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LETTER

Can Post-Menopausal Osteoporosis Be Prevented by Essential Fatty Acids? [Letter]

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Dear editor

Based on their study, Damani et al[1] suggest that post-menopausal osteoporosis is due to enhanced production of inflammatory cytokines. Osteoporosis seen in inflammatory conditions such as rheumatoid arthritis is due to excess production of IL-6, TNF-α, and other inflammatory cytokines.[2] These results imply that anti-inflammatory strategies including use of corticosteroids[3] should prevent osteoporosis. Yet they induce osteoporosis. These results imply that there could be some other mechanism(s) by which IL-6 and TNF-α produce osteoporosis that also need to explain the mechanism of post-menopausal osteoporosis and steroids-induced decrease in bone mineral density.

Previously, we showed that corticosteroids inhibit not only phospholipase A2 (PLA2), COX-2 (cyclo-oxygenase-2) and lipoxygenase (LOX) enzymes to reduce the synthesis of pro-inflammatory prostaglandins (PGs), and leukotrienes (LTs) but also the activities of desaturases (both Δ^6 and Δ^5) that are needed for the conversion of dietary essential fatty acids (EFAs) linoleic acid (LA, 18:2 n-6) and alpha-linolenic acid (ALA, 18:3 n-3) to their respective long-chain metabolites arachidonic acid (AA, 20:4 n-6) and eicosapentaenoic acid (EPA, 20:5 n-3) and docosahexaenoic acid (DHA, 22:6 n-3) respectively. Thus, corticosteroids not only suppress the release of AA, EPA and DHA from the cell membrane phospholipids but also reduce their (AA, EPA and DHA) formation by blocking desaturases[4] that explains their potent anti-inflammatory actions. Glucocorticoids by inducing AA, EPA and DHA deficiency also reduce the synthesis of anti-inflammatory lipoxin A4 (LXA4) from AA and resolvins, protectins and maresin from EPA and DHA.

In addition, TNF-α and IL-6 suppress the activities of desaturases[5] suggesting that these cytokines induce AA, EPA and DHA deficiency (similar to glucocorticoids) that results in reduced formation of lipoxins, resolvins, protectins and maresins. AA, EPA, DHA, lipoxins, resolvins and protectins suppress TNF-α and IL-6 production.[4,5] Thus, there exists a feedback regulation between bioactive lipids and pro-inflammatory cytokines.

Estrogen enhances the formation of LXA4 that may explain some of its beneficial actions including its anti-osteoporotic action. Thus, it is envisaged that AA/EPA/DHA and LXA4/resolvins/protectins are the downstream mediators of the actions of cytokines, estrogen, and corticosteroids. IL-6 and TNF-α activate PLA2 and COX-2 and LOX enzymes inducing the release of AA/EPA/DHA and increased formation of PGs and LTs; estrogen ienhances the formation of LXA4, whereas corticosteroids inhibit PLA2 and COX-2 and LOX enzymes so that formation of pro-inflammatory PGs and LTs are decreased. PGs produce osteoporosis. Estrogen enhances LXA4 formation that suppresses PGE2 formation and thus, prevents osteoporosis;[5] corticosteroids decrease the release of AA/EPA/DHA and formation of LXA4, resolvins, protectins and maresins that suppress IL-6, TNF-α, and PGE2 production. Thus, IL-6 and TNF-α have pro-inflammatory actions and produce osteoporosis; post-menopausal osteoporosis is due to excess generation of cytokines; glucocorticoids are anti-inflammatory but produce osteoporosis; estrogen is anti-inflammatory and prevents osteoporosis; AA/EPA/DHA/lipoxins/resolvins/protectins/maresins are anti-inflammatory and prevent osteoporosis. Hence, understanding the interaction(s) among estrogen, cytokines, glucocorticoids, and bioactive lipids may throw newer insights into the pathobiology of not only osteoporosis but also inflammation and immune response.[4,5]

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Disclosure

The author reports no conflicts of interest in this communication.

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