Author's response to reviews

Title: Lactobacillus casei strain GG in the treatment of infants with acute watery diarrhea: A randomized, double-blind, placebo controlled clinical trial

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June 25, 2004 Ms. Emma Parkin Editorial Administrator The BioMed Central Editorial Team Re: "Lactobacillus casei strain GG in the treatment of infants with acute watery diarrhea: A randomized, double-blind, placebo controlled clinical trial" Dear Ms. Parkin, I'm pleased to submit the revised version of our manuscript for your consideration. We have addressed all the reviewers' comments and made the following changes in the manuscript: (Reviewer #1) 1) An intention-to-treat analysis has been performed and text and tables have been changed accordingly to present this analysis instead of the per-protocol analysis used in the original manuscript. The most relevant change found, as compared to the per-protocol analysis, is that the difference between means of the total stool output has increased slightly (from -47.9 ml/kg to -52.8 ml/kg) and the p value is now 0.047 (in the original manuscript was 0.137). To our concept, this does not modify the main conclusion of our study, i.e., we have found no beneficial effect of LGG on the clinical outcome of acute diarrhea in Peruvian infants. 2) Dose of LGG used in the study and details of the clinical outcomes data have been added to the Abstract section. 3) A whole new section defining primary and secondary outcomes used in this study has been added right before the Working definitions section. 4) The diagram showing the flow of participant patients throughout the study has been added. 5) The paragraph describing the policy of withdrawal replacement has been deleted. We believe it lacks of relevance when presenting an intention-to-treat analysis since this involves all patients recruited. 6) A statement that no adverse effect due to the study formula was noticed during the study has been added in the Results section. 7) A new reference (#15 Pediatrics 2002;109:678-684) has been added to support our new statement that we have used in our study a daily LGG dose above the suggested daily dose threshold found in the meta-analysis of the reference. 8) Difference between means (with 95% CI) is presented in Table 3 in addition to p values. (Table 2 does not contain means.) (Reviewer #2) 1) We have substituted "unresolved diarrhea" for "prolonged diarrhea" or "persistent diarrhea" throughout the manuscript when we describe those of our patients who still had diarrhea on day 5. We are doing this in order to avoid any confusion the readers may have with the well coined term "persistent diarrhea", which refers to a diarrhea lasting more than 14 days. This trial was designed to follow-up the patients for only the first 5 days after randomization. We have no data on what was the patient's status after then. 2) We are providing the cut-off point (0.75 g %) to define a positive reaction for reducing substances in stools. 3) We are highlighting in both the Result section and the Discussion section the finding of more rotavirus in the placebo group than in the LGG group. 4) The typo in the statement about the amount of lactose offered to patients in this study has been corrected. Other relevant changes in the manuscript: 1) Statistical Analysis section: We did not use logarithmic transformation of any variable to perform the ITT analysis; only Chi-square Yates corrected and not Fisher’s Exact Test was used for discrete variables. 2) Table 1 and Table 2: Some variables shown in the original manuscript have been deleted in order to simplify the table. The variables deleted are mostly a detailed breakdown of one main variable; we believe they do not convey any further relevant information to the readers. 3) Table 2: Study formula intake, caloric intake, volume of vomitus, and volume of urine are now expressed as ml/kg or Kcal/kg, as correspond, without adjusting them per day in order to make it more uniform with the way the other variables are presented. I look forward to your kind response. Yours sincerely, Eduardo Salazar-Lindo, M.D. Professor and Chair Department of Pediatrics Cayetano Heredia Hospital Av. El Polo 740 Of. C-410 Surco, Lima 33, PERU