

## Correspondence: Probiotic (*Lactobacillus reuteri* Protectis) in premature infants

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*This correspondence refers to the following article:*

Jerković Raguž M, Brzica J, Rožić S, Šumanović Glamuzina D, Mustapić A, Novaković Bošnjak M, Božić T.  
*The impact of probiotics (Lactobacillus reuteri Protectis) on the treatment, course and outcome of premature  
infants in the Intensive Care Unit in Mostar. J Pediatr Neonat Individual Med. 2016;5(2):e050228.  
doi: 10.7363/050228.*

*Authors' reply can be found in the following article:*

Jerković Raguž M, Brzica J, Rožić S, Šumanović Glamuzina D, Mustapić A, Novaković Bošnjak M, Božić T.  
*Correspondence: Probiotic (Lactobacillus reuteri Protectis) in premature infants – Authors' reply.  
J Pediatr Neonat Individual Med. 2017;6(1):e060130. doi: 10.7363/060130.*

### Keywords

Neonatal sepsis, feeding intolerance, necrotizing enterocolitis.

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### How to cite

Mandal A, Sahi PK. Correspondence: Probiotic (*Lactobacillus reuteri* Protectis) in premature infants.  
J Pediatr Neonat Individual Med. 2017;6(1):e060129. doi: 10.7363/060129.

**Dear Editor,**

We read with great interest the article by Jerković Raguž et al. [1] published in the latest issue of your journal. First, we would like to commend the authors for their endeavor. We have the following comments regarding the methodological issues which require further clarification by the authors for the benefit of the readers of JPNIM:

1. The authors have included two retrospective cohorts of preterm newborns belonging to the year 2013 and 2014. Each cohort consisted of 50 newborns. Given the retrospective nature of the study it is not clear as to how they have chosen these 50 newborns each because given the exclusion criteria mentioned it is very unlikely that exactly 50 newborns were born during both 2013 and 2014. This is of utmost importance as there is scope for selection bias [2].
2. It is stated that “the children’s parents gave their consent for the administration of probiotics, as they purchased it individually for their child and brought it to the Department”. However, even if the parents buy the interventional agent, this cannot be taken as consent for its application. Further, the authors also do not mention whether any ethical clearance was obtained from the Institutional/University Ethics committee for the study.
3. The definition/criteria used for the following terminologies in the present study are not mentioned: feeding intolerance, early onset sepsis, late onset sepsis, necrotizing enterocolitis. The protocol for stopping ranitidine therapy is also not provided; it is of importance as duration of ranitidine therapy was one of the outcome measures significantly different in the two groups.
4. It is mentioned in the discussion that “premature infants in 2014 had a more severe clinical state of infection accompanied by significantly lower values of thrombocytes, a higher concentration of CRP and leucocytes compared to the children from the 2013 study, but spent significantly fewer days in the ICU” (Intensive Care Unit). The authors also went on implicating this as a “possible positive impact of the probiotics”. But

the results show that the two cohorts only had significantly different platelet count which again could be affected by many other conditions such as toxemia of pregnancy in mother, etc., apart from sepsis.

5. The outcome measures of number of treatment days in ICU and days of feeding intolerance is affected by many other factors apart from those studied here. These factors such as intrauterine growth status (small for gestational age vs. appropriate for gestational age), flow abnormalities in the uterine artery (absent/reversal of end-diastolic flow), hemodynamically significant patent ductus arteriosus, type of milk (human milk vs. formula), hemodynamic instability, mechanical ventilation, etc. were needed to be compared between the two groups. As the sample was a time-cohort, the risk of these factors working as confounders is very high.
6. Discussion also mentions that “probiotics significantly affect the time of commencement of peroral feeding ... This was also confirmed in our study: on average, the infants began feeding perorally without signs of feeding intolerance on the 3<sup>rd</sup> day of life in 2014 and on the 5<sup>th</sup> day in 2013”. But no such data is presented in the results; further, the authors methodologically mention that “peroral feeding ... was introduced to the premature infants from the 1<sup>st</sup> to the 3<sup>rd</sup> day of life”. So, it makes one wonder whether the protocol for starting feeding was the same during these two years.

**Declaration of interest**

The Authors declare that there is no conflict of interest.

**References**

1. Jerković Raguž M, Brzica J, Rozić S, Šumanović Glamuzina D, Mustapić A, Novaković Bošnjak M, Božić T. The impact of probiotics (*Lactobacillus reuteri* *Protectis*) on the treatment, course and outcome of premature infants in the Intensive Care Unit in Mostar. *J Pediatr Neonat Individual Med.* 2016;5(2):e050228. doi: 10.7363/050228.
2. Davies HT, Crombie IK. Bias in cohort studies. *Hosp Med.* 2000;61(2):133-5.