



Can Ursodeoxycholic acid be Considered as an Alternative Treatment for Postmenopausal Osteoporosis?

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SUMMARY. Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to bone fracture. Bone tissue undergoes constant remodeling. Under the physiologic conditions, bone formation and resorption are in a fair balance. After the third decade of life, bone resorption exceeds bone formation and leads to osteopenia and, in severe situations, osteoporosis. The result is fragile bones and an increased risk for fracture with even minimal trauma. Postmenopausal osteoporosis is thought to result from gonadal (ie, estrogen) deficiency. Estrogen deficiency have been reported to make decrease in 1-25 vitamin D, PTH levels and also calcium absorption and increased of some cytokines (ie. IL-1, TNF-alpha) may cause. it was noticed that Ursodeoxycholic acid (UDCA) may decrease these cytokines and increase fractional calcium absorption. Consequently, we hypothesize that UDCA might be useful Postmenopausal osteoporosis.

INTRODUCTION

Postmenopausal osteoporosis is thought to result from estrogen deficiency. Estrogen deficiency, regardless of age of occurrence, results in accelerated bone loss. The result is fragile bones and an increased risk for fracture with even minimal trauma ^{1,2}. Moreover, it is associated with significant morbidity, mortality, reduction in quality of life, and increasing health care costs ³. Thus, the prevention and treatment of postmenopausal osteoporosis vital degree is important. In this article has been discussed that whether ursodeoxycholic acid may an alternative treatment for postmenopausal osteoporosis.

Can Ursodeoxycholic acid be used in the treatment of Postmenopausal Osteoporosis?

Osteoporosis is a progressive metabolic bone disease that decreases bone density (bone mass per unit volume), with deterioration of bone structure ⁴. It is a common ailment seen in

postmenopausal women, resulting in fragile and weak bones highly susceptible to fractures of hips, spine and wrist ⁵. Women lose 30-40% of their cortical bone and 50% of their trabecular bone over their lifetime ⁶. At menopause, bone remodeling becomes unbalanced and results in bone loss at each remodeling site. In addition, an increase in number of remodeling (that is, bone turnover) sites results in an accelerated bone loss throughout the entire skeleton ⁵. Postmenopausal osteoporosis is thought to result from gonadal (ie, estrogen, testosterone) deficiency ⁷. Estrogen or testosterone deficiency, regardless of age of occurrence, results in accelerated bone loss. The exact mechanisms of this bone loss potentially are numerous, but, ultimately, an increased recruitment and responsiveness of osteoclast precursors and an increase in bone resorption, which outpaces bone formation, occurs. Estrogen inhibits osteoclasts, cells that mediate bone resorption; estrogen stimulates osteoblasts, cells that mediate bone formation. Osteoblasts produce many growth

KEY WORDS: Postmenopausal Osteoporosis, Treatment, Ursodeoxycholic Acid.

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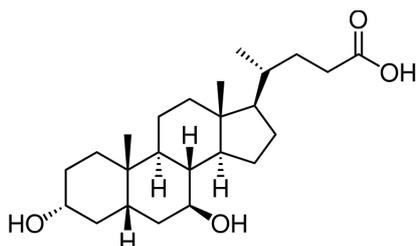


Figure 1. Ursodeoxycholic acid structure.

factors and cytokines that mediate estrogen action, some of which regulate the osteoclasts indirectly. Estrogen deficiency stimulates osteoblast production of IL-1, IL-6, and TNF- α and inhibits apoptosis and extends the life span of osteoclasts ⁷. In conclusion, estrogen make an effect protective on bone mineral density. In addition, low estrogen levels have been reported to make decrease in 1-25 vitamin D, PTH levels and also calcium absorbson ⁸.

Ursodeoxycholic acid (UDCA) is one of the secondary bile acids (Fig. 1), which has cytoprotective, antiapoptotic and immunomodulatory properties ⁹. The UDCA decreases levels of endogenous hydrophobic bile acids while increasing the fraction of non-toxic hydrophilic bile acids. It helps regulate cholesterol by reducing the rate at which the intestine absorbs cholesterol molecules while breaking up micelles containing cholesterol. Because of this property, ursodeoxycholic acid is used to treat (cholesterol) gallstones non-surgically ¹⁰.

UDCA has also been shown experimentally to suppress immune response such as immune cell phagocytosis ¹¹. Hepatoprotective properties have lead to UDCA being used to treat liver diseases such as primary biliary cirrhosis (PBC), primary sclerosing cholangitis and cystic fibrosis-related cholestasis. It is stated that UDCA decreased the inflammatory markers (IL-1, TNF α) in some organs ^{12,13}. Recently, a study showed that UDCA has improved fractional calcium absorbtion in patients with PB ¹⁴. In the light of this information, it may be proposed that UDCA might be used in treatment of postmenopausal osteoporosis.

CONCLUSION

We hypotesize that, considering these properties, UDCA might be useful in treatment of postmenapousal osteoporosis by increasing fractional calcium reabsorbson and decreasing inflammatory cytokines in postmenopausal osteoporosis treatment. Future studies are needed to confirm this hypothesis.

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