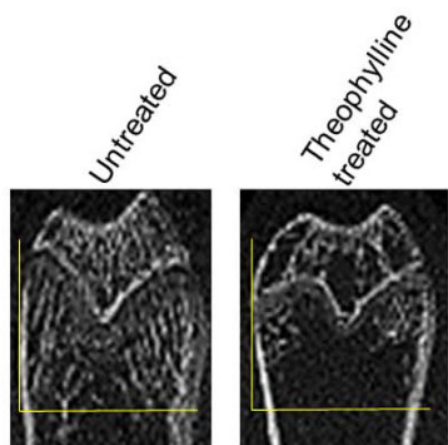


Theophylline, a drug to treat asthma increases risk of fracture and causes vitamin D deficiency

Incidence of chronic obstructive pulmonary diseases (COPD) of which asthma is the commonest manifestation is growing by leaps and bounds in two most populous countries, India and China due to rapid growth of industrialization and associated rise in air pollution. Not surprisingly, the major burden of COPD of the world is shared by these two countries.

Theophylline, a methylxanthine drug is a bronchodialator (dilates airways of lungs) and also has anti-inflammatory property and thus mitigates the distressing symptom of COPD such as breathing trouble. Theophylline is also used as an additive to some 50 medicines sold as fixed dose combination for the treatment of COPD in India.

Side effect # 1: Osteoporosis induction



Severe loss of bony structure by theophylline treatment is shown in the perpendicularly marked region

Side effect # 2

Theophylline causes marked vitamin D deficiency and hormonal and mineral (calcium and phosphate) imbalances

Adverse effects of theophylline on bone and mineral regulation.

Our research on laboratory animals has shown that theophylline kills the bone-forming cells, osteoblasts, and simultaneously hyper-activates the bone degrading cells, osteoclasts and together these processes induce severe bone loss. This drug causes loss of both long and vertebral bones and makes them osteoporotic. As a result bones become brittle and fracture prone. In addition, when animal bones were surgically fractured, theophylline treatment delayed fracture healing. Our research therefore suggests that theophylline not only increases the risk of fracture but also impairs

body's ability to repair fracture.

Medical management of COPD involves a combination of drugs that include not only theophylline but also synthetic corticosteroids because of their anti-inflammatory properties. Corticosteroids are already included in the list of bad-to-bone drugs. Our research showed that the bone loss caused by theophylline was equal to that by methylprednisone (a synthetic corticosteroid present in COPD medication). Therefore, a combination of corticosteroid and theophylline that is generally prescribed to COPD patients is expected to heighten fracture risk.

In addition to making bones porous, the drug also causes deficiency of vitamin D and alters hormones that maintain body's calcium and phosphate balance. Our research showed that theophylline inhibits vitamin D producing enzymes in liver causing a marked fall in vitamin D levels in blood. Vitamin D is a hormone that maintains healthy immune system to fight against infection and required for bone, cardio-vascular and metabolic health. In addition, theophylline increases parathyroid hormone (PTH) and fibroblast growth factor-23 (FGF-23) levels in blood. Excess PTH causes bone loss and excess FGF-23 causes loss of phosphate in urine causing phosphate deficiency. Deficiency of phosphate impairs the ability of bone to deposit minerals that gives the required toughness to bone. Therefore, theophylline causes havoc to body's endocrine system (a network of biochemical signaling systems integrated by hormones) that is necessary for maintaining bone health and its associated minerals (calcium and phosphate).

One good news from our research is that vitamin D supplementation mitigates the adverse impacts of theophylline on bone and bone-related regulating hormones and minerals. Because theophylline suppresses the liver enzymes responsible for the synthesis of vitamin D, a COPD patient who is otherwise vitamin D replete, if taking theophylline would require vitamin D supplementation, or else the patient will quickly become vitamin D deficient and become osteoporotic as well as suffer from imbalances in hormones and minerals that maintain bone health causing rise in fracture risk.

Overall, our research should create awareness among clinicians about increasing the risk of osteoporosis and altering mineral regulation in COPD patients who are prescribed theophylline and preventing adverse impacts by supplementing the patients with vitamin D.

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Publication

[Theophylline, a methylxanthine drug induces osteopenia and alters calciotropic hormones, and prophylactic vitamin D treatment protects against these changes in rats.](#)

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