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"EXPLORING THE GUT-BONE AXIS: IMPACT OF GUT MICROBIOTA DYSBIOSIS AND DIETARY INTERVENTIONS ON BONE HEALTH"

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ABSTRACT:
Osteoporosis is a prevalent global health issue characterized by bone fragility and an increased risk of fractures. Dysbiosis of the gut microbiota, marked by an imbalance in microbial communities, has emerged as a potential contributor to impaired bone health. Age, diet, and disease influence gut microbiota composition, disrupting bone metabolism signalling pathways, impairing calcium absorption, and dysregulating osteoclast activity, ultimately impacting bone strength and quality. This paper examines the intricate relationship between the gut microbiota and bone health, highlighting the role of dysbiosis in promoting osteoporosis and related disorders. Gastrectomy, neuropeptide secretion, and bacterial variance exacerbate bone loss by influencing calcium metabolism and systemic inflammation. The gut-bone axis, governed by interactions between gut physiology and microbial populations, is crucial in regulating bone metabolism. Dietary interventions, particularly involving prebiotics such as galactooligosaccharides (GOSs) and fructooligosaccharides (FOSs), promote bone health by modulating the gut microbiota. These prebiotics stimulate beneficial bacteria growth, enhance osteoblast activity, and improve calcium absorption and mineralization. Clinical trials in postmenopausal women and animal studies demonstrate the beneficial effects of prebiotic supplementation on bone density and turnover markers. Furthermore, randomized controlled trials and animal studies reveal that supplementation with calcium plus short-chain fructooligosaccharides (CaFOS) or fructooligosaccharides (FOS) increases femoral bone area and calcium content, reduces bone resorption, and decreases inflammation. These findings underscore the potential of dietary interventions targeting the gut microbiota to mitigate bone loss and prevent osteoporosis.

Keywords: *Bone, Growth Factor, Galactooligosaccharides, Fructooligosaccharides, Xylooligosaccharides, Lactulose*

INTRODUCTION:

Osteoporosis, a global health concern, affects approximately two hundred million people (Pisani P, 2016). This condition, characterized by unhealthy or fragile bones, can manifest in both adults and the elderly. It leads to structural changes, osteoporosis, and low bone mineral density, all of which significantly increase the risk of fractures (Ferrari, 2016).

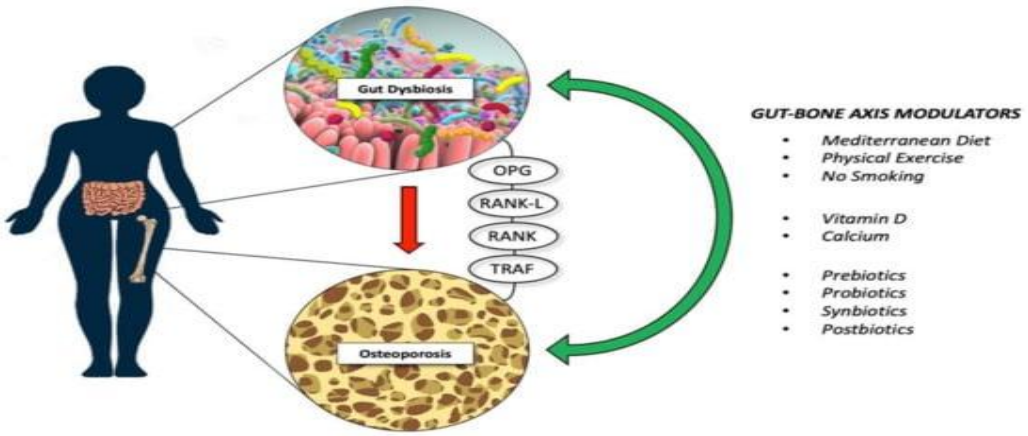
These conditions can end up in severe consequences of surgeries, lifelong disabilities, and even death. Because low-energy trauma can cause fragility fractures, hospitalization and surgical procedures may be necessary. These procedures have adverse effects, including increased mortality risk and lifelong disability. Disrupted intestinal metabolism is a culprit and an additional risk factor for poor bone health. Currently, researchers are studying the possibility that changes in intestinal homeostasis may contribute to a higher risk of decreased bone health. This could also serve as a new target for therapeutic interventions. The human gut microbiota consists of over 1000 microorganisms living in a mutually beneficial relationship with their host. While most of these microbes are specific to each healthy individual, a joint, stable, and abundant component includes different bacteria (Nagpal, 2014).

DYSBIOSIS:

A term used for changes in the gut microbiota that create an imbalance in a human's gut microflora and ultimately result in dysregulation of metabolism, IBS, RA, and other diseases (Rosser EC, 2016). Many factors cause dysbiosis, such as depression, ageing, and inflammation. After healing, it is corrected naturally (Ozaki D, 2021). Disturbance can also occur in microbial communities due to an environment linked with host genetic factors that can ultimately modify their immunity. The gut microbiome influences bone metabolism signalling pathways by generating and translocating metabolites. Gut microbial dysbiosis affects bone by impairing the absorption of calcium in the intestines and disrupting osteoclast activity by altering the amounts of IGF-1 in the blood. Moreover, alterations in the microbiota diminish the robustness and excellence of bones and affect the OPG/RANKL pathway in osteoclasts. (Novince CM, 2017)

GUT BONE AXIS:

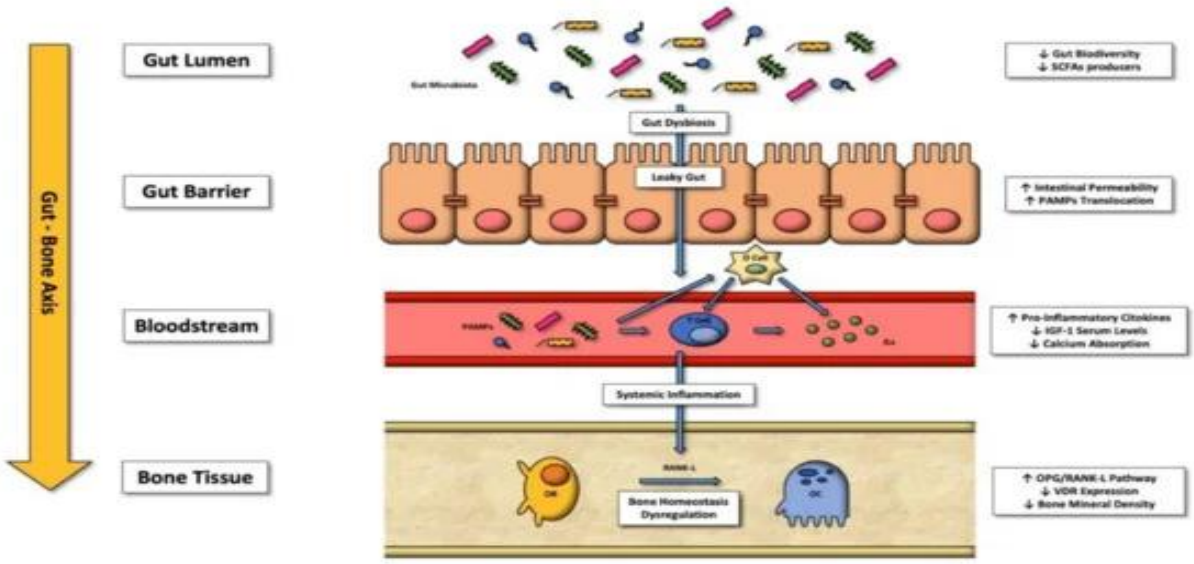
The composition of the gut microflora is subject to variation based on factors such as age, sex, food, environmental conditions, and diseases. Similarly, bone is an active organ that continuously undergoes remodelling to preserve bone mass and regulate serum calcium levels. The gut's physiology and the population of microbes in the gut have distinct functions in controlling bone metabolism at various levels.



A gastric bypass leads to decreased BMD in animals and humans, as disturbed gastric acid affects calcium metabolism and absorption. Additionally, various neuropeptides released by the GIT stimulate osteogenesis or hinder osteoclast activity, while others, like stomach inhibitory polypeptide,

serotonin, and gastrin, have osteoporosis-promoting effects. Variations in the composition of the bacterial gut and the prevalence of specific microbial organisms can affect the absorption of micronutrients, calcium, a mineral and beta-carotene, contributing to systemic infection (Rizolli, 2018).

The relationship between the gut-bone axis and the immune system is complicated. In normal conditions, the gut's microflora regulates the development of the host's natural immune systems. However, dysbiosis in the gut microflora can produce excessive inflammatory mediator production, as demonstrated in animal studies. During dysbiosis, metabolites produced by bacteria are transported to the liver through the bloodstream, increasing immune response. Also, they influence CD4+ T lymphocytes located within the bone marrow, resulting in an osteoclastic-promoting effect. (Chen YC, 2017)



DIET AND BONE HEALTH:

Diet, a factor within our control, plays a crucial role in shaping the composition of the gut microbiota, which, in turn, affects the health of our bones. For instance, a high-fat diet has been shown to decrease microflora diversity in mice, while a diet high in sugars can lead to glucose intolerance. The diet associated with the Mediterranean region is characterized by a high content of dietary fibres, fermented dairy products, and phytonutrients, which have been linked to beneficial effects on the human gut microflora. These changes promote bone health and lower the risk of fractures (Gentile CL, 2018).

ROLE OF PREBIOTICS:

These substances are non-digestible dietary components that stimulate the growth or function of microorganisms in the large intestine by acting as a substrate. They are usually generated by chemically converting glucose, such as GOSs, FOSs, inulin, digestion-resistant cellulose, XOSs, and lactic acid. Galactooligosaccharides, which consist of a series of galactose units (usually 2-8) with glucose at the end, have demonstrated encouraging benefits. They stimulate the proliferation of advantageous bacteria, boost the number and efficiency of bone-forming cells, and enhance the absorption of calcium and magnesium in the intestines, as well as the process of bone mineralization. During a double-anonymized experiment, adolescent girls administered 5 grams of GOSs twice daily for three weeks exhibited enhanced calcium absorption in the lower gastrointestinal tract and increased faecal excretion (Whisner CM, 2018).

FOSs are composed of 3–10 fructose units, with the last fructose unit being connected to a remaining glucose molecule. Fructooligosaccharides have comparable impacts to galactooligosaccharides in stimulating the proliferation of Bifidobacteria, resulting in an elevated level of the compound butyrate in the colon. A short-chain fatty acid that stimulates the gut microbiota, particularly its influence on

bone metabolism. In animal models, the consumption of FOS has been linked to enhanced bone strength, mineral formation, and decreased bone decay. A recent study found that FOSs can increase the maximum density of bones and blood level of butyrate in rats that experience bone loss as a result of estrogen deprivation. In postmenopausal women, the addition of FOS (fructooligosaccharides) at a dosage of 3.6 grams per day for a duration of 12 months, together with calcium dietary changes, resulted in a decrease in the levels of bone renewal markers in the blood. However, this supplementation did not have any impact on bone mineral density. (Tanabe K, 2019) (Slevin MM, 2014)

METHODS:

A study was conducted at the University of Lahore, Pakistan, following established guidelines. The study involved 45 male mice fed a modified diet with specific components for 31 weeks. Various samples were collected at different intervals using culturally dependent methods, including blood, urine, and cecal contents. The bone health of the mice was assessed through soft X-rays, and other biomarkers were also evaluated using different techniques.

Statistical analysis:

The data were reported as a mean and a standard deviation (SD). After verifying the mice's normal or abnormal dispersion, a one-way analysis of variance test was applied. This test was used to evaluate the effect of a modified diet on mice. A P-value below 0.05 was deemed statistically significant. The IBM SPSS program was utilized for data analysis.

The correlation between the amount of calcium in the femur bone and all other measurement characteristics was evaluated at 24 and 36 weeks of age using Spearman's rank correlation coefficient test (Tanabe K, 2019).

Group	Total Food Intake (g)	Body Weight Gain (g)	Diet Efficiency
Control	Not significantly different from FOS	Not significantly different from FOS	Not significantly different from FOS
FOS	Not significantly different from Control	Not significantly different from Control	Not significantly different from Control
GM	Significantly higher than Control ($p < 0.05$)	Lowest among groups	Not significantly different from Control

Another double-anonymized, randomized controlled trial was conducted in August 2008 after screening 693 postmenopausal women using a questionnaire. A second screening of 372 women was done to assess their BMD and other risk factors for osteoporosis. In the next step, only 300 women were randomly added to one of the three groups: calcium, Ca plus short-chain fructooligosaccharides, or placebo (maltodextrin). These participants underwent their respective treatments for 24 months and consumed their supplements daily. Data was collected through different assessment methods at three intervals: baseline, 12 months, and 24 months. Assessment methods include Anthropometric measurements, dietary intake, physical activity, and BMD. Other biochemical tests were performed at three intervals, including CTX, PTH, and 25-hydroxyvitamin D.

Recruitment and First Screening (August 2008 - June 2009):

- Postmenopausal women were recruited through various means including information leaflets, media appeals, and senior citizens groups.
- Initial screening involved 693 women who were screened by telephone using a questionnaire to exclude those who did not meet the inclusion criteria.
- Exclusion criteria included premenopausal or perimenopausal status, previous diagnosis of osteoporosis, use of medications or dietary supplements affecting bone metabolism, diagnosis of bone-degenerative chronic diseases, and menopause before age 40.

Second Screening (October 2008 - June 2009):

- A total of 372 women who passed the first screening attended the study center for the second screening.
- Additional screening involved assessing individual BMD and gathering information on risk factors for osteoporosis through a questionnaire.

Intervention Phase (February 2009 - June 2011):
- 300 eligible postmenopausal women proceeded to the intervention phase and were randomly assigned to one of three treatment groups: Ca, CaFOS, or placebo.
- Random assignment was performed by an independent researcher using a computer-generated code.
- Participants were provided with visually identical supplements, and were required to consume 2 supplements per day for 24 months.
- The supplements included: 1) 800 mg/d Ca, 2) 800 mg/d Ca and 3.6 g/d scFOS, or 3) 9.8 g/d maltodextrin.
- Compliance with supplement intake was assessed through questionnaires and blood samples.

Outcome Measures:
- Anthropometric measurements, dietary assessments, and physical activity assessments were conducted at baseline and throughout the study.
- BMD was measured for total body, lumbar vertebrae, and left proximal femur by DXA at baseline and 24 months.
- Biochemical analyses including serum osteocalcin, CTX, PTH, 25(OH)D, and urinary DPD were performed at baseline and throughout the study.

Statistical Analysis:
Changes were assessed in BMD and bone turnover markers at intervals between the treatment groups, with significance at less than 0.05. A minimum sample size of forty-six for each group was calculated, and 300 members were chosen for the study, with 46 participants in each treatment group. The effects of supplements were monitored throughout the study. There are two main outcomes: primary and secondary. The primary outcome includes a change in BMD in grams per centimetre squared, and the secondary outcome includes a change in BTMs. ANCOVA test was conducted for the primary outcomes, and ANOVA was conducted for the secondary outcomes. Data are reported as means ± SDs, statistically significant at $P < 0.05$ (Slevin MM, 2014).

In one study, 35 adolescent girls aged between 15 and 15 were recruited from the Niagara Region, Ontario, Canada, through local media, clinics, and schools. The study's eligibility criteria were that the girls be between 12 and 16.9 years old, menarcheal, minimally active, and healthy. The study focused on bone turnover from participants assigned to the recommended dairy and low dairy intervention group.
The study scheme involved classification by BMI (overweight or obese) and random classification into one of three assigned groups: RDa, LDa, or no intervention control group. The RDa group was given the recommended amount of dairy compared to the LDa group. The present study focused only on these two groups. This study lasted 12 weeks and included some exercise sessions, dietary counselling, and the provision of dairy products. In data collection, anthropometric measurements, food records, somatic maturity offset, and fasting venous blood samples were collected at the initial level and after eighty-four days post-intervention. Blood samples related to bone density and health were also collected.

Variable	RDa Pre (Mean ± SD)	RDa Post (Mean ± SD)	LDa Pre (Mean ± SD)	LDa Post (Mean ± SD)	p-value (Group)	p-value (Time)	p-value (Group × Time)
Years from peak height velocity	2.0 ± 0.9	2.1 ± 0.9	2.5 ± 0.9	2.6 ± 0.9	0.12	<0.001	0.23
Height (cm)	163.4 ± 8.4	163.8 ± 8.4	164.0 ± 6.0	163.8 ± 5.5	0.98	0.002	0.53
Body weight (kg)	79.7 ± 15.5	79.7 ± 14.4	80.5 ± 14.0	77.6 ± 13.4	0.76	0.26	0.28

Variable	RDa Pre (Mean ± SD)	RDa Post (Mean ± SD)	LDa Pre (Mean ± SD)	LDa Post (Mean ± SD)	p-value (Group)	p-value (Time)	p-value (Group × Time)
BMI percentile (%)	96.5 ± 4.6	95.6 ± 6.4	94.4 ± 6.1	93.3 ± 6.9	0.27	0.027	0.75
Energy (kcal/day)	1749.2 ± 369.7	1756 ± 364.7	1591.6 ± 468.2	1510.9 ± 180.5	0.065	0.56	0.49
Protein (g/day)	67.0 ± 18.8	86.7 ± 12.3*	65.5 ± 17.6	74.2 ± 11.0*	0.12	<0.001	0.044
Carbohydrates (g/day)	216.2 ± 50.9	207.5 ± 47.2	194.3 ± 57.0	177.3 ± 31.1	0.076	0.10	0.54
Vitamin D (mcg/day)	2.2 ± 1.5	5.7 ± 1.0*	1.4 ± 0.9	1.7 ± 1.0	<0.001	<0.001	<0.001
Calcium (mg/day)	699.3 ± 269.3	1295.7 ± 185.2*	789.3 ± 179.7	804.2 ± 222.0	<0.001	<0.001	<0.001
Phosphorous (mg/day)	828.6 ± 332.2	1335 ± 204.8*	722.5 ± 205.8	877.3 ± 166.5*	<0.001	<0.001	0.001
Potassium (mg/day)	1555.8 ± 623	2359.4 ± 489.7*	1508.5 ± 494.6	1881.7 ± 437.6*	0.086	<0.001	0.031
Magnesium (mg/day)	167.3 ± 72.6	244.6 ± 54.6*	158.5 ± 51.4	256.0 ± 71.0*	0.94	<0.001	0.42

STATISTICAL ANALYSIS:

Table 1.1: The table presents data on anthropometric measurements and nutritional intake before and after an intervention in two groups of overweight and obese adolescent girls: recommended dairy (RDa) and low dairy (LDa). The years from peak height velocity, height, body weight, BMI percentile, energy intake, and macronutrient intake (protein, carbohydrates, fat) were assessed. The results show no significant differences in years from peak height velocity and height between the two groups, but there was a significant increase over time in both groups. Body weight and energy intake did not significantly change over time or differ between groups. However, there was a significant decrease in BMI percentile over time for both groups. Protein intake significantly increased in the RDa group but remained unchanged in the LDa group. There were no significant differences in carbohydrate or fat intake between groups or over time. Both groups showed significant increases in vitamin D, calcium, phosphorous, potassium, and magnesium intake over time. These findings suggest that the intervention, particularly in the RDa group, led to improvements in nutritional intake, with notable increases in key micronutrients.

Data were assessed using histogram, z scores, kurtosis, and Kolmogorov-Smirnov test. All variables were examined using two-way repeated ANOVA in pre- and post-intervention, time effect. Differences between groups at an initial level were also examined using independent t-tests. The study also conducted Pearson correlations to examine the relationships among nutrition diary servings, change in BTM, and maturity offset. The significance level was established at an alpha level of less than 0.05. The statistical analyses were conducted using the SPSS software (Josse AR, 2020).

RESULTS:

Overall, the randomized controlled trial conducted on women who have reached menopause found that supplementation with calcium (Ca) or calcium plus NutraFlora short-chain fructooligosaccharide did not have a substantial impact on the rate of bone loss compared to maltodextrin after 24 months. However, CaFOS supplementation showed some benefits, including decreased total-body bone mineral density and reduced bone turnover compared to Ca alone. These effects were more pronounced in women with osteopenia, where CaFOS supplementation resulted in a significantly smaller decline in total-body BMD compared to maltodextrin.

Characteristic	Ca (n = 100)	CaFOS (n = 100)	MD (n = 100)	P-value
Age (years)	61.3 ± 6.6	61.3 ± 6.4	60.4 ± 6.3	0.53
Age at menarche (years)	12.5 ± 1.5	13.1 ± 1.5	13.1 ± 1.5	0.35
Age of menopause (years)	48.2 ± 5.0	49.4 ± 4.8	47.8 ± 5.6	0.08
Surgical menopause (%)	25	15	19	0.20
Years since menopause	13.1 ± 8.1	12.0 ± 7.2	12.6 ± 7.5	0.67
- Total body	0.1 ± 1.0	0.2 ± 1.2	0.1 ± 1.1	0.51
Daily total calcium intake (g)	0.9 ± 0.4	0.9 ± 0.4	0.9 ± 0.4	0.68
Daily vitamin D intake (mg)	4.9 ± 2.6	4.6 ± 2.8	5.1 ± 2.8	0.24

Characteristic	Ca (n = 100)	CaFOS (n = 100)	MD (n = 100)	P-value
Daily fiber intake (g)	17.2 ± 5.7	18.8 ± 6.4	18.2 ± 5.9	0.17
Estimated osteopenia (%)	63	54	57	0.42
Serum CTX (mg/L)	0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.32
Serum osteocalcin (mg/L)	20.6 ± 7.8	18.9 ± 6.7	19.6 ± 8.3	0.35
Serum vitamin D (nmol/L)	56.2 ± 19.6	55.8 ± 17.7	53.4 ± 17.8	0.47
Insufficient (,<50 nmol/L) vitamin D (%)	40.2 ± 6.0	40.1 ± 6.7	38.3 ± 7.4	0.34
Serum total calcium (mmol/L)	2.2 ± 0.1	2.2 ± 0.1	2.2 ± 0.1	0.87
Plasma PTH (ng/mL)	61.1 ± 25.5	58.4 ± 18.6	63.1 ± 31.1	0.88

Table 1.2: The table presents baseline characteristics of participants in three treatment groups: Ca, CaFOS and MD (maltodextrin). It includes demographic information, anthropometric measurements, dietary intake, bone health indicators, and physical activity levels. Statistical significance (P-values) indicates differences among the groups. Key findings include similar ages across groups, higher alcohol use in the MD group, and higher physical activity in the Ca group. There are no significant differences in most bone health indicators and dietary intakes among the groups.

	Baseline	24 months	Change (%)
Lumbar vertebrae 1–4			
Ca	1.078	1.061	-1.7
CaFOS	1.121	1.115	-0.5
MD	1.096	1.082	-1.3
Femur			
Ca	0.885	0.877	-0.9
CaFOS	0.903	0.897	-0.7
MD	0.897	0.887	-1.1
Total body			
Ca	1.126	1.119	-0.6
CaFOS	1.142	1.141	-0.1
MD	1.130	1.127	-0.3

In an animal study involving mice, supplementation with fructooligosaccharide (FOS) or galactooligosaccharide (GM) increased femoral bone area and calcium content compared to the control group. FOS and GM groups also showed lower urinary deoxypyridinoline (DPD) excretion, indicating reduced bone resorption, and lower serum high-sensitivity C-reactive protein levels, indicating reduced inflammation.

	Control	FOS	GM
Bifidobacterium	3.2 ± 1.1	139 ± 305	1.4 ± 0.7
Lactobacillus	7.0 ± 6.0	37.0 ± 32.5*	1.6 ± 0.9
Bacteroides	35.6 ± 33.1	371 ± 268*	80.3 ± 51.0
Clostridium	8.2 ± 7.7	5.2 ± 2.9	919 ± 642*

Values are expressed as mean ± SD (n = 15 per group). *Significant difference from the control group at $p < 0.05$ by Dunnett's post hoc test.

The third study found no significant differences in anthropometric measures, dietary intakes, or bone biochemical markers between groups at baseline. Both groups showed improvements in diet over time, with increased intakes of several nutrients. The BMI percentile dropped in both groups without

a change in body weight. The RDa group had higher intakes of dairy-related nutrients than the LDa group.

Two-way repeated measures of the ANOVAs revealed significant interactions between the groups and time for β-CTX and OC, indicating decreases in these markers in the RDa group. It increases in the low dairy group from pre- to post-intervention. Post-hoc analyses revealed significant decreases in OC and a trend towards a decrease in CTX in the RDa group, with no change in the LDa group.

variable	**RDa**	**LDa**	**RMANOVA (p values)**
	N = 19	N = 16	
Pre	**Post**	**Pre**	**Post**
P1NP (µg/l)	376.9 ± 308.7	300.1 ± 224.8	258.3 ± 200.0
β-CTX (ng/l)	1015.4 ± 331.3	918.9 ± 364.6†	831.6 ± 290.7
Osteocalcin (pg/ml)	15380.1 ± 6081.0	14434.9 ± 4992.1†,*	12611.3 ± 5475.3
Sclerostin (pg/ml)	2667.6 ± 1057.1	2576.8 ± 1200.6	2175.5 ± 1011.6
25-hydroxyvitamin D (nmol/l)	81.7 ± 20.9	83.7 ± 22.3	77.2 ± 25.3
Parathyroid hormone (pg/ml)	113.2 ± 68.2	108.0 ± 70.2	81.9 ± 37.2
Bone turnover ratio (P1NP:β-CTX)	337.8 ± 164.4	304.8 ± 121.9	280.9 ± 127.7

Table 1.3: Values are expressed as mean ± SD. † Significant within-group pre-post difference, $p < 0.05$; post-hoc paired t test.

Pearson correlations showed negative correlations between Modifications in β-CTX and OC levels with dairy servings ingested during the trial. Additionally, correlations at baseline indicated that maturity offset exhibited a negative correlation with β-CTX, P1NP, and OC, suggesting that as maturity increases, bone turnover decreases.

The RDa group demonstrated more workout commitment with more scheduled sessions than the LDa group. Both groups adhered to the dairy routine, with the RDa group consuming significantly more dairy servings than the LDa group.

In summary, the study suggests that the RDA group, which had higher dairy intake, experienced decreases in bone resorption markers and improvements in bone turnover compared to the LDa group, indicating the potential benefits of dairy consumption on bone health.

DISCUSSION:

The discussion aims to interpret and contextualize the findings from the reviewed studies, providing insights into the implications of gut microbiota dysbiosis and dietary interventions on bone health.

Impact of Gut Microflora Dysbiosis on Bone Health:

The reviewed studies collectively emphasize the significant role of intestinal microflora dysbiosis in contributing to impaired bone health. Dysbiosis disrupts bone metabolism signalling pathways, leading to decreased calcium absorption, dysregulated osteoclast activity, and compromised bone strength and quality. Factors such as age, diet, and diseases exacerbate dysbiosis, highlighting the complexity of the gut-bone axis.

Dietary Interventions and Prebiotics:

Dietary interventions targeting the gut microflora offer potential avenues for improving bone health. Prebiotics like galactooligosaccharides (GOSs) and fructooligosaccharides (FOSs) have shown promising effects in modulating gut microbiota composition, stimulating beneficial bacteria growth, and enhancing osteoblast activity. These prebiotics also improve calcium absorption and mineralization, as evidenced by clinical trials and animal studies.

Investigations conducted in clinical trials and animal studies:

The reviewed clinical experiments and animal trials provide valuable insights into the efficacy of prebiotic supplementation in preserving bone health. Supplementation with calcium plus short-chain

fructooligosac charides (CaFOS) or fructooligosac charides (FOS) has demonstrated positive effects on bone density, BTM, and inflammation reduction. These findings underscore the potential of dietary interventions to mitigate bone loss and prevent osteoporosis.

Discussion of Results from Randomized Controlled Studies:
The results from randomized controlled studies in postmenopausal women highlight the benefits of dietary supplementation with CaFOS in reducing bone loss and improving bone turnover compared to calcium alone. These findings suggest that prebiotic supplementation may offer additional benefits for individuals at risk of osteoporosis, particularly those with osteopenia.

Exercise Compliance and Dairy Intake:
The discussion also addresses the importance of exercise compliance and dairy intake in promoting bone health. Participants in the intervention groups demonstrated varying levels of compliance, with the group receiving recommended dairy intake showing improvements in bone turnover markers. This highlights the potential benefits of dairy consumption in enhancing bone health.

Limitations and Future Directions:
It is essential to understand the limitations of the reviewed studies, including small sample sizes, short durations of intervention, and variations in study designs. Future research should focus on elucidating the mechanisms underlying the gut-bone axis and optimizing dietary interventions for improving bone outcomes. Long-term, well-designed clinical experiments are needed to validate the effectiveness of prebiotic supplementation and its potential as a preventive strategy for osteoporosis.

CONCLUSION:

In conclusion, the findings from the reviewed studies underscore the complex interplay between gut microbiota and bone health. Dysbiosis of the intestinal microflora contributes to impaired bone metabolism, while dietary interventions targeting the gut microflora show promise in preserving bone health and reducing the risk of osteoporosis. More research is warranted to fully understand the processes involved and optimize dietary strategies for improving bone outcomes.

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