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Letter to the Editor

Acute Effects of Intravenous Administration of Pamidronate in Patients with Osteoporosis

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To the Editor

We read the interesting article "Acute Effects of Intravenous Administration of Pamidronate in Patients with Osteoporosis" in the Journal of Korean Medical Science by Lim et al. (1). We would like to comment and compare these data to a study recently published by our research group (2). The two studies had different initial aims, but still they share the same results in determining the modulatory effect of inflammation of aminobisphosphonates, such as pamidronate. The pamidronate belongs to the family of aminobisphosphonates (N-BPs), currently the major class of drugs used for the treatment of osteoporosis and other diseases characterized by increased bone resorption. The immune modulation exerted by pamidronate has not yet fully been understood (3). In vitro experiments have shown an anti-inflammatory effect of this N-BP; (4, 5) as well as a pro-inflammatory one (6, 7). Moreover contrasting results were obtained when pamidronate was used for the treatment of different inflammatory or immunologic diseases, such as rheumatoid arthritis (8, 9) or systemic sclerosis.

The aminobiphosphonates act on farnesylpyrophosphate synthase (FPPS) and inhibit the mevalonate pathway, the latter being responsible for production of cholesterol and isoprenoid lipids. In particular we can hypothesize that the inflammatory phenotype is due to lack of enzymes downstream the FPPS, and in particular the lack of geranylgeranyl-pyrophosphate (GGPP) could be associated to the activation of caspase-1 and the high IL-1β release.

Lim et al. (1) emphasized that in vivo infusion of pamidronate at a therapeutic dose of 30 mg increased production of two inflammatory cytokines, IL-6 and TNF-α in serum. The increase is an acute effect after intravenous injection (1).

Recently, our group demonstrated that pamidronate is able to increase the sensitivity to bacterial compounds both in the murine macrophagic cell line (Raw 264.7) and in Balb/c mice, by an incremental release of IL1β. These findings are in agreement with published data concerning inflammatory modulation in alendronate treated-mice (2). Moreover the effect of pamidronate does not depend on its concentration, whereas it may be involved in the increase of susceptibility to pro-inflammatory compounds such as muramildipeptide or lipopolysaccaride (2).

In summary, we agree with the study by Lim et al. (1) and we emphasize the pivotal role of pamidronate in the modulation of inflammatory response.

Sincerely.

REFERENCES

1. Lim MJ, Kwon SR, Park SG, Park W. *Acute effects of intravenous administration of pamidronate in patients with osteoporosis. J Korean Med Sci 2010; 25: 1277-83.*
2. Marcuzzi A, Crovella S, Pontillo A. *Geraniol rescues inflammation in cellular and animal models of mevalonate kinase deficiency. In Vivo 2011; 25: 87-92.*
3. Slobodin G, Rosner I, Feld J, Rimar D, Rozenbaum M, Boulman N, Odeh M. *Pamidronate treatment in rheumatology practice: a comprehensive review. Clin Rheumatol 2009; 28: 1359-64.*
4. Cecchini MG, Fleisch H. *Bisphosphonates in vitro specifically inhibit, among the hematopoietic series, the development of the mouse mononuclear phagocyte lineage. J Bone Miner Res 1990; 5: 1019-27.*
5. Pennanen N, Lapinjoki S, Urtti A, Mönkkönen J. *Effect of liposomal and free bisphosphonates on the IL-1 beta, IL-6 and TNF alpha secretion from RAW 264 cells in vitro. Pharm Res 1995; 12: 916-22.*
6. Mandey SH, Kuijk LM, Frenkel J, Waterham HR. *A role for geranylgeranylation in interleukin-1beta secretion. Arthritis Rheum 2006; 54: 3690-5.*
7. Thiébaud D, Sauty A, Burckhardt P, Leuenberger P, Sitzler L, Green JR, Kandra A, Zieschang J, Ibarra de Palacios P. *An in vitro and in vivo study of cytokines in the acute-phase response associated with bisphosphonates. Calcif Tissue Int 1997; 61: 386-92.*
8. Van Offel JF, Schuerwegh AJ, Bridts CH, Bracke PG, Stevens WJ, De Clerck LS. *Influence of cyclic intravenous pamidronate on proinflammatory monocytic cytokine profiles and bone density in rheumatoid arthritis treated with low dose prednisolone and methotrexate. Clin Exp Rheumatol 2001; 19: 13-20.*

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9. Carbone LD, Warrington KJ, Barrow KD, Pugazhenthi M, Watsky MA, Somes G, Ingels J, Postlethwaite AE. *Pamidronate infusion in patients with systemic sclerosis results in changes in blood mononuclear cell cytokine profiles. Clin Exp Immunol 2006; 146: 371-80.*

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