Regulatory Role of PPAR-gamma Agonist Pioglitazone in Osteoclastogenesis of Type2 Diabetic Postmenopausal Women

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Pioglitazone, a class of Thiazolinediones (TZDs) is an effective oral drug used for management of type2 diabetes mellitus. Pioglitazone exerts its action through the activation of peroxisome-proliferator activator receptor-ã (PPAR-gamma) and turning on gene transcription. Activation of PPARg by TZDs play an important role in bone metabolism by promoting hematopoietic stem cells to differentiate into osteoclast, thus increasing bone resorption. Many observational studies have suggested the effect of TZDs on bone loss and high fracture incidence in diabetic postmenopausal women; few studies have shown the role of TZDs in estrogen synthesis. The effect of pioglitazone on osteoclastogenesis which may involve the suppression of estrogen function in type2 diabetic postmenopausal women has not been previously studied. In this connection, we have identified osteoclasts in type2 diabetic postmenopausal women using an invitro technique from peripheral blood monocytes in the presence of macrophage colony stimulating factor (M-CSF) and soluble RANKL.

The study were divided into three groups, healthy control postmenopausal women (n=13) (mean age 44.61±17.10), type 2 diabetic postmenopausal women (n=13) (mean age 48.87±16.98) and type 2 diabetic premenopausal women (mean age 32.12 ± 7.10) (n=13). PBMCs were treated with different concentrations of pioglitazone (2-10µM) and 17 beta estradiol (0.1-1nM) for 7-15 days. TRAP-positive multinucleated cells containing three or more nuclei were considered as osteoclasts. Pioglitazone treated cells showed a significant increase in osteoclasts as compared with untreated cells from healthy and diabetic pre and postmenopausal women .Reduction in osteoclast cells were observed in estradiol treated cells as compared to untreated cells.