The Relationship of Mineral and Bone Metabolism to the Systemic Response to Neurotrauma of Adult Males with Spinal Cord Injury

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ABSTRACT

Biochemical assays and radioabsorptiometry evaluated the relationship of mineral and bone metabolism to the systemic response to neurotrauma or orthopaedic trauma of adult males. Forty-one adult males (29.4±9.3 years) participated of which 37 had a primary diagnosis of traumatic spinal cord injury (SCI) and four were vertebral fracture controls. Biochemical abnormalities found included hyperphosphataemia, in association with low or low normal serum levels of 1,25-dihydroxyvitmain D ($1,25(OH)_2D$) and of parathyroid hormone (PTH), whilst patients remained normocalcaemic. These disturbances of phosphate and vitamin D metabolism and the markedly accelerated resorption of bone were strongly associated with the interval since injury and the severity of injury, but none of these relationships was correlated with the level of the injury, the sensory status of a patient or the presence of spine fracture.

The disturbances of phosphate and vitamin D metabolism and the markedly accelerated resorption of bone found in this study are a mirror image of the data of patients with the heritable disorders autosomal dominant hyperphosphataemic rickets (ADHR), which results from an inactivating mutation of the gene encoding fibroblast growth factor 23 (FGF23) and autosomal recessive hypophosphataemic rickets (ARHR), which is caused by a mutation of the gene encoding dentin matrix protein-1 (DMP-1). It is potentially important that the hormone/proteolytic enzyme/extra-cellular matrix protein cascade associated with these disorders is counter-regulated by $1,25(OH)_2D$, acting either directly or indirectly. The present results suggest that the serum levels of $1,25(OH)_2D$ of the neurotrauma patients chosen for study may have been inappropriately high with respect to the "physiological and metabolic set" of serum levels of phosphate and ionised calcium in the period corresponding to the uncoupling of the resorption and formation of bone, at least in males, prompting further investigation. The findings are consistent with a new "physiological set," possibly involving

an abnormality in the synthesis or processing of the endocrine fibroblast growth factors or other circulating phosphatonins, which may act as an additional level of regulation of the renal–bone axis, rather than renal failure. Strongly supporting this was the dynamic pattern of the biochemistry and radiological data of these neurotrauma patients and also, preliminary evidence of disturbances in circulating levels of other systemic modulators of mineral and bone metabolism.

The relationships that were observed potentially may be explained by the diversity of the physiological activities of the endocrine fibroblast growth factors and the modes of actions of secreted FGF23 in bone.

The findings provide an understanding of why bone loss occurs and may form the target for safe and cost effective interventions.

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