EFFECTS OF ZOLEDRONIC ACID ON CATHEPSIN K CIRCULATING LEVELS IN PATIENTS WITH BONE METASTASIS

Tumminello Francesca M[1]., Badalamenti Giuseppe[2], Incorvaia Lorena[2], Fulfaro Fabio[2] Crescimanno Marilena[1], Flandina Carla[1], Gebbia Nicola[2] and Leto Gaetano [1]

[1] Lab. Chemioter. Sperimentale and [2]U.O. di Oncologia Medica, Dipartimento di Discipline Chirurgiche ed Oncologiche; Policlinico Universitario P. Giaccone, 90127 Palermo, Italy

Background: Cathepsin K (CathK) is a cysteine proteinase predominantly expressed in the osteoclasts. The enzyme appears to play a key role in osteoclast mediated bone resorption. Therefore, we have undertaken some investigations to assess whether the blood levels of this proteinase may be altered in patients with bone metastasis and whether this enzyme may have a role as additional marker for the therapeutic monitoring of patients undergoing serial treatments with zoledronic acid (ZA), a third generation bisphosphonate derivative endowed with a powerful osteoclast inhibiting activity. ***Patients and Methods:*** Cath K serum levels were determined by a commercially available ELISA kit in patients with bone metastases from breast cancer(BC) or prostate cancer(PC) administered with ZA (4mg i.v. by a 15 min. infusion, every 21days).The circulating levels of this enzyme were measured before starting drug treatments (baseline) and then 1 month after the first ZA administration. Additionally, Cath K concentrations were also assessed in the peripheral blood of patients with localized BC or PC, in patients with non-malignant diseases and in healthy blood donors (control group). ***Results:*** Mean Cath K serum levels were significantly more elevated in healthy subjects or patients with primary osteoporosis as compared to BC patients ($p=0.0008$ and $p=0.0009$ respectively). Conversely, no significant difference was highlighted between PC patients and patients with benign prostatic hyperplasia (BPH) or healthy subjects. Furthermore, in patients with metastatic bone disease Cath K circulating levels were not significantly different from those measured in patients primary tumor. Surprisingly, the administration of ZA to patients with bone metastasis from breast or prostate cancer induced a marked increase of CK serum levels as compared to baseline values, being this phenomenon statistically significant only in the case of PC patients ($p=0.016$). ***Conclusion***: ZA administration induced a marked increase of serum Cath K in patients with bone metastasis. As this proteinase has been shown to be actively secreted also by osteoblasts it is conceivable to speculate that the changes in Cath K levels induced by ZA may reflect an enhanced osteoblastic activity related to bone remodelling processes elicited by the drug treatment. Therefore, the circulating levels of this enzyme may be regarded also as a possible additional marker of osteoblastic activity and may be useful for the monitoring of the therapeutic response of patients to treatments with bisphosphonates.

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