ECTS
Rome, May 15th 2016
Poster # P395

Acute kidney injury (AKI) after a single intravenous zoledronic acid administration in patients with osteoporosis

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Introduction

Safety data on zoledronic acid (ZA) administration for osteoporosis suggest potential kidney toxicity; indeed, it is not indicated in patients with impaired renal function. Patients' clinical monitoring usually includes glomerular filtration rate (GFR) evaluation; no study addressed the issue of the early kidney injury.

We evaluated the early (within 3 months) effect of iv ZA on renal function defining the potential role of AKI biomarkers in unveiling subtle damage.

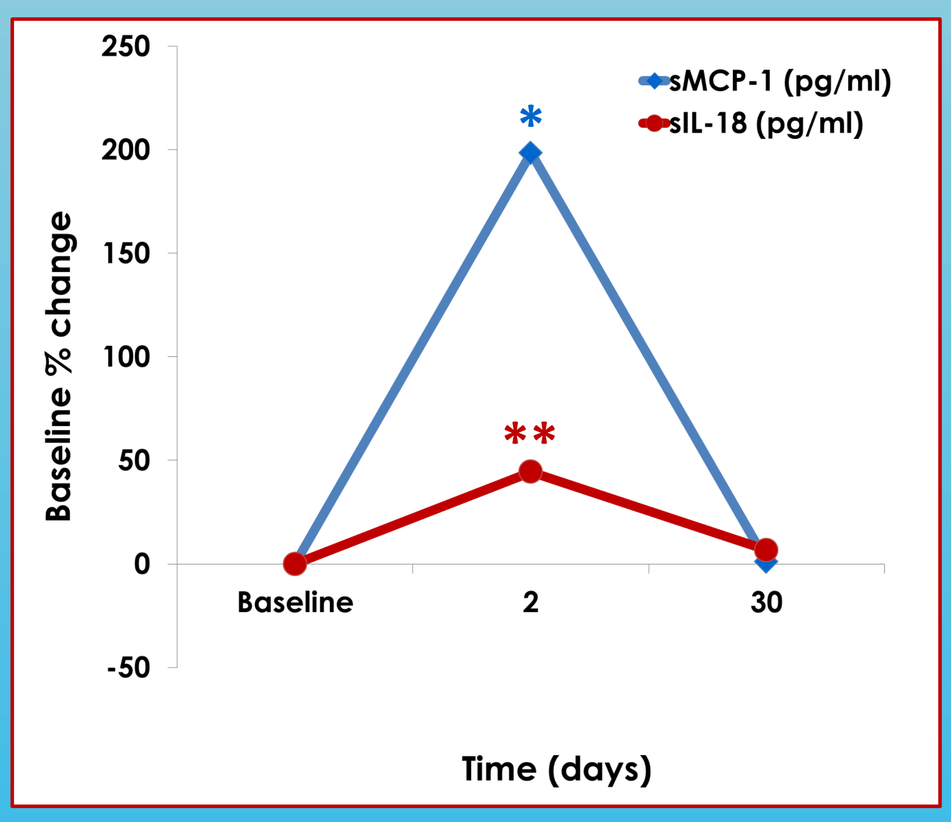
Patients and Methods

Five mg i.v. ZA infusion was administered for the first time to 23 patients with osteoporosis and normal renal function (17 women and 6 men, mean age 73±7 SD years). AKI biomarkers [urinary (u) NGAL, KIM-1, and MCP-1; serum (s) MCP-1 and IL-18] were assessed at baseline and at day (d) 2 and 30 after administration. Serum calcium (sCa), Creatinine clearance (CrCl), parathyroid hormone (PTH), plasma C-terminal FGF-23, sKlotho, calcium excretion (CaEx) and renal threshold phosphate concentration/GFR ($TmPO_4$/GFR) were also measured.

Results

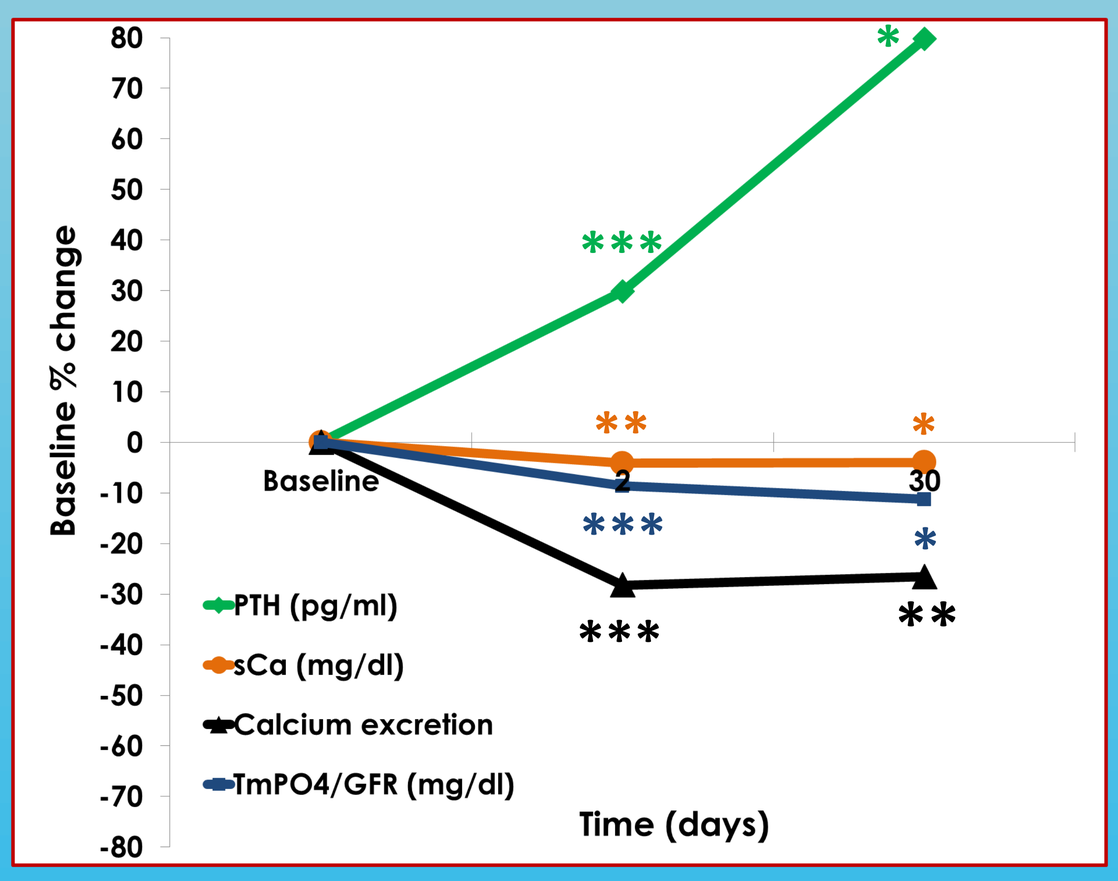
No significant changes in mean levels of urinary markers were detected. Mean values of sIL-18 and sMCP-1 significantly increased at d 2 (44±88%; p<0.01 and 198±237%; p<0.001) and returned to baseline levels at d 30 (*Figure 1*). There was a significant decrease in sCa at d 2 (-4.1±2.8%; p<0.01) and d 30 (-3.9±4%; p<0.001). Mean CrCl values did not significantly change at d 30. Serum PTH significantly increase by 29.8±37.7% at d 2 (p<0.05) and 79.8±95.8% at d 30 (p<0.001) (*Figure 2*). There was a 28±59% and 26±43% decrease in CaEx at d 2 (p<0.05) and d 30 (p<0.01), respectively (*Figure 2*). $TmPO_4$/GFR significantly decreased at d 2 and d 30 (-8.6±15.9%, p<0.05 and -11.3±13.5%, p<0.001) (*Figure 2*). We observed no difference in mean levels of plasma C-terminal FGF-23 and sKlotho at any time.

Figure 1. Mean values of serum MCP-1 and serum IL-18 percent basal difference at any time point



*p < 0.001; **p<0.01

Figure 2. Mean values of serum Calcium, PTH, calcium excretion and $TmPO_4$/GFR percent basal difference at any time point



*p < 0.001; **p<0.01 ***p<0.05

Conclusions

Our data show that there is an acute renal damage as early as 24 hours after ZA infusion in osteoporotic patients with normal renal function. Renal injury is apparently reversible after 1 month.

Among the AKI biomarkers, serum MCP-1 and IL-18 have the best sensitivity in assessing the acute kidney injury.

Hyperparathyroidism, secondary to reduced serum calcium levels, is responsible for reduction in $TmPO_4$/GFR and calcium excretion.