ACTIVATED PLATELET SUPERNATANT CAN AUGMENT THE ANGIOGENIC POTENTIAL OF PERIPHERAL BLOOD STEM CELLS IN STEM CELL-BASED THERAPY

Poster Contributions
Hall C
Sunday, March 30, 2014, 3:45 p.m.-4:30 p.m.

Session Title: Acute Coronary Syndromes: Basic II
Abstract Category: 2. Acute Coronary Syndromes: Basic
Presentation Number: 1224-224

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Background: Although platelets are known to play a role in hemostasis, they also promote angiogenesis and tissue recovery by releasing various cytokines. Here, we examined autologous ‘activated platelet supernatant (APS)’ as a priming agent for stem cells; thereby enhance their proangiogenic potential and efficacy of stem cell-based therapy against ischemic diseases.

Methods: Granulocyte-colony stimulating factor mobilized peripheral blood stem cells (mobPBSC) were isolated from healthy volunteers, while APS was collected separately by thrombin (0.5IU/L) activation of the platelet rich plasma. The characteristics of APS-primed mobPBSCs were examined and the 36-hour cell culture supernatant was measured to check the paracrine effect of APS-primed mobPBSCs. We used athymic mice ischemic hindlimbs and Matrigel plugs as in vivo models. Safety analysis for clinical application was done by checking the platelet activity of whole blood mixed with APS-primed mobPBSCs.

Results: APS contained high levels of various angiogenic cytokines such as IL8, PDGF and VEGF. 6-hour mobPBSC priming with APS increased the expression of angiogenic factors such as CXCR4, CD34 and cell surface integrin b1, b2 subunits. This enabled APS-primed mobPBSCs to promote transwell migration to SDF-1 and increase adhesion to fibronectin and HUVECs. APS-primed mobPBSCs were also polarized toward CD14++/CD16+ pro-angiogenic monocytes. The supernatant of 36-hour cultured APS-primed mobPBSCs contained high levels of IL8, IL10, IL17 and TNFa, which augmented proliferation and capillary network formation in HUVECs. In vivo transplantation of APS-primed mobPBSCs into athymic mice ischemic hindlimbs and Matrigel plugs elicited vessel differentiation, which improved vasculogenesis and tissue repair. Safety analysis of APS-primed mobPBSC showed platelet activity increased when APS-primed mobPBSCs were mixed in whole blood. However pretreatment with aspirin could decrease platelet activity.

Conclusions: Collectively, our data identify that APS priming can enhance the angiogenic potential of mobPBSCs, which can be used as a novel method in increasing efficacy of stem cell-based therapy for ischemic diseases.