RESTORATION OF ANGIOGENIC ACTIVITY OF HYPERGLYCEMIA-INSULTED BONE MARROW STEM CELLS BY OXYTOCIN VIA KLF2 UP-REGULATION

ACC Poster Contributions
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Background: Angiogenesis has been demonstrated to be a main therapeutic mechanism of stem cell therapy to cardiovascular diseases containing myocardial infarction, atherosclerosis, and heart failure. Oxytocin was reported to promote the migration of stem cells and glucose uptake of cardiomyocytes. From these background, we examined whether hyperglycemia would impair the function of stem cells and could be regressed by oxytocin.

Methods: Streptozotocin (65mg/kg) was intraperitoneally injected to Sprague-Dawley rat to induce hyperglycemia. After four weeks MSCs were isolated from bone marrow. The angiogenic potential and cell proliferation were evaluated by tube formation assay and WST-1 assay, respectively. The migratory activity was assayed by using Boyden chamber, and Kruppel-like factor 2 (KLF2) mRNA level was assessed by reverse transcriptase-polymerase chain reaction (RT-PCR).

Results: The cell proliferation of stem cells isolated from hyperglycemic rat was slower than cells from normal rat. Tube formation was attenuated whereas transwell migration was not different in MSCs from DM rat. To examine whether oxytocin treatment could induce the functional change of diabetic MSCs, 100 nM oxytocin was pretreated for 24 hours. Oxytocin pretreatment showed significant improvement of proliferation rate and tube formation in diabetic MSCs. To explain the effect of oxytocin on angiogenesis, we screened KLF2 expression pattern in MSCs. KLF2 was well studied transcription factor involved in and vascular formation and maturation. Interestingly, KLF2 mRNA was significantly reduced in diabetic MSCs and restored to normal level by oxytocin treatment.

Conclusions: Here we suggested that cellular activity of stem cells would be deteriorated by cardiovascular risk factors such as hyperglycemia and oxytocin could be an attractive therapeutic drug for restoring impaired function of hyperglycemia-exposed stem cells.