

Effect of Enriched Lactoferrin Supplementation (ELS) on Bone Health in Post-Menopausal Women

(This study is ongoing)

PURPOSE

The purpose of this study is to determine whether a daily “Enriched Lactoferrin Supplement (ELS)” will improve bone health among post-menopausal women.

Condition	Intervention
Post-menopausal women	Enriched Lactoferrin Supplement (ELS)

Study Type: Interventional
Study Design: Supplementation

Official Title: Effect of Enriched Lactoferrin Supplementation (ELS) on Bone Health in Post-Menopausal Women

Primary Outcome Measures:

- Change in bone turnover markers in serum and urine compared to baseline at 1, 2, 3 and 6 months.
- Change from baseline in bone-specific alkaline phosphatase (BSAP) levels, the serum marker for bone formation.
- Change from baseline in N-telopeptide of type 1 collagen (NTx) levels, the serum marker for bone resorption.

Total Enrollment: 50

Study start: May 2007

Osteoporosis affects both men and women, in particular, the women undergoing post-menopause. The most serious complication of osteoporosis is a broken bone or fracture. Fractures due to osteoporosis can result in long hospital stays, dependence on others, and premature death. While there are several medications that prevent osteoporosis they all have side effects. For example, postmenopausal women who take hormone replacement therapy (HRT) are at increased risk of breast cancer and heart disease. In addition, drugs to prevent osteoporosis are expensive and not available worldwide. Therefore, it is essential that researchers continue to identify and test new medications for the prevention of osteoporosis.

Milk contains a number of growth factors that are vital for mammalian growth and development, in general. While milk calcium provides raw materials for bone mineralization, other specific milk compounds directly stimulate the modeling and remodeling of bone [1]. Recent studies have indicated that lactoferrin (LF); a specific metal-binding glycol-protein is uniquely able to boost the growth-multiplication of human osteoblast cells [2]. Furthermore, LF could reduce, up to 50-70%, the rate at which osteoblast (cells responsible for bone formation) die, and also decrease the formation of

osteoclasts (cells responsible for bone resorption). LF affects osteoblasts by binding to cell surface proteins called low-density lipoprotein receptors. In addition, LF has also been shown to increase the multiplication of chondrocytes, the cells that build cartilage [3]. In mammals, LF production rises in an embryo during the last half of gestation, and indication that it promotes skeletal development [4].

LF is also a major bioactive component of the synovial fluid in the bone joints with a regulatory role in bone growth and repair. Biosynthesized in the bone marrow, LF can modulate inflammatory responses by scavenging toxic 'free' iron [5]. This mechanism is important at the sites of inflammation, such as in the rheumatoid joint. LF can bind 'free' iron in the synovial fluid and reduce joint inflammation during arthritis [6]. Orally administered LF has preventive and therapeutic effects on joint inflammation and pain. The ability of LF to modulate the immune system could be beneficial in the treatment of rheumatoid arthritis [7].

LF is present in milk, saliva, tears, gastric mucus, bronchial mucus, synovial fluid, seminal fluid, amniotic fluid, cerebrospinal fluid, blood and tissue throughout the body. This metal-binding protein is secreted by exocrine glands located at the gateways of digestive, respiratory and reproductive systems [8]. Specific receptors for LF are present on immune cells including neutrophils, monocytes, lymphocytes and on tissues of liver, intestinal, urogenital and respiratory tracts. Interaction of LF with these receptors is essential for several body functions such as hormone regulation, tissue repair, bone regeneration, blood detoxification and energy generation. Numerous functions have been reported and continue to be reported for LF, some of which are related to its iron-binding properties [9]. LF plays a critical role in the intestinal absorption and physiological transport of several essential metals including iron, zinc, manganese, and selenium. The ability of LF to bind iron in the presence of bicarbonate anion contributes to antibacterial, antiviral, antifungal, anti-inflammatory, antioxidant and immuno-modulatory activities [10]. LF is a multifunctional replenishment highly critical for a bone health, in particular.

LF is endowed with millions of distinct receptors all over the body, intestinal brush border cells, in particular, to promote active transport [11, 12]. It is like having a designated master key or swipe card to move around the body! LF can also facilitate the co-entry of other compounds under specialized conditions [13, 14]. An appropriate structure of LF protein, similar to the grooves and indents of a key, is highly critical for such unlock and entry process.

Enriched Lactoferrin Supplement (ELS) is a patented formulation specifically developed to exploit the functional properties of LF for intestinal transport and maximum bioavailability of specific bio-replenishments and supplements that are important for bone health. *In the ELS, a milk ribonuclease (RNase)-enriched fraction of LF creates the key component and a highly potent free-form of LF in excess, that provides the essential bone replenishment. The complex further contains hyaluronic acid and bromelain as functional synergists.*

Healthy bone depends on continuous regeneration, carried out by the two main types of bone cells; *osteoclasts*, which break down old bone; and *osteoblasts*, which form new bone. Osteoporosis occurs when there is an imbalance in this process and the old bone develops fine fractures. Bone formation is indicated by the change in levels of bone specific alkaline phosphatase (BSAP) in the serum [15] and bone resorption as indicated by the change in levels of N-telopeptides (NTx) in the serum and urine [16].

The participants of this clinical study are selected based on the inclusion/exclusion criteria and then randomly assigned to a "Control group" or a "Test group", based on their medical history. The subjects in the **Test group** will receive supplementation of two ELS capsules of 125 mg actives each along with 100% RDA (Recommended Daily Allowance) of Calcium administered orally, from Day 1 to Day 180. The subjects in the **Control group** will receive calcium supplementation only. There will be a total of eight visits in this six month study. During the first informational meeting, the participants will fill up a study questionnaire. After selection based on the questionnaire, selected subjects will have visits on Day (0), Day (+15), Day (+30), Day (+60), Day (+90), Day (+180) of the study. There will be a general check up of weight and blood pressure, blood and urine collection and a study satisfaction and feedback survey / opportunity at each of these visits. This will be followed by the analysis of urine and serum samples for bone turnover markers.

ELIGIBILITY

Ages Eligible for Study: 45 to 60 years

Genders Eligible for Study: Female

CRITERIA

Inclusion Criteria

- Post-menopausal - no menses for 18 months; and if less than 50 years of age - no menses for 12 months if more than 50 years of age
- Generally healthy as determined by standard medical assessment on physical and mental health
- Willing to comply with the study procedures
- Willing to accept use of all nameless data, including publication, and the confidential use and storage of all data
- Having received both oral and written explanations about the study
- Having provided written informed consent
- Willing to travel to the study site

Exclusion Criteria

- Active Paget's disease
- Hyperthyroidism
- Hypothyroidism
- Diabetes mellitus type 1
- Calcium intolerance
- Kidney problems
- Cancer diagnosis for solid malignancies within the 18 months prior to study
- Treatment with estrogens, progesterone, raloxifene, or tamoxifen
- Active inflammatory bowel disease
- Life expectancy of less than 2 years
- Current and ongoing use of methotrexate, phenytoin, phenobarbital, or inhaled corticosteroids at a dose of greater than 800 mcg/day
- Current use of antiresorptive agents (e.g., calcitonin or bisphosphonates).
- Body mass index (BMI) greater than 32 or less than 20

Withdrawal Criteria

- Voluntary withdrawal by the subject
- In the event of adverse effects to study
- At the recommendation of the Principal Investigator
- Non-compliance with the study protocol

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