The Variance of the Expressions of Extracellular Matrix Components and the Effects of the Anti-osteoporotic Drugs on Mönckeberg's Arteriosclerosis

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Arterial calcification is a common event in the pathogenesis of arteriosclerosis, especially Mönckeberg type and occurs as a complication in diabetic, uremic patients or postmenoposal women. It has been shown that arterial calcification generates the loss of elasticity in tunica media. We had already reported that the expression of tropoelastin (TE), the precursor protein of elastin, is suppressed by the arterial calcification. Without changes of mRNA expressions of the other elastic fiber components, such as fibrillins, did not show the variance of the mRNA expressions on arterial calcification. We examined the effects of bisphosphonates, known as the anti-osteoporotic drugs, in inorganic phosphate (Pi)-induced calcified bovine aortic smooth muscle cells (BASMCs) (*in vitro* arterial calcification model). Treatment of pamidronate, a kind of bisphosphonates, significantly inhibited the calcium deposition on the arterial calcification model. Pamidronate also inhibited the suppression of TE mRNA expression and the progression of osteopontin (OPN) and core binding factor-α1 (Cbfa1), an osteogenic transcription factor, by BASMCs calcification. Basically, bisphosphonates could inhibit the phenotypic transition, such as SMC to osteoblast-like cell. The inhibitory effects of bisphosphonates were also shown in retired female Sprague-Dawley rats with calcinosis induced by the administration of the over-dose vitamin D_2 (*in vivo* arterial calcification model).

It has been known that arterial calcification was accelerated by the oxidative low density lipoprotein (oxLDL). Therefore, we examined the effects of 7-ketocholesterol (7kc), a component of oxLDL, on Pi-induced *in vitro* arterial calcification model. Thereupon, it was revealed that 7kc drastically accelerated the Pi-induced calcification. But 7kc could not induce the calcification alone. And risedronate, a kind of bisphosphonates, completely restored the calcification and these mRNA expressions accelerated by 7kc.