

Effect of infant vitamin D drops on fecal glycerol, propylene glycol, and microbiota at 3 months of age

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AIM: Health Canada recommends exclusively breastfed, healthy, term infants are supplemented with vitamin D. Vitamin D liquid formulations contain non-medicinal excipients, such as glycerin or propylene glycol (PG). Digested glycerin and PG are fermentable by gut microbiota, producing bioactive metabolites. Therefore, we aimed to investigate fecal glycerin and PG levels concerning vitamin D supplementation and their association with gut microbiota and metabolites.

METHODOLOGY: Fecal samples and questionnaires were collected at three months of age from 575 infants in the Canadian Healthy Infant Longitudinal Development (CHILD) Cohort Study. Fecal metabolites and microbiota were quantified using NMR Spectroscopy and 16S rRNA sequencing, respectively. Logistic regression was used to determine the association between vitamin D supplementation and fecal glycerol and PG. Spearman's rank correlation was used for the relationship between fecal microbiota and metabolites with glycerol or PG.

RESULTS: Infants using vitamin D drops had higher fecal PG (aOR = 1.58, $p < 0.05$), but lower fecal glycerol (aOR=0.59, $p < 0.05$) on average at 3 months of age, adjusting for breastfeeding modes and confounders. Fecal PG levels were positively correlated with *Lactobacillaceae* ($r = 0.3$, $p < 0.05$), *Enterobacteriaceae* ($r = 0.2$, $p < 0.05$), *Bifidobacteriaceae* ($r = 0.2$, $p < 0.05$) but inversely related to *Lachnospiraceae* ($r = -0.3$, $p < 0.05$). Vitamin D drops use might influence microbial metabolism of glycerol and PG in the gut, resulting in elevated lactate ($r = 0.1$, $p < 0.05$), but reduced propionate ($r = -0.4$, $p < 0.05$) and butyrate ($r = -0.4$, $p < 0.05$).

CONCLUSION: The novel link between fecal PG and probiotic microbiota, notably *Bifidobacterium*, and microbial acetate, butyrate, and propionate, may have implications for infant health.