SERUM CONCENTRATIONS OF CATHEPSIN K IN PAGET'S DISEASE OF BONE BEFORE AND AFTER BISPHOSPHONATES INTRAVENOUS TREATMENT

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Cathepsin K is a cysteine protease enzyme with high expression in bone. It is synthesized by the resorbing osteoclast, and regulates the degradation of the organic matrix of bone. It cleaves both helicoidal and telopeptide regions of collagen type I. Importantly bone resorption is impaired in cathepsin K deficiency. The aim of the present study was to evaluate serum cathepsin K levels in 60 patients affected with Paget's disease of bone (PDB) before and after treatment with different intravenous bisphosponates compared to control age-matched women (n=30) and men (n=20). Circulating cathepsin K levels were determined by a specific sandwich enzyme immunoassay. The detection limit was 1.1 pmol/l, and the CV were 4-6%. Serum total alkaline phosphatase (ALP), crosslaps (sCTX) and bone-specific ALP (BALP) were also measured. After recruitment, 28 of the 70 PDB patients were treated with intravenous pamidronate and 12 with zoledronate with follow-up serum sampling at days 3, 30, 90 and 180 after each treatment. Pre-treatment cathepsin K levels were significantly higher in PDB patients than controls. Moreover, in PDB subjects baseline cathepsin K positively correlated with sCTX and urinary calcium but not with ALP and BALP. Similar but weaker correlations were observed in controls. Overall, intravenous bisphosphonate treatment significantly reduced cathepsin K levels by 28%, 34%, 45% and 29% at respectively 3, 30, 90 and 180 days. The reduction at each time point was significantly higher in patients treated with zoledronic acid than in those treated with pamidronate. With pamidronate, a trend for an increase in cathepsin K levels at 180 vs. 90 days of follow-up was observed. On the opposite, ALP and BALP levels significantly decreased at 30, 90 and 180 days, without any significant increase between 90 and 180 days.

Our data suggest that serum cathepsin K could be a valuable parameter in the evaluation of subjects with PDB as well as in the follow up of different bisphosphonate treatments. The observed increase in cathepsin K levels with respect to ALP or BALP observed 180 days after pamidronate treatment may suggest a better sensitivity of cathepsin K in predicting the recurrence in disease activity.