

## Abstract

# Daily Lactose Supplementation in Lactase Non-Persistent Individuals Induces Colonic Adaptation and Reduces Intolerance Symptoms <sup>†</sup>

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**Abstract:** Background and objectives: Globally, about 70% of the adult population is lactase non-persistent (LNP), lacking the enzyme required for lactose digestion. The main consequence of intolerance is withholding nutrient-rich dairy foods, while the literature shows that many LNPs are able to consume  $\leq 12$  g of lactose, comparable to 250 mL of milk, without experiencing gastrointestinal discomfort. Repetitive consumption of lactose may improve intolerance symptoms even further via colonic adaptation. This study aimed to assess the effects of daily consumption of incremental lactose doses on microbiota composition and function, and intolerance symptoms. Methods: Twenty-five healthy adults of Asian origin (age 22–44 yrs, BMI 19–28 kg/m<sup>2</sup>), carrying the LNP genotype and avoiding lactose in their habitual diet, were included in this 12-week single-blinded intervention trial. Participants consumed lactose twice daily, with doses being gradually increased from 3 to 6 g, to finally 12 g twice daily, each dose being provided for 4 consecutive weeks. Before and after the 12-week intervention, participants underwent a 25 g lactose challenge hydrogen breath test (HBT) and handed in stool samples. Daily gastrointestinal symptoms and acute intolerance symptoms during the HBT were recorded. Results: There was a significant increase in Bifidobacterium after 12 weeks of lactose consumption ( $p = 0.009$ ), accompanied by a two-fold increase ( $p < 0.001$ ) in fecal  $\beta$ -galactosidase activity. There was a 1.5-fold decrease (AUC;  $p = 0.01$ ) in expired hydrogen during the second compared to the baseline HBT. There was a non-significant decrease in total symptom score ( $p = 0.09$ ) during this second HBT, which was already relatively low during the baseline HBT. Daily consumption of lactose was generally well tolerated, with mild to no gastrointestinal complaints reported during the intervention. Discussion: Repetitive consumption of incremental doses of lactose increases lactose tolerance in LNP individuals via colonic adaptation, most likely through increasing the relative abundance of lactose-fermenting Bifidobacterium. Repetitive lactose consumption is well tolerated and able to reduce expired hydrogen during a 25 g lactose HBT. Here, we show that regular and incremental exposure to lactose in LNP individuals leads to colonic adaptation without any increase in gastrointestinal symptoms. This lifts the necessity to remove dairy foods completely from the diet.



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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Data described in the manuscript and analytic code will not be made available because this was not stated in the ethics application.

**Conflicts of Interest:** E.L., R.T. and, J.G. were employees of FrieslandCampina at the time of conceptual development and submission of the manuscript. L.J. was employee of FrieslandCampina at the time of conceptual development but switched employment prior to study execution.

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