The effect of kefir and milk intake on intestinal permeability

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Abstract

We performed a longitudinal intervention study that lasted 4 months at the UP Faculty of Health Sciences in Izola. The participants were divided into two groups, each alternately consuming kefir or milk for 21 days, with two washout periods in-between. Venous blood was sampled (fasted) after each phase and the participants completed a questionnaire on gastrointestinal symptoms and a Bristol stool scale. Kefir supplementation resulted in a greater improvement of serum zonulin levels whereas significant yet similar improvement in lipid profile, serum glucose levels, inflammation markers and appetite were found in both supplementations. We did not observe significant changes in the incidence of gastrointestinal symptoms, with the exception of significantly decreased sensation of bloating after kefir intake. The average number of defecations increased after kefir intake and decreased after milk intake. The percentage of participants who defecated at a consistent time each day decreased after kefir intake and increased after milk intake. We conducted one of the first studies comparing the effects of kefir and milk on the human intestine. Our research shows that daily kefir consumption could be an effective strategy for individuals with constipation and bloating. There is still a lack of solid evidence for the use of probiotics for most medical conditions.

Keywords: kefir, milk, zonulin, intestinal permeability, inflammation

Introduction

Cow's milk and fermented dairy products, such as yogurt, buttermilk and kefir, have been a major part of our diet for many years (Kok and Hutkins, 2018) and have beneficial health effects (Bourrie et al., 2016). The intake of dairy products has been linked with reduced risk of obesity, hypertension, type 2 di-

abetes and heart disease (Li et al., 2018). Kefir is a fermented dairy product containing a large number of lactic acid bacteria and yeasts (Kim et al., 2017). The largest bacterial community in the human body is located in the gastrointestinal tract (Bischoff et al., 2014) and it's known that a diverse gut microbiota and increased intestinal permeability plays a key role in inflammation that accompanies chronic diseases and in maintaining health (Kim et al., 2017). It modulates the expression of many genes in the gut that are associated with immunity, nutrient absorption, energy metabolism, and gut barrier function (Bell et al., 2018). The human gut is surrounded by a layer of epithelial cells that forms a barrier between the environment and the host. Increased intestinal permeability is thought to be an important element in the pathogenesis of chronic inflammatory diseases, in addition to genetic and environmental factors. Zonulin is so far the only known physiological intercellular modulator of intestinal tight junctions (Sturgeon and Fasano, 2016) and it's a biomarker showing altered intestinal barrier function in many autoimmune, neurodegenerative and tumor diseases (Fasano, 2012). The specific pathophysiological role of zonulin in various diseases is not well known, but elevated zonulin levels are thought to be a key factor in the onset of the inflammatory process (Sturgeon and Fasano, 2016). Despite the prevalence of dairy products, there has been very little research done on the effects of kefir and milk intake on the intestine, especially in humans.

Methods

We performed a longitudinal intervention study, which lasted from March to June 2018 at the Faculty of Health Sciences in Izola. The study included 28 healthy individuals (13 men and 15 women) aged between 31 and 64 years, with a BMI between 25 and 30 kg/m². The exclusion criteria were: any acute or chronic illness, lactose intolerance or milk allergy, taking medication, BMI < 25 kg/m² or BMI > 30 kg/m², pregnancy and lactation, significant body weight change in the last 3 months. The participants were divided into two groups, each alternately consuming kefir (250 ml daily) or milk (250 ml daily) for 21 days, with two washout periods in-between. During the washout periods complete abstinence from fermented dairy products was required. After each phase venous blood was sampled (fasted) and was then analyzed with Cobas c 111 analyzer (Roche Diagnostics) and with enzyme-linked immunosorbent assay (ELISA) for serum zonulin levels. After each phase participants completed a questionnaire on gastrointestinal symptoms – nausea, bloating, borborygmus, stomach pain, flatulence and heartburn. They also completed a Bristol stool scale. Participants were instructed to try to keep their diet as normal as possible throughout the study.

Results

Serum zonulin levels

Table 1 shows the mean and standard deviation of serum zonulin values before and after kefir and milk intervention.

Table 1: Mean serum zonulin levels before and after kefir and milk intervention

	Before kefir	After kefir	Before milk	After milk
	Mean	Mean	Mean	Mean
Serum zonulin levels (ng/ml)	1,089±1,425	0,940±0,923	0,866±0,864	0,837±0,913

The results of the Wilcoxon test of predicted ranks showed that both kefir intervention ($z = -0,222$; $p = 0,824$) and milk intervention ($z = -0,336$; $p = 0,737$) did not have a statistically significant effect on the change in serum zonulin levels.

Analysis of covariance (ANCOVA), with gender, age, BMI and baseline zonulin levels as covariates, showed that the change in serum zonulin levels after kefir intervention was statistically significant ($p < 0,001$), but not after milk intervention ($p = 0,162$). Kefir supplementation resulted in a greater improvement of serum zonulin levels whereas significant yet similar improvement in lipid profile, serum glucose levels, inflammation markers and appetite were found in both supplementations. CRP and adiponectin were not significantly affected by neither of the two interventions (Jenko Pražnikar et al., 2020).

Gastrointestinal symptoms

Table 2 shows the mean value of the occurrence of gastrointestinal symptoms before and after kefir and milk intervention and the results of paired-samples t-test. It showed a statistically significant change only in the feeling of bloating before and after the kefir intervention ($p = 0,043$), whereas the other changes in the incidence of gastrointestinal symptoms were not statistically significant.

Table 2: The occurrence of gastrointestinal symptoms before and after kefir and milk intervention and paired-samples t-test

	Before kefir	After kefir	Paired-samples t-test		Before milk	After milk	Paired samples t-test	
Gastrointestinal symptoms*	Mean	Mean	t	p	Mean	Mean	t	p
Nausea	0,29±0,76	0,29±0,71	0,000	1,000	0,12±0,43	0,31±0,79	-1,044	0,306
Bloating	1,00±0,96	0,70±0,87	2,126	0,043	0,92±0,93	1,13±1,15	-0,816	0,423
Borborygmus	0,92±0,94	0,92±0,94	0,000	1,000	0,84±0,80	0,60±0,96	1,186	0,247

Gastrointestinal symptoms*	Before kefir	After kefir	Paired-samples t-test		Before milk	After milk	Paired samples t-test	
	Mean	Mean	t	p	Mean	Mean	t	p
Stomach pain	0,74±1,06	0,52±0,89	1,185	0,247	0,64±0,92	0,50±0,93	0,485	0,632
Flatulence	1,50±0,91	1,35±0,94	0,811	0,425	1,52±0,92	1,52±1,05	0,000	1,000
Heartburn	0,89±1,07	0,58±0,90	1,397	0,175	0,72±0,94	0,56±0,87	0,778	0,444

Legend: * Gastrointestinal symptom values are expressed on a scale from 0 to 5, with 0 representing the absence of a gastrointestinal symptom and 5 representing the maximum intensity of occurrence of a gastrointestinal symptom.

An independent samples t-test to compare changes in the occurrence of gastrointestinal symptoms after intervention with kefir and milk has shown no statistically significant difference in the the altered incidence of nausea (t = -0,895; p = 0,375), bloating (t = -1,788; p = 0,080), borborygmus (t = 1,051; p = 0,298), stomach pain (t = -0,712; p = 0,480), flatulence (t = -0,786; p = 0,435) and heartburn (t = -0,907; p = 0,369) between the groups.

Stool consistency, frequency and time of defecation

Table 3 shows stool consistency, frequency and time of defecation. Participants rated their stool consistency with a Bristol stool scale from 1 to 7, with 1 and 2 representing harder stool, 3 and 4 stool of appropriate consistency, and 5, 6 and 7 representing softer stool. Stool consistency became softer after both kefir and milk intervention. In each stage of the study participants defecated on average from 0,5 to 3 times per day. Frequency of defecation was slightly increased after kefir intervention and decreased after milk intervention. The percentage of participants who defecated at a consistent time each day decreased after kefir intervention and increased after milk intervention.

Table 3: Average number of defecation before and after intervention with kefir and milk

	Before kefir	After kefir	Before milk	After milk
Stool consistency	3,6	3,8	3,8	3,9
Number of defecations	1,3	1,4	1,4	1,3
Defecating at a consistent time (%)	78,3	70,0	69,9	77,3

Discussion

Kefir intervention resulted in a greater improvement of serum zonulin levels than milk intervention. Some studies have found beneficial effects of various probiotics on the serum zonulin levels and intestinal permeability (Liu et al.,

2013; Stenman et al., 2016), while some haven't (Stadlbauer et al., 2015; Mekkala et al., 2018). CRP and adiponectin were not significantly affected by neither of the two interventions. We did not observe significant changes in the incidence of gastrointestinal symptoms, with the exception of significantly decreased sensation of bloating after kefir intervention. In most studies, consumption of kefir or other probiotics had beneficial effects on most gastrointestinal symptoms (Kato-Kataoka et al., 2016; Lee et al., 2018; Yilmaz et al., 2019). Stool consistency became softer after both kefir and milk intervention. The average number of defecations increased after kefir intervention and decreased after milk intervention. The percentage of participants who defecated at a consistent time each day decreased after kefir intervention and increased after milk intervention. Some other studies also found a beneficial effect of both kefir and milk on stool consistency or there were no differences compared to the control group (Moreira et al., 2017; Maki et al., 2018), while some studies have shown a beneficial effect of kefir or other probiotics on stool consistency, with the effect being significantly different from the control group (Lee et al., 2018; Yoon et al., 2018).

Conclusions

We conducted one of the first studies comparing the effects of kefir and milk on zonulin levels and gastrointestinal symptoms in healthy asymptomatic individuals. We have shown that daily consumption of kefir could be an effective strategy for individuals with constipation and bloating problems. There is still a lack of solid evidence for the use of probiotics for most medical conditions.

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