Effects of Gadodiamide on cell proliferation and collagen production in cultured human dermal fibroblasts

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Introduction

Symptoms of NSF largely occur in the skin (redness and hardness accompanied by pain and itching sensation of the extremities and trunk) and articular symptoms (contracture and articular immobility). The fibrosis-affected skin in NSF patients is histopathologically characterized by thickening of the collagen fiber bundles, presence of numerous fibroblast-like cells and positive results for CD34. The present study was designed to evaluate the influence of GA on the proliferation activity, collagen production activity and expression levels of the collagen genes in healthy human dermis-derived fibroblasts, with the goal of exploring the mechanism underlying the development of Gd-induced fibrosis.

Figure 1. Effects of gadodiamide (GA) on the growth of cultured dermal fibroblasts.

The number of cells was counted 24(day 1), 48(day 2), and 72(day 3) hours after the start of incubation with GA. The results shown are mean $\pm$ S.E.M.

Figure 4. Effects of gadodiamide (GA) on DNA synthetic activity by cultured dermal fibroblasts.

Figure 5. Effects of gadodiamide (GA) on production of collagens by cultured dermal fibroblasts.

Figure 6. Effects of GA on the gene expression levels of the genes encoding $\alpha 1(I)$ collagen, $\alpha 2(I)$ collagen and $\alpha 1(III)$ collagen in cultured dermal fibroblasts Real-time reverse transcriptase- polymerase chain reaction (PCR) analysis of the genes encoding $\alpha 1(I)$ collagen (a), $\alpha 2(I)$ collagen (b) and $\alpha 1(III)$ collagen (c)

Figure 2. Phase contrast images of fibroblasts with / without treatment by GA.

Cell division images (arrows) were more frequently observed in the culture containing GA at $5 \times 10^{-5} M$ as compared to those in the culture without GA .

Figure 3. Immunofluorescence staining of CD34 (red) in fibroblasts culture with / without treatment by GA at $5 \times 10^{-5} M$.

Conclusion

We conclude that, addition of GA to the culture medium resulted in elevation of the fibroblast growth activity, while the collagen expression level did not differ significantly between the GA-added group and the control group.

These results suggest that the formation of sclerosing lesions in patients with NSF may be attributable to the effect of GA of enhancing the growth activity of CD34 positive fibroblasts.