VIEW POINT

Heparin Effect on Osteoblast-Like Cells In Vitro

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We have read the comprehensive article by Hausser et al. [2004] with great interest. Since our own work has been cited, we would like to take the opportunity for a few remarks. The authors state that heparin interferes with the ligand binding activities of heparan sulfate chains by competing with binding sites on "heparin-binding" proteins, thus interfering with normal growth factor responses to cells. This facts is crucial and underlines a possible pathomechanism in heparin-induced osteoporosis. Other growth-factor interactions of heparin have been described: insuline-like growth factor (ILGF) binding protein-5 is expressed on the osteoblast surface and regulates osteoblast replication and proliferation [Song et al., 2000]. Heparin has the ability to bind to the ILGF binding protein 5, which reduces the affinity of this receptor for ILGF and possibly interfering with physiological osteoblast regulation [Andress, 1995].

Furthermore, the authors discuss the dual effect of low and high heparin concentrations described before [Kock and Handschin, 2002; Matziolis et al., 2002]. Inhibitory effects of heparin preparations were observed in both of these studies in high concentrations (50 and 100 mcg/ml), while low concentrations (0.1–0.2 IU/ml) caused a stimulating effect on osteoblast proliferation in one study. The findings of Matziolis et al. [2002] do not contribute to explain to phenomenon of heparin induced osteoporosis, because inhibitory effects on bone in vivo have been predominantly observed in high dose and long term treatment (>10.000 I.E./day, several weeks of heparin therapy) but not in therapeutical doses used in their experiment. Short-term low-dose heparin administration does not change biochemical parameters of bone resorption [van der Wiel et al., 1993]. We suggest, that in future in vitro experiments on heparin osteoporosis, high doses should be chosen to reach a biological effect on osteoblasts.

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Received 26 April 2004; Accepted 28 April 2004

DOI 10.1002/jcb.20176

Published online 8 July 2004 in Wiley InterScience (www.interscience.wiley.com).