Gadolinium promotes osteogenic differentiation in MC3T3-E1 cells and human adipose tissue-derived mesenchymal stem cells: a possible role of gadolinium on ectopic calcification of nephrogenic systemic fibrosis

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Keywords: Gadolinium, nephrogenic systemic fibrosis, osteoblasts, mesenchymal stem cells, calcification

Objective: Recent studies have suggested a close association between the administration of gadolinium (Gd)-based contrast agents and the development of nephrogenic systemic fibrosis (NSF), an acquired disorder characterized by systemic fibrosis and ectopic calcification in patients with severe renal dysfunction. However, causative roles of Gd has remained unknown. The aim of this study is to investigate the effect of Gd on the development of fibrosis and calcification in cultured cells.

Methods: MC3T3-E1 cells (pre-osteoblastic cells), human adipose tissue-derived mesenchymal stem cells (AMSCs), human osteoclasts, human preadipocytes and human dermal fibroblasts (HDFs) were cultured in each differentiation medium with or without gadolinium chloride (GdCl₃). Osteogenic differentiation of MC3T3-E1 cells and AMSCs was determined by Alizarin Red staining. Adipogenic differentiation of human preadipocytes and AMSCs was determined by Oil Red O staining. Osteoclast differentiation was determined by TRAP staining. Fibrogenesis of HDFs was determined by real time PCR for the mRNA expression of type I collagen.

Results: GdCl₃ promote osteogenic differentiation and osteoclast differentiation, but not adipogenic differentiation. In addition, gadodiamide also promote osteogenic differentiation in MC3T3-E1 cells. GdCl₃ did not increase the mRNA expression of type I collagen in HDFs.

Conclusions: We have demonstrated a direct relationship between Gd and osteogenic differentiation that may be involved in the development of ectopic calcification of NSF patients.