Re: “Oral Administration to Nursing Women of Lactobacillus fermentum CECT5716 Prevents Lactational Mastitis Development: A Randomized Controlled Trial” by Hurtado et al. (Breastfeed Med 2017;12:202–209)

To the Editor:

We would like to point out several items that we believe invalidate the authors’ conclusions in the article “Oral Administration to Nursing Women of Lactobacillus fermentum CECT5716 Prevents Lactational Mastitis Development: A Randomized Controlled Trial” by Hurtado et al.¹

There is an incongruence between the objective of the study, the method, and the conclusion: the stated objective is “to evaluate the preventive effect of oral administration of Lactobacillus fermentum CECT5716 on mastitis incidence in lactating women”; however, the study was done on “women who received preventive dose of antibiotic in the context of delivery.” Therefore, the conclusion should not state results as “an efficient strategy to prevent development of lactational mastitis in women,” but “in women who received preventive dose of antibiotic in the context of delivery.”

The high rate of cesarean section among the recruited women (both in the control and the experimental groups) is surprising: 31.4% and 34.7%, respectively, both higher than the average in Spain (26.7% in 2015). The high incidence in both groups of mixed feeding (49.4% and 54.3%), pacifier use (30.5% and 31.2%), and sucking difficulties (26% and 29%) makes it doubtful that the study participants received effective breastfeeding support, resulting in a high incidence of difficulties known to be predisposing factors for mastitis.²

The distribution of previous episodes of mastitis in the study women among the control and experimental groups should have been more homogeneous, or even an exclusion criterion, being a known risk factor for subsequent mastitis. Women in the control group had a higher incidence of previous mastitis (17.3%) than those of the probiotic group (11.5%) with a statistically very low p (p < 0.126), low enough as to possibly alter results.

The basal characteristics shown pertain to the women originally included in the study (322 in the control group and 303 in the probiotic group), but there is no information about the women who were finally studied (152 and 139, respectively) and whether there were statistical differences among the groups.

The high incidence of women who discontinued breastfeeding is surprising (53% in the control group, 54% in the probiotic group), barely explained in the discussion. And there were no comparing data between women who discontinued breastfeeding and those who did not. The percentage of breastfeeding discontinuation is similar in both groups: 23.6% (76 of 322) in the control group and 21.6% (70 of 303) in the probiotic group. Therefore, taking probiotics was not effective for maintaining breastfeeding.

The mastitis rate presented is 20%, very high compared with that in other studies,² so the study group might have suffered selection. The global recurrence rate, 26%, is also much higher than that in the literature. Recurrence rate was 33% in the control group and 12.5% in the probiotic group. We wonder why the women in this study had so many mastitis and so many recurrences (both globally and by groups) and whether there were correct breastfeeding support interventions for these women. There is no information about the treatment the women received for their mastitis, nor is there mention of a unified protocol to manage those episodes in the women studied.

The abstract does not mention that there were no statistical differences (p > 0.058) in the percentage of mothers who had mastitis in both groups.

The authors mention a statistically significant lowering of Staphylococcus spp. in the probiotic group, but not whether it is Staphylococcus aureus or Staphylococcus epidermidis. Since S. aureus is the main etiological agent for mastitis,² it is an important distinction, more so because these authors have previously declared that S. epidermidis is the main causal agent for mastitis.³

Some authors, including those in the PROLAC group, have a conflict of interest, having ties to the company that owns the patent and markets the probiotic under study. This company,

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Biosearch Life, has signed an agreement to license its strain of L. fermentum to Nestlé in December 2017. It is to be marketed at a global level as “nutritional complement for breastfeeding women for maintaining healthy breastfeeding.”

The recommendation for lactating women to take probiotics to prevent mastitis, based on such unclear evidence, could be a dangerous marketing operation, as such a recommendation could delay or interfere with evidence-based interventions and be economically onerous for families.

Disclosure Statement

No competing financial interests exist.

References


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Response to Paricio-Talayero and Baeza re: “Oral Administration to Nursing Women of Lactobacillus fermentum CECT5716 Prevents Lactational Mastitis Development: A Randomized Controlled Trial”

José A. Hurtado¹ and Juristo Fonollá²

To the Editor

We read with interest the letter to the editor from Baeza and Paricio-Talayero¹ commenting on our study.² We appreciate their comments; however, we believe none of the points made in their letter, in any way, invalidate nor alter the report or conclusions of our study.

The letter from Baeza and Paricio-Talayero suggests an incongruence between our objective (to evaluate the preventive effect of oral administration of Lactobacillus fermentum CECT5716 on mastitis incidence in lactating women) and the conclusion (Consumption of L. fermentum CECT5716 might be used during breastfeeding as an efficient strategy to prevent development of lactational mastitis). The results analyzed and the conclusion reflect the population of breastfeeding mothers only, and are, therefore, consistent with the objective. It is correct the population was selected from women who received antibiotics in the context of delivery, and although this may lead to limitations in the

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**References**


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generalization of results, it is not an incongruency in objective and conclusions. This limitation is specifically stated in the discussion section of the article, wherein we indicate that we selected women at higher risk of suffering mastitis based on receiving antibiotic treatment during delivery as reported by others, with an increased odds ratio of 1.53. However, it is worthwhile to note that current estimations suggest >40% of pregnant women are given some type of antibiotic immediately before delivery (Spanish data published by Martínez de Tejada, 2014).

Baeza and Paricio-Talayero suggest that the cesarean section rates of 31.4 and 34.7 in the study groups are higher than average and that mixed feeding and pacifier use were high and an indicator of ineffective breastfeeding support. We do not consider this to be the case. In all 12 participating hospitals, breastfeeding is promoted and all mothers receive information about breastfeeding. Taking into account that the population was selected among those receiving antibiotic treatment, it is not surprising to have 5–8 more percentage points of C-sections. Women who have had a C-section can suffer delay when milk first comes in so it could also influence the percentage of mixed feeding during first days as data of mixed breastfeeding at the beginning of the study correspond to the first days after delivery. In fact, the percentage of mixed breastfeeding reduced along the time, and at 4 weeks it dropped to 29–39%. These data can be considered normal as it is estimated that about 32% of breastfed infants receive mixed breastfeeding at 4 months of age (www.iesa.csic.es/publicaciones/010920110.pdf).

Regarding the use of baby soothers in Spain it is widespread and the percentages observed in the study are not considered unusual. Sucking difficulties are very common during first days after delivery when basal data were collected. The percentage is reduced to 10% at the next visit at 4 weeks and to 2–6% at the end of the study. Therefore, the population showed usual basal characteristics for women during the first days of breastfeeding.

Regarding the distribution of previous mastitis and selection criteria, previous episodes of mastitis were included as a covariate in the statistical analysis of the outcomes and no interaction was observed. Furthermore, the analysis of the same subject characteristics mentioned at baseline was performed and no significant differences were observed.

The percentage of women who discontinued breastfeeding was 23.6% in control group and 21% in probiotic group. The percentage of women who discontinue breastfeeding in Spain before 3 months is estimated around 33% and that before 6 months is around 53%. Therefore, the discontinuation rates in the study were not surprising.

Baeza and Paricio-Talayero “wonder why the women in this study had so many mastitis” (20%) and recurrences (26%). As discussed in the article, there is great variability in reporting incidence of mastitis globally, from single digits to 33%, as published by WHO. These and other recent data are consistent with the incidence in our study, especially in a population with greater risk, based on having received antibiotics. Both groups received similar lactation support.

The incidence rate of mastitis was statistically different between the groups ($p = 0.021$) and is stated in the abstract. The difference in the estimated OR did not reach to be statistically significant, and its $p$-value was also included in the abstract (0.058).

Baeza and Paricio-Talayero indicate that we did not carry out speciation of the *Staphylococcus* spp. This is correct. The PCR technique used in our study allows quantifying all species of the genus *Staphylococcus*. Analyzing *Staphylococcus aureus* and *Staphylococcus epidermidis* independently would have been interesting. However, a previous study demonstrated that *L. fermentum* CECT5716 is able to reduce both, *S. aureus* and *S. epidermidis*, in women suffering from mastitis. Noteworthy, it has been previously reported that *S. epidermidis* is not the main causal agent for mastitis but that “*S. epidermis* could be an additional and underrated cause of lactational mastitis…”

Baeza and Paricio-Talayero suggest that “recommendations for lactating women to take probiotics” could be a dangerous and onerous “marketing operation.” Our article does not make recommendations, it just exposes the scientific results of a clinical trial and concludes that, based on those results, “the consumption of the probiotic strain might be an efficient strategy to prevent the development of lactational mastitis.” Previous studies have evidenced that the proliferation of *Staphylococcus* in breast is related to a dysbiosis of the breast milk microbiota that might be counteracted by probiotic intervention. Recommendations to prevent mastitis are focused on good practices of breastfeeding, management of engorgement, to avoid milk stasis, etc. Our results do not question these beneficial practices to prevent mastitis, and simply discuss the management of dysbiosis in breast milk as one more strategy to decrease the risk of mastitis development.

**Ethical Report**

Regarding the potential conflicts of interest, the article includes full disclosure of affiliations of all the authors, and the clinical trial was carried out following all standard good clinical practice procedures.

**Disclaimer**

The discussion, criticism, and speculation regarding commercial practices and agreements by or between any parties have no place in the scientific context nor in a serious academic exchange in a clinical research journal.

**Disclosure Statement**

Juristo Fonollá is an employee of Biosearch Life, owner of the patent for *Lactobacillus fermentum* CECT5716.

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