials (RCTs) evaluating the effect of yogurt consumption in children with AGE. The risk of bias was assessed using the Cochrane risk of bias tool.
Results: Four RCTs ($n = 448$) that were generally low in methodological quality, all performed in hospital setting, were included. Compared with placebo/no intervention, yogurt consumption had no significant effect on stool volume. The data on the effect of yogurt consumption on the duration of diarrhea and stool frequency were not consistent. The chance of treatment success (or failure) was similar in both groups. Compared with placebo, the duration of hospitalization was shorter in children who received yogurt, but the difference was of a borderline significance. Total weight gain increased for those treated with yogurt.
Conclusions: The consumption of yogurt had a positive effect on weight gain, but no consistent effect on AGE outcomes in hospitalized children. Given the limited data and the methodological limitations of the included trials, the evidence should be viewed with caution. The effect of yogurt consumption in the ambulatory setting is unknown.

1. Introduction

In May 2014, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society of Paediatric Infectious Diseases (ESPID) published updated evidence-based guidelines for the management of acute gastroenteritis (AGE) for practitioners at all levels of health care [1]. Rehydration is the key treatment and should be applied as soon as possible. Regular feeding should not be interrupted and should be carried on immediately after initial rehydration. Drugs are generally not necessary, although some have an impact on the duration and symptoms of AGE. The ESPGHAN/ESPID guidelines state that treatment with racecadotril (an enkephalinase inhibitor) or smectite (an adsorbent) may be considered in the management of AGE. Apart from drugs, certain probiotics may reduce the duration and intensity of symptoms [1,2]. Following a recent meta-analysis [3], the possibility of avoiding lactose in specific circumstances in the hospital setting has been highlighted. The use of yogurt in the management of AGE was not addressed, although it is commonly used as a home remedy for the management of diarrheal diseases [4].

Yogurt, as defined by the Codex Alimentarius standard for fermented milks (CODEX STAN 243-2003), is a form of fermented milk that contains symbiotic cultures of *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. *bulgaricus* that 'shall be viable, active and abundant in the product to the date of minimum durability.' To be called 'yogurt', a fermented milk product must contain

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milk protein, milk fat, lactic acid, ethanol, microorganisms, and yeasts in the proper proportions [5,6]. It has been postulated that yogurt may act on gut health by modulating the gastrointestinal flora and immune response. The immunologic effects of yogurt were thoroughly reviewed by Meydani & Ha (for review, see reference [7]). In brief, while a number of animal (mainly) and human studies suggest that yogurt has immunostimulatory effects, it remains unclear which components are responsible for these effects. In principle, the immunostimulatory effects of yogurt are attributed to bacterial components only. However, non-bacterial components of yogurt, such as whey protein, short peptides, and conjugated linoleic acid, may be responsible for these effects as well. Thus, further studies are needed to address the mechanism(s) by which yogurt exerts its action.

High-level evidence in the form of randomized controlled trials (RCTs) is needed to recommend or warn against the use of yogurt in the management of AGE. To our knowledge, this question has not been addressed in any previously published systematic review. Thus, our objective was to systematically evaluate the efficacy of yogurt consumption for the management of AGE in children.

2. Methods

The protocol for this systematic review was registered with PROSPERO, registration number CRD42014010454.

2.1. Criteria for considering studies for this review

Only randomized and quasi-randomized trials were eligible for inclusion. Participants had to be children with AGE (as defined by the authors of the original studies) who were treated as out- and/or inpatients. Trials that included children with persistent/chronic diarrhea or included children with other causes of diarrhea than a gastrointestinal infection present (e.g., antibiotic-associated diarrhea) were excluded.

The intervention had to be the administration of yogurt as defined by the Codex Alimentarius standard for fermented milks (CODEX STAN 243-2003), at any dosage scheme and duration of delivery. Studies eligible for inclusion in the scoping review included the following interventions: Consumption of yogurt, or any of its synonyms (Yoghurt; Yoghourt; Yaourt; Joghurt; Yogourt; Yaghourt; Yahourth; Yoghurd; Joghourt; Jogourt; Maas (Amasi); Dahi; Doi; Perugu; Thayir; Mosaru; Curd; Matsun; Matsoon; Matsoun; Matxoun; Madzoon; Madzoun; Mancun; Matson; Matsoni; Dadiah; Dadih; Stragisto). Studies were also eligible for inclusion when consumption of yogurt was featured as an intervention in combination with consumption of any other non-probiotic substance. Only studies reporting the oral consumption of yogurt were relevant. Topical application of yogurt as an intervention was not a relevant intervention. As in the scoping review, studies only reporting the following interventions were not eligible for inclusion: (i) Consumption of the following products: yogurt supplemented with probiotics; yogurt used as the carrier base for other substances alone when the other substance is the focus of the study; fermented milk, kefir and kumys; fermented baby formula; and milk. (ii) Subjects who consumed yogurt that was reported to contain bacteria other than *S. thermophilus* and *L. delbrueckii* subsp. *bulgaricus*.

A trial was included if it included any of the following control groups: placebo or no fermented milk products or no intervention.

The p*rimary outcomes* measures were as follows: duration of diarrhea, stool output, diarrhea lasting $\geq$3 days, diarrhea lasting $\geq$4 days, diarrhea lasting $\geq$7 days, and treatment failure. The *secondary outcome* measures were stool frequency, vomiting/duration of vomiting, need for hospitalization (outpatients), length of hospital stay (inpatients), weight gain, and adverse events. A lack of data regarding the above-listed outcomes was not a criterion for study exclusion.

2.2. Search methods for identification of studies

2.2.1. Electronic searches

The first electronic search was part of a larger, scoping review (unpublished) of the evidence of the health benefits conferred by the consumption of yogurt as defined by the Codex standard for fermented milks. This electronic search of various databases, societies, and conference proceedings (date of search: March 2014) is shown in Tables A and B (see online Supporting Information). There was no restriction on the language imposed. The second electronic search included a search of Ovid MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials (CENTRAL) for trials published from March 2014 (date of search for the scoping review) until July 2014.

2.2.2. Selection of studies

Initially, the title, abstract, and key words of every record identified with the search strategy were screened. Irrelevant articles were excluded by title or abstract. Full texts were obtained for all potentially relevant studies. Differences between reviewers were resolved by discussion until a consensus was reached.

2.2.3. Data extraction and management

The following data were extracted from the articles into a Microsoft Excel spreadsheet: author; year of publication; baseline characteristics of the participants (age, setting, country of origin, sample size); type of intervention: active product dosage; comparator; duration of the intervention; outcome measures, and results. If feasible, the data were entered into Review Manager [Computer program. version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012].

2.2.4. Assessment of risk of bias in included studies

Two reviewers independently (BPG and HS), but without being blinded to the authors or journal, assessed the risk of bias in the studies that met the inclusion criteria. The tool of the Cochrane Collaboration for assessing risk of bias was used, which includes the following criteria: adequacy of sequence generation, allocation concealment, and blinding of participants, personnel, and outcome assessors and determination of the extent of loss to follow-up (incomplete outcome data). In all cases, an answer of 'yes' indicates a low risk of bias and an answer of 'no' indicates a high risk of bias.

2.2.5. Measures of treatment effect

If appropriate, the data were analyzed using Review Manager (RevMan) software. The dichotomous measures for individual studies are reported as the risk ratio (RR) between the experimental and control groups with 95% confidence intervals (CIs). The mean difference (MD) between treatment and control groups was selected to represent the difference in continuous outcomes (with 95% CIs). Missing standard deviations were obtained from standards errors, confidence intervals, or a *P* value by the method described in the Cochrane Handbook for Systematic Reviews of Interventions [8]. For one outcome (duration of diarrhea), following Hozo et al. [9] a conversion of a result expressed as median (range) into mean (standard deviation) was performed in order to pool data together. However, we realize that such data conversion may result in overestimation of the mean and standard deviation. Thus, caution is needed in the interpretation of the pooled results on the duration of diarrhea. If no data were available, we report the results

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