Are probiotics safe for use during pregnancy and lactation?

Jackie Elias RPh Pina Bozzo Adrienne Einarson RN

Abstract

Question There has been a great deal of discussion in both the medical and lay literature about the use of probiotics to improve general health. Subsequently, pregnant women have been asking me if probiotics used for treating conditions such as bacterial vaginosis and diarrhea are safe to use during pregnancy and lactation.

Answer Current data suggest that probiotic supplementation is rarely systemically absorbed when used by healthy individuals. One meta-analysis and several randomized controlled trials conducted with women during the third trimester of pregnancy did not report an increase in adverse fetal outcomes. There have been no published studies addressing *Saccharomyces* species use in pregnancy. Probiotics are unlikely to be transferred into breast milk.

Résumé

Question On a beaucoup parlé, dans les ouvrages médicaux et les médias populaires, de l'utilisation des probiotiques pour améliorer l'état de santé général. Depuis, des femmes enceintes me demandent si les probiotiques utilisés pour traiter des problèmes comme la vaginose bactérienne et la diarrhée sont sécuritaires durant la grossesse et l'allaitement.

Réponse Selon les données actuelles, les suppléments de probiotiques sont rarement absorbés systémiquement quand ils sont utilisés par des personnes en santé. Une méta-analyse et quelques études randomisées contrôlées réalisées auprès de femmes durant le troisième trimestre de la grossesse n'ont pas relevé d'augmentation de résultats indésirables pour le fœtus. Aucune étude portant sur l'utilisation des suppléments de *Saccharomyces* durant la grossesse n'a encore été publiée. Il est peu probable que les probiotiques passent dans le lait maternel.

Probiotics are live microorganisms (in most cases bacteria) that are similar to beneficial microorganisms found naturally in the human gut. They are available to consumers mainly in the form of dietary supplements and foods, and "when administered in adequate amounts confer a health benefit on the host."[1] The most widely used probiotics in Canada are live bacteria such as *Lactobacillus* and *Bifidobacterium* species and nonpathogenic yeast such as *Saccharomyces*. They are available alone or in combination as tablets, drops, liquids, and oral or vaginal capsules; they are also contained in various fermented foods, most commonly yogurt. Probiotics have been used for the treatment of acute diarrhea, antibiotic-associated diarrhea, *Clostridium difficile*, and yeast and bacterial vaginosis. In healthy humans, lactobacilli are normally present in the oral cavity, ileum, colon, and vagina.

Product safety

When ingested orally or used vaginally, probiotics are generally considered safe and are well tolerated. One theoretical concern associated with probiotics is the potential for these organisms to cause systemic infections. Although rare, probiotic-related bacteremia and fungemia have been reported.[2] It is estimated that the risk of developing bacteremia from ingested *Lactobacillus* probiotics is less than 1 per 1 million users,[3] and the risk of developing fungemia from *Saccharomyces boulardii* is estimated at 1 per 5.6 million users, and is estimated to be lower in healthy individuals.[4] There have been no reports of bifidobacterium sepsis associated with the use of probiotics in healthy individuals.[5] Risk factors for systemic infections include immunosuppression, critical illness, central venous catheters, and impairment of the intestinal epithelial barrier.[3] Probiotics administered orally to combat urogenital infections are not systemically absorbed but rather get to the site of action by passage through the gastrointestinal system and ascending into the vagina.[6]

Use in pregnancy

Because the risk of probiotic-induced bacteremia and fungemia is low, probiotics are unlikely to reach the systemic circulation of the fetus, and therefore are unlikely

to cause harm. A meta-analysis and systematic review of 8 randomized control trials of probiotic use in more than 1500 pregnant women was published.[7] Most of the women began probiotic treatment between 32 and 36 weeks' gestation and continued until delivery. The studies included in the meta-analysis compared *Lactobacillus* spp alone or in combination with *Bifidobacterium* spp with placebo. There was no increase in the incidence of miscarriages or malformations, which was expected because probiotic use mostly occurred in the third trimester and was therefore unlikely to affect organogenesis. There was no significant difference in birth weight, gestational age, or the incidence of cesarean section.

Several randomized control trials conducted in pregnant women in the third trimester of pregnancy were published following the meta-analysis (**Table 1**).[8-15] These studies examined *Lactobacillus* spp and *Bifidobacterium* spp as monotherapy or in combination. Although not designed to directly evaluate pregnancy outcomes, these studies did not suggest an increase in adverse outcomes related to probiotics. Two observational studies examining the use of lactobacilli in the first trimester of pregnancy reported no increased risk of malformations.[16,17]

There are 2 published randomized control trials[11,15] of women exposed to probiotics commencing in the

Table 1. Randomized placebo-control trials of probiotics exposure during pregnancy

STUDY	NO. OF PATIENTS	PERIOD OF EXPOSURE	PROBIOTICS	PREGNANCY OUTCOMES	COMMENTS
Boyle et al,[8] 2008	73	36 weeks' gestation to delivery	*Lactobacillus rhamnosus* GG	Not reported	None
Kopp et al,[9] 2008	68	4-6 weeks before expected delivery to 6 months after delivery	*L rhamnosus* GG	No significant difference in gestational age, birth weight, or method of delivery	Selected women with uneventful pregnancies and without underlying chronic disease (ie, diabetes mellitus, rheumatoid arthritis, chronic infectious disease)
Kukkonen et al,[10] 2008	1223	4 weeks before expected delivery	*L rhamnosus* GG and LC705; *Bifidobacterium breve* Bb99; and *Propionibacterium freudenreichii* ssp *shermanii* JS	No significant difference in birth weight, birth length, and incidence of vaginal delivery	Excluded birth at <37 weeks' gestation and infants born with major malformations. Babies also received treatment for 6 months after delivery
Huurre et al,[11] 2008	140	First trimester to end of exclusive breastfeeding	*L rhamnosus* GG and *Bifidobacterium lactis* Bb12	No significant difference in gestational age or incidence of cesarean section	Women with chronic or metabolic disease before or during early pregnancy were excluded
Kuitunen et al,[12] 2009	1223	36 weeks' gestation to delivery	*L rhamnosus* LC705, *B breve* Bb99, and *P freudenreichii* ssp *shermanii* JS	No significant difference in birth weight	Babies received treatment for 6 months after delivery
Niers et al,[13] 2009	156	6 weeks before expected delivery to delivery	*Bifidobacterium bifidum* W23 and *B lactis* W52	No significant difference in the incidence of cesarean section, birth weight, or prematurity or gestational age	Babies received treatment for 12 months after delivery
Allen et al,[14] 2010	454	36 weeks' gestation to delivery	*Lactobacillus salivarius* CUL61 and *Lactobacillus paracasei* CUL08	No significant difference in adverse events related to pregnancy or childbirth	Babies received treatment for 6 months after delivery
Luoto et al,[15] 2010,	256	First trimester to end of exclusive breastfeeding	*L rhamnosus* GG and *B lactis* Bb12	No significant differences in incidence of adverse outcomes; significantly lower birth weight (P=.035) and shorter birth length (P=.028)	None

first trimester until the end of exclusive breastfeeding (**Table 1**).[8-15] Both studies examined the combination of *Lactobacillus rhamnosus* strain GG and *Bifidobacterium lactis* compared with placebo. Neither study was specifically designed to examine pregnancy outcomes; therefore, malformations were not reported. Luoto et al[15] found that infants born to women in the probiotics group had statistically significant lower risk of increased birth weight ($P=.035$) and birth length ($P=.028$); however, the clinical significance of this slight difference is unknown. This finding was not confirmed in the study by Huurre et al.[11] Both studies demonstrated no significant difference in gestational age or the incidence of cesarean section. There have been no published studies addressing *Saccharomyces* spp as an intervention for pregnant women.

Use in breastfeeding

Because probiotics are rarely systemically absorbed, they are not expected to transfer into breast milk. One randomized control trial examined *Lactobacillus reuteri* levels in 174 colostrum samples after maternal and infant oral supplementation of this probiotic.[18] Although higher in the active than in the placebo group, the prevalence of *L reuteri* in colostrum was low and not clinically important. Abrahamsson et al[18] suggested that the most likely origin of *L reuteri* in colostrum was external contamination from the gastrointestinal tract. There are no published data regarding adverse effects in breastfed infants. In several of the studies previously mentioned,[10,12-14] infants received probiotic therapy after delivery without an increase in adverse effects.

Conclusion

Probiotics do not appear to pose any safety concerns for pregnant and lactating women. Systemic absorption is rare when probiotics are used by healthy individuals, and the current literature does not indicate an increase in adverse pregnancy outcomes.

Competing interests
None declared

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MOTHERISK Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. **Ms Elias** is a doctoral candidate in the Faculty of Pharmacy at the University of Toronto. At the time this paper was written, **Ms Bozzo** was a member and **Ms Einarson** was Assistant Director of the Motherisk Program. **Ms Bozzo** is now Assissant Director and **Ms Einarson** continues to be a member of the Motherisk Program.

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