Reviewer's report

Title: Polymorphism in the oxytocin promoter region in patients with lactose intolerance is not related to symptomatology

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Reviewer: Irma E Jarvela

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Truedsson et al. Polymorphism in the oxytocin promoter region in patients with lactose intolerance is not related to symptomatology

The group has studied the association of oxytocin (OXT) and oxytocin receptor (OXTR) polymorphisms in patients genotyped for the most common variant associated with lactase persistence/non-persistence, C/T-13910, residing in the MCM6 gene in order to understand the GI symptomatology in lactase persistence/non-persistence. The term lactose intolerance mean all milk-related symptoms, not only hypolactasia or lactase non-persistence related symptoms. Since the diagnosis is based on genotyping of the lactase persistence SNP C/T-13910, lactose intolerance is too unspecific here.

The major drawback of the study is the missing clinical data. What kind of symptoms the patients had? How many of them had inflammatory bowel disease. The clinical data could be presented in a Table.

The question is interesting but requires detailed analysis of symptoms of the patients, see above. OXT has been shown to be expressed in the gut and stimulate colonic activity and leads to increased gastric emptying, the symptom resembling lactose intolerance. Whereas OXTR antagonist, atosiban has an opposite effect delaying gastric emptying.

The following questions arise from the text:

1. Subjects
Although the correlation between milk consumption and lactase persistence/non-persistence is poor, it is essential that the lactose-related symptoms are mentioned in this kind of study. The major problem of the work is that clinical symptoms are totally missing. Being aware that both lactase persistent and non-persistent subjects are suffering from GI-symptoms, the clinical data would be vital.

Ethical question: If the DNA samples were anonymized after routine genetic testing from whom the written informed consent was obtained and why? Please describe this in detail.

2. DNA-analysis
If only the C/T-13910 variant was analyzed, there is a possibility that in patients
originating outside Europe, other SNPs could be found to be responsible for lactase persistence. This was not mentioned in the study.

The C/T-13910 variant is located inside the MCM6 gene. LCT means gene encoding lactase. It is misleading to call the analysis of the C/T-13910 variant LCT-genotyping since lactase gene is not analyzed here.

3. Statistical analyses
P-value of 0.05 is not strong enough as a limit in genetic association studies. Significant P-values are much smaller, reaching up to a 1x10^-7.

4. Discussion
The authors do not use the newest literature of genotypes associated with lactase persistence/non-persistence. Really, the ethnicity has become crucial since several new SNPs in the vicinity of the C/T-13910 genotype have been reported.

As a summary, the p-values are not strong enough to claim that there is a significant association. Therefore, the result remains unreliable. The poor description of clinical diagnoses is another revision needed before the paper can be resubmitted.

Spelling mistakes:
Introduction
-previously

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.