Catecholamines accelerate BMP-induced osteoblastic differentiation and bone formation

+1Uemura T; 1Ohta Y; 1Nakao Y; 1Takaoka K
+1Osaka City University Graduate School of Medicine, Osaka, Japan
uemuratakuy@mbr.nifty.com

INTRODUCTION:
It has recently been reported that the sympathetic nervous system is involved in regulation of osteoblastic function mainly through β-type adrenergic receptors on the cell surface [1]. The stimulatory effects of the sympathetic nervous system are mediated by catecholamines, such as epinephrine, norepinephrine and dopamine, which elevate the intracellular cyclic adenosine 3', 5'-monophosphate (cAMP) level through the Gs-coupled receptors. In a previous study, we showed that intracellular cAMP accumulation consistently enhanced bone morphogenetic protein (BMP)-induced osteoblastic differentiation, predominantly via the protein kinase A (PKA) signaling pathway [2], [3]. This study was designed to substantiate the potential of these catecholamines to enhance BMP-induced bone formation.

METHODS:
To investigate the ability of catecholamines to augment the bone-inducing action of BMP under in vivo condition, 30 mg of polymer discs (poly-D, L-lactic acid-p-dioxanone-polyethylene glycol block copolymer; PLA-DX-PEG) containing rhBMP-2 (5 µg) with or without catecholamines (10, 20, 40 µg) were implanted into the dorsal muscle pouch of mice. All ossicles induced by BMP were harvested 3 weeks later and examined by radiological analyses. Next, in mouse osteoblastic cell lines- ST2 cells, changes of alkaline phosphates (ALP) levels by BMP with or without catecholamines treatment and changes of cAMP levels after addition of catecholamines in time sequence were assayed.

RESULTS:
The ossicles induced by rhBMP-2 when used in conjunction with each catecholamine (epinephrine; 10, 20, 40 µg, norepinephrine; 40 µg, and dopamine; 10, 20, 40 µg) were significantly larger in size on soft X-ray radiogram and higher in bone mineral content (BMC) and bone mineral density (BMD) on dual-energy X-ray absorptiometry, compared with those induced by rhBMP-2 alone (Figure 1, 2, 3).

DISCUSSION:
In this study, we showed that catecholamines accelerate BMP-induced osteoblastic differentiation and bone formation both under in vitro and in vivo condition and the intracellular cAMP level was maintained by pulse treatment with epinephrine longer than by epinephrine single treatment. Catecholamines accelerate BMP-induced osteoblastic differentiation probably by increasing cAMP via the PKA signaling pathway. Catecholamine secretion and response in the body may interact with BMP signaling and influence bone metabolism.

REFERENCES: