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Study of skeletal health in elderly patients with kidney disease

Submission date	Recruitment status	[_] Prospectively registered
06/11/2025	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/11/2025	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
12/11/2025	Urological and Genital Diseases	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Chronic kidney disease (CKD) has a global prevalence of approximately 10–15%, with the rate rising to over 30% in individuals aged 65 years and older. A major complication of CKD is bone disorders: up to 60% of patients with moderate CKD (stage 2–3) develop osteoporosis, a rate significantly higher than that of age-matched individuals with normal kidney function.
Standard osteoporosis treatments (e.g., bisphosphonates like alendronate sodium) are less effective in CKD patients compared to the general population, and their effectiveness further declines as kidney function worsens.
Bifidobacterium animalis subsp. lactis BB-12 is a well-studied probiotic strain with proven safety in the elderly. However, clinical evidence supporting the use of probiotics for bone health in CKD patients remains limited.
This study aims to evaluate whether combining Bifidobacterium animalis subsp. lactis BB-12 with standard alendronate sodium/vitamin D3 therapy improves bone mineral density (BMD), bone metabolism markers, and T cell immune-related metabolism in elderly patients with CKD stage 2–3 and osteoporosis.

Who can participate?
Patients aged 65 years and over with stage 2–3 CKD and osteoporosis

What does the study involve?
Participants are randomly assigned to two groups. The intervention group receives standard osteoporosis treatment: alendronate sodium and vitamin D3 (once weekly, via tablets) and elemental calcium (daily, as calcium carbonate) plus probiotic supplementation with Bifidobacterium lactis BB-12 (daily, in capsule form). The control group receives the same standard osteoporosis treatment as the intervention group plus placebo supplementation with identical-looking capsules containing maltodextrin (once daily). Alendronate sodium/vitamin D3 tablets are taken in the morning on an empty stomach with a full glass of water; participants must remain upright for at least 30 minutes post-ingestion. Probiotic/placebo capsules are taken in the evening with cold or lukewarm drinks. Participants are followed for 12 months with evaluations at baseline, 3 months, 6 months, and 12 months.

What are the possible benefits and risks of participating?
Possible benefits:
1. Improved skeletal health, which may lower the risk of bone loss and fractures.
2. Enhanced immune-metabolic balance, which may alleviate the chronic inflammation associated with CKD.
3. Access to structured care: regular follow-up visits, free study medications (alendronate sodium /vitamin D3, calcium, probiotic/placebo), and comprehensive health monitoring (e.g., scans, laboratory tests).
Possible risks:
1. Mild adverse events: common, non-serious side effects include gastrointestinal symptoms (abdominal discomfort, diarrhea, constipation), musculoskeletal pain (back pain, joint pain), upper respiratory tract infections, headache, or dizziness
2. Rare serious adverse events: infrequent serious events (e.g., hospitalization)
3. No increased renal risk
4. No specific probiotic-related risks

Where is the study run from?
First Affiliated Hospital of Xinxiang Medical College (China)

When is the study starting and how long is it expected to run for?
March 2020 to January 2023

Who is funding the study?
Bethune Charitable Foundation (China)

Who is the main contact?
Yun Liu, liuyun_593@163.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Gut-bone-immune modulation with probiotic-enhanced alendronate sodium/vitamin D3 and Bifidobacterium lactis BB-12 improves skeletal health in elderly patients with stage 2–3 chronic kidney disease

Study objectives
Evaluate whether combining Bifidobacterium animalis subsp. lactis BB-12 with standard alendronate sodium/vitamin D3 therapy improves bone mineral density (BMD), bone metabolism markers, and T cell immune-related metabolism in elderly chronic kidney disease (CKD) stage 2–3 patients with osteoporosis.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 01/12/2022, First Affiliated Hospital of Xinxiang Medical College (No.88, Jiankang Road, Weihui City, Xinxiang, 453100, China; +86 (0)18738501860; liuyun_593@163.com), ref: EC-022-117

Study design
Single-center double-blind randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic kidney disease (CKD)

Interventions
128 elderly patients (≥65 years) with CKD stage 2–3 and osteoporosis were randomly assigned to receive either alendronate sodium/vitamin D3 plus B. lactis BB-12 (intervention group, n = 64) or alendronate sodium/vitamin D3 plus placebo (control group, n = 64).

Intervention group (n = 64):
Dosage: alendronate sodium 70 mg + vitamin D3 2800 IU/week; Bifidobacterium lactis BB-12 1×10^{10} CFU/day; Elemental calcium 500 mg/day (as calcium carbonate)
Administration method: alendronate sodium/vitamin D3 tablets taken in the morning on an empty stomach with a full glass of water; B. lactis BB-12 capsules taken in the evening with cold or lukewarm drinks; calcium carbonate taken as routine

Frequency: alendronate sodium/vitamin D3 once weekly; B. lactis BB-12 and calcium carbonate once daily

Control group (n = 64):
Dosage: alendronate sodium 70 mg + vitamin D3 2800 IU/week; placebo capsules (containing maltodextrin) one capsule/day; elemental calcium 500 mg/day (as calcium carbonate)
Administration method: alendronate sodium/vitamin D3 tablets taken as the intervention group; placebo capsules taken in the evening with cold or lukewarm drinks; calcium carbonate taken as routine
Frequency: alendronate sodium/vitamin D3 once weekly; placebo and calcium carbonate once daily
Total treatment time: 12 months
Follow-up duration: 12 months (key timepoints: baseline, 3 months, 6 months, 12 months)

Randomization process:
Randomization ratio: 1:1 allocation to intervention and control groups.
Randomization method: computer-generated random number sequence with permuted blocks of variable sizes (4 and 6)
Stratification factors: sex, baseline T-score (≤-3.0 or >-3.0), eGFR category (35-44 or 45-59 mL/min /1.73 m^2).
Blinding: double-blinding (participants and investigators including outcome assessors); probiotic and placebo preparations are identical in appearance, taste, smell, and packaging; randomization code sealed in opaque envelopes, broken only after data analysis or for serious adverse events.
Implementer: statistician not involved in patient recruitment or assessment.

Intervention Type
Mixed

Primary outcome(s)
1.Lumbar spine (L1-L4) bone mineral density (BMD) percentage change is measured using dual-energy X-ray absorptiometry (DXA, Lunar Prodigy, GE Healthcare) at baseline and 12 months
2. Femoral neck BMD percentage change is measured using dual-energy X-ray absorptiometry (DXA, Lunar Prodigy, GE Healthcare) at baseline and 12 months

Key secondary outcome(s))
1. Serum levels of bone turnover markers (C-terminal telopeptide of type I collagen [CTX-I] and procollagen type I N-terminal propeptide [P1NP]) are measured using electrochemiluminescence immunoassays (Roche Diagnostics) at baseline, 3 months, 6 months and 12 months.
2. Serum levels of mineral metabolism parameters (calcium, phosphate, intact parathyroid hormone [iPTH], 25-hydroxyvitamin D [25(OH)D] and fibroblast growth factor 23 [FGF23]) are measured using laboratory routine tests at baseline, 6 months and 12 months.
3. T cell subsets (Th1, Th2, Th17 and regulatory T cell [Treg]) are measured using flow cytometry (BD FACSCanto II) with fluorochrome-conjugated antibodies (CD3, CD4, CD8, CD25, FOXP3, IFN-γ, IL-4 and IL-17A) at baseline and 12 months.
4. T cell metabolic parameters (oxygen consumption rate [OCR], extracellular acidification rate [ECAR], OCR/ECAR ratio and spare respiratory capacity) are measured using a Seahorse XFe96 Extracellular Flux Analyzer (Agilent Technologies) with mitochondrial and glycolysis stress tests at baseline and 12 months.
5. Serum levels of inflammatory markers (pro-inflammatory cytokines IL-6, IL-17, TNF-α and anti-inflammatory cytokines IL-10, TGF-β) are measured using multiplex immunoassays at baseline and 12 months.

6. Gut microbiota composition (diversity and genus relative abundance) is measured using 16S rRNA gene sequencing (Illumina MiSeq platform) with QIIME2 software analysis at baseline and 12 months.
7. Kidney function parameters (estimated glomerular filtration rate [eGFR] and urinary albumin-to-creatinine ratio [UACR]) are measured using laboratory routine tests at baseline, 3 months, 6 months and 12 months.
8. Adverse events are recorded throughout the study period, and laboratory parameters for safety assessment (complete blood count, liver function tests and renal function tests) are measured using laboratory routine tests at baseline, 3 months, 6 months and 12 months.
9. Bifidobacterium lactis BB-12 colonization in feces is measured using strain-specific quantitative PCR (qPCR) targeting the hsp60 gene at baseline, 3 months and 12 months.

Completion date
01/01/2023

Eligibility

Key inclusion criteria
1. Age ≥65 years
2. Confirmed CKD stage 2–3 [estimated glomerular filtration rate [eGFR] = 36-59 mL/min/1.73m² consistently exceeds for more than three months (stage 3); GFR = 60-89 mL/min/1.73m², accompanied by other kidney abnormalities for more than three months (stage 2) calculated using the CKD-EPI equation], with all enrolled patients having eGFR ≥35 mL/min/1.73m²at baseline to align with drug safety guidelines for alendronate use
3. Diagnosis of osteoporosis according to WHO criteria (T-score ≤-2.5 at lumbar spine or femoral neck, or presence of fragility fracture)
4. Stable renal function (eGFR change <5 mL/min/1.73m² in the preceding 3 months)
5. Ability to provide informed consent.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
65 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. History of gastrointestinal disorders affecting absorption (e.g., inflammatory bowel disease, celiac disease)
2. Use of antibiotics, probiotics, or synbiotics within 3 months prior to enrollment
3. Current use of medications affecting bone metabolism other than vitamin D and calcium (e.g., glucocorticoids, hormone replacement therapy, denosumab, teriparatide)
4. Contraindications to bisphosphonate therapy (e.g., esophageal abnormalities, inability to remain upright for 30 minutes)
5. Secondary causes of osteoporosis other than CKD (e.g., hyperthyroidism, hyperparathyroidism)
6. History of malignancy within 5 years
7. Active infection or inflammatory disease
8. Life expectancy <12 months

Date of first enrolment
15/03/2020

Date of final enrolment
26/06/2021

Locations

Countries of recruitment
China

Study participating centre
First Affiliated Hospital of Xinxiang Medical College
China
453100

Sponsor information

Organisation
First Affiliated Hospital of Xinxiang Medical College

Funder(s)

Funder type
Charity

Funder Name
Bethune Charitable Foundation

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
China

Results and Publications

Individual participant data (IPD) sharing plan
The datasets used and analyzed during the current study are available from the corresponding author Dr Yun Liu (liuyun_593@163.com) on reasonable request.

IPD sharing plan summary
Available on request