chymase prevented fibrosis and maintained left ventricle function after left ventricular repair in a rat chronic myocardial infarction model.

Heart failure is a chronic syndrome in which cardiac remodeling plays an important role in the pathogenesis; furthermore, cardiac mast cells may be one of the mainstays of pathologic mechanism according to the current studies [2,3]. Protein kinase C signaling is a relatively new signal transduction pathway of mast cell degradation which currently attracts attention. Palaniyandi and co-workers introduced protein kinase C inhibition to prevent cardiac mast cell degranulation without affecting mast cell density and they performed V1-2 treatment for rat cardiac mast cell degranulation and decreased myocardial fibrosis [4]. Although Kanemitsu and co-workers underlined that inhibition of fibrosis established by cardiac chymase via transforming growth factor-β, our study also demonstrated that chymase, mediator of mast cell degranulation, related with myocardial fibrosis especially by basic-FGF [2].

These new findings and our previous studies [2–5] demonstrate that chymase-positive mast cells were associated with not only increased fibrosis but degradation of these cells may contribute in decreased cardiac inflammation and remodeling. One of my concerns about this excellent study by Kanemitsu is that he and his colleagues may be performing chronic chymase inhibition with oral medications, when according to previous studies, cardiac mast cells have several mediators as tryptase, 5-lipoxygenase, cytokins, histamin, serglycin, proteoglycans, carboxypeptidase. Chymase, tryptase and carboxypeptidase are also known as mast cell-specific proteases. Recent studies show promising progress of mast cell specific proteases, so how can Kenemitsu help us by reducing fibrosis by only preventing one mast — cell specific protease, instead of direct mast cells inhibition.

References


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We recognize the significance of mast cell function. The point raised by Akgul is important, but it is very difficult to determine whether chymase inhibition or mast cell inhibition is more useful for prevention of fibrosis [1]. This is because chymase has many functions including the production of angiotensin II, activation of transforming-growth factor (TGF)-β and attraction of mast cells [2]. Like angiotensin II, TGF-β plays a crucial role in the acceleration of cardiac fibrosis, and blockade of either angiotensin II or TGF-β has inhibited fibrosis in cardiac tissues. In patients with liver cirrhosis, the augmentation of chymase-positive cells was accelerated along with that of angiotensin II-positive cells by the progression of fibrosis, and there were significant correlations between the number of chymase-positive cells and the number of angiotensin II-positive cells, between the number of chymase-positive cells and the degree of fibrosis, and between the number of angiotensin II-positive cells and the degree of fibrosis [3]. Chymase significantly increases the proliferation of cultured human dermal fibroblasts and this increased cellular proliferation can be completely suppressed by a chymase inhibitor, but not by an angiotensin II receptor blocker [2]. On the other hand, in a mast cell-deficient model, cardiac fibrosis is attenuated, suggesting the significance of mast cells in the fibrosis [4]. In cardiomyopathic hamsters, chymase inhibition resulted in attenuation of cardiac fibrosis along with reduction of mast cell numbers in cardiac tissues [2]. Chymase is known to play an important role in the accumulation of mast cells by activating stem cell factor [5]. Therefore, attenuation of mast cell numbers in cardiac tissues may be involved in the mechanism by which chymase inhibitors prevent cardiac fibrosis in vivo. Thus chymase may be involved in cardiac fibrosis through various enzymatic functions, and in other words chymase inhibition may contribute to the attenuation of cardiac fibrosis by mechanisms that are multiple rather than simple.

References


Letter to the Editor

Guideline on antiplatelet and anticoagulation management in cardiac surgery

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We congratulate Dunning and colleagues for their guideline on antiplatelet and anticoagulation management in cardiac surgery [1]. However, we disagree with the authors’ statement regarding a lack of studies demonstrating safety of perioperative tranexamic acid (TA) administration and venous graft patency.

Our research group conducted a double-blind prospective randomized controlled trial exploring the very issue of intraoperative administration of TA and early saphenous vein graft patency (SVG) patency in patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass (CPB) [2]. A total of 312 patients were randomized to receive either TA or placebo. The primary objective of this study was to determine the equivalence of SVG patency rates between the treatment and placebo groups. In 237 patients saphenous vein graft patency was assessed with magnetic resonance imaging during the first month postoperatively. Our results showed insignificant variation in graft patency rates between the two groups. Consequently, TA could be advocated for routine use in patients undergoing coronary revascularization procedures with CPB to minimize postoperative bleeding and reduce perioperative blood product transfusion rates.

References


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Reply to the Letter to the Editor

Reply to Katznelson et al.
Tranexamic acid is safe with regard to vein graft patency

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Thank you for alerting the EJCTS to this excellent paper [1, 2]. Your paper used MRI scanning to show that the patency of vein grafts between 5 and 30 days after coronary surgery was 87% (231/265) in the placebo group and 85% (253/297) in patients who received 100 mg/kg of tranexamic acid after induction of anaesthesia. We are also aware that you used this important information in the creation of the BART trial [3], a landmark paper in the assessment of drug therapy to minimise bleeding after cardiac surgery. Your paper is available full-text for free currently from the Journal of Thoracic and Cardiovascular Surgery and I encourage readers to download it and read it in full including the optimal dosages of tranexamic acid for patients undergoing coronary surgery.

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