

Letter: ginger as anti-emetic for acute gastroenteritis in children: interpreting evidence gingerly. Authors' reply

We thank Drs. Cyriac and Libin¹ for their interest in our paper reporting the efficacy of ginger as anti-emetic in children with acute gastroenteritis (AGE).²

We disagree with their personal interpretation of our introductory remarks. We clearly stated that previous investigations were performed only in adults and that no data were available in paediatric patients. This reason and the increased availability on the market of many ginger-based food supplements without any proof of efficacy for the treatment of children prompted the first randomised controlled trial (RCT) designed to test ginger in children with AGE-associated vomiting.

Criticism of the selection of placebo specifically regarding the content of stevia and anise is unfounded because these agents were equally present at the same concentration in both placebo and ginger products (as shown in Table 1 of our paper).² Thus, any potential negative effects elicited by these compounds would have been observed equally in both groups. Drs. Cyriac and Libin also ignored the fact that these unpleasant symptoms were observed only in subjects exposed to products with higher concentrations of stevia or anise than used in our study and with sugar alcohols, and that symptoms occurred in individuals who are very sensitive to these chemicals.³ In this trial, we used sugar- and alcohol-free products.

Regarding the sample size calculation, as there were no previous studies on the effect of ginger in children, we were inspired by the only methodologically rigorous study available which reported the results of another therapeutic strategy in a similar clinical setting.⁴ We feel that this was a methodologically appropriate way for a first exploratory investigation on the efficacy of ginger in this specific setting. As we stated, future investigations (also including non-inferiority trials) are warranted to confirm our findings, to define the most effective dose of ginger, and to test whether ginger could be effective in improving vomiting of different aetiologies in childhood. Lastly, in the selection of 5-HT₃ receptor antagonist for future non-inferiority trials, the possible occurrence of relevant side effects (such as prolonged QT interval, headache, lightheadedness, constipation, diarrhoea)⁵ should be also considered.

Other limitations proposed by Drs. Cyriac and Libin regarding the lack of pharmacokinetics, storage kinetics, dosing rationale and

ginger-associated active compounds are acknowledged but are not strictly relevant to our RCT that explored, for the first time, the potential clinical efficacy of ginger for the treatment of the most common cause of vomiting in children. Ginger reduced vomiting associated with AGE in children.

Thus, the results of our trial, conducted with a rigorous methodology, could be considered the first step towards an "organized knowledge" in the field of ginger use for the treatment of paediatric vomiting. This will be expanded with future preclinical and clinical studies.

ACKNOWLEDGEMENT

The authors' declarations of personal and financial interests are unchanged from those in the original article.²

LINKED CONTENT

This article is linked to Nocerino et al and Philips & Abraham papers. To view these articles, visit <https://doi.org/10.1111/apt.16404> and <https://doi.org/10.1111/apt.16474>

DATA AVAILABILITY STATEMENT:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Rita Nocerino^{1,2} 

Gaetano Cecere¹

Maria Micillo¹

Giulio De Marco¹

Pasqualina Ferri¹

Mariateresa Russo¹

Giorgio Bedogni^{2,3}

Roberto Berni Canani^{1,2,4,5} 

¹Department of Translational Medical Science, University of Naples Federico II, Naples, Italy

²CEINGE Advanced Biotechnologies, University of Naples Federico II, Naples, Italy

³Clinical Epidemiology Unit, Liver Research Center, Basovizza, Trieste, Italy

⁴European Laboratory for the Investigation of Food-induced Diseases, University of Naples Federico II, Naples, Italy

⁵Task Force on Microbiome Studies, University of Naples Federico II, Naples, Italy

Email: berni@unina.it

ORCID

Rita Nocerino  <https://orcid.org/0000-0003-4681-546X>

Roberto Berni Canani  <https://orcid.org/0000-0002-5169-9574>

REFERENCES

1. Phillips CA, Abraham L. Letter: ginger as anti-emetic for acute gastroenteritis in children - interpreting evidence gingerly. *Aliment Pharmacol Ther.* 2021;54:858-859.
2. Nocerino R, Cecere G, Micillo M, et al. Efficacy of ginger as antiemetic in children with acute gastroenteritis: a randomised controlled trial. *Aliment Pharmacol Ther.* 2021;54:24-31.
3. Momtazi-Borojeni AA, Esmaili SA, Abdollahi E, Sahebkar A. A review on the pharmacology and toxicology of steviol glycosides extracted from *Stevia rebaudiana*. *Curr Pharm Des.* 2017;23:1616-1622.
4. Freedman SB, Adler M, Seshadri R, Powell EC. Oral ondansetron for gastroenteritis in a paediatric emergency department. *N Engl J Med.* 2006;354:1698-1705.
5. Romano C, Dipasquale V, Scarpignato C. Antiemetic drug use in children: what the clinician needs to know. *J Pediatr Gastroenterol Nutr.* 2019;68:466-471.