Probiotic safety in pregnancy: a systematic review and meta-analysis of randomized controlled trials of Lactobacillus, Bifidobacterium, and Saccharomyces spp

Dugoua JJ, Machado M, Zhu X, Chen X, Koren G, Einarson TR

CRD summary
This review concluded the use of probiotics Lactobacillus and Bifidobacterium during pregnancy had no effect on the incidence of caesarean section, birth weight, or gestational age; the safety of Saccharomyces was not evaluated. The authors' conclusions appeared to reflect the data presented, but given possible overlap of patient populations between the trials, the reliability of their conclusions is not clear.

Authors' objectives
To assess the safety of probiotic strains of Lactobacillus, Bifidobacterium and Saccharomyces during pregnancy.

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), DARE, AMED, Cochrane Database of Systematic Reviews, AltHealthWatch, Complete German Commission E Monographs (by the American Botanical Council), Natural Database and Natural Standard were searched from inception to September 2007. No language restrictions were applied. Reference lists of relevant studies were handsearched. Additionally, experts in the field were contacted for unpublished studies. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that administered probiotic strains of Lactobacillus, Bifidobacterium, Saccharomyces, or placebo to pregnant women, for at least one week, were eligible for inclusion. Additionally, trials were required to report data on birth weight, gestational age, incidence of caesarean section, malformations or miscarriage.

The probiotic interventions evaluated were either Lactobacillus spp. alone or in combination with Bifidobacterium spp. There were no trials on Saccharomyces spp. In most trials, the probiotic intervention occurred at 32 to 34 weeks of gestation and was administered to pregnant women with a family history of atopic disease. The daily dosage used varied from $1 \times 10^8$ to $1 \times 10^{10}$ colony forming units.

Two reviewers independently selected studies, with any disagreements resolved by a third reviewer.

Assessment of study quality
Two reviewers independently assessed the trial quality based on reporting, external validity, internal validity (bias and confounding/selection bias) and power. Any disagreements were resolved by consensus, or by a third reviewer. Additionally, trials were assigned an evidence level of harm based on a standardised criterion.

Data extraction
Data on birth weight, gestational age, and incidence of caesarean section were extracted in order to calculate odds ratios, mean differences, and associated 95% confidence intervals (CI). Where possible, authors were contacted for additional data.

Two reviewers performed the data extraction independently.

Methods of synthesis
Studies were combined in random-effects meta-analyses. Heterogeneity was assessed using $I^2$ test. Publication bias was assessed using the Begg-Mazumdar test.

Results of the review
Eight papers reporting on six RCTs were included in the review (there appeared to be some discrepancy in number of trial participants reported between the text and the tables, ranging from 1,423 to 1,691 women). Trial quality was graded as either very strong or strong, with scores ranging from 29 to 87.1%.

Compared with placebo, there were no statistically significant increases in incidence of caesarean section (odds ratio 0.88, 95% CI 0.65 to 1.19; five RCTs), birth weight (weighted mean difference 45g, 95% CI -181 to 271; six RCTs) or gestational age (weighted mean difference 0.4 weeks, 95% CI -0.4 to 1.2; three RCTs) in the probiotic group. Heterogeneity was not statistically significant.

Only one trial reported data on incidence of malformations, with three cases reported in the placebo group. Based on Caesarean section outcomes, there were little evidence of publication bias (τ=0.2, p=0.624).

Authors’ conclusions
*Lactobacillus* and *Bifidobacterium* spp. had no effect on the incidence of caesarean section, birth weight or gestational age. The safety of *Saccharomyces* spp. during pregnancy was unknown.

CRD commentary
This review focused on a clear research question and was supported by well defined inclusion criteria. The literature search appeared adequate, with several sources being searched, with no language restrictions. There were also specific attempts to identify unpublished studies, minimising the risk of language and publication bias. The authors appeared to have taken steps to minimise bias and errors during the process by independent, duplicate assessment of trial eligibility, quality assessment and data extraction.

The method of synthesis appeared appropriate. However, it appeared that some of the included trials were on subgroups of patients included in another RCT eligible for this review, and may be reporting on same patients.

The authors’ conclusions appeared to reflect the data presented. However, because of the possible overlap of patient cohorts between the included trials, the reliability of conclusions is not clear.

Implications of the review for practice and research
Practice: The authors stated that it is not prudent to administer *Saccharomyces* spp. to pregnant women.

Research: The authors stated that future studies should avoid using carrier solutions that are known allergens or hypersensitising agents, such as peanuts and coconut.

Funding
Not stated.

Bibliographic details

PubMedID
19646321

Original Paper URL
http://www.sogc.org/jogc/abstracts/200906_DrugsinPregnancy_1.pdf

Indexing Status
Subject indexing assigned by NLM
MeSH
Bifidobacterium; Female; Humans; Lactobacillus; Pregnancy; Pregnancy Outcome; Probiotics /therapeutic use; Randomized Controlled Trials as Topic; Saccharomyces

AccessionNumber
12009108393

Date bibliographic record published
10/03/2010

Date abstract record published
30/06/2010

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.