Pengaruh Bone Marrow Mesenchymal Stem Cells terhadap pertumbuhan Tunika Muskularis Aneurisma Intrakranial: Uji eksperimental in Vivo pada tikus = The role of Bone Marrow Mesenchymal Stem Cells in Vascular Smooth Muscle Regeneration of Intracranial Aneurysm: Experimental Study in rats.

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Abstrak

Aneurisma intrakranial sakular terjadi akibat lemahnya dinding pembuluh darah karena hilang atau rusaknya tunika muskularis. Belum ada penelitian yang bertujuan memperkuat dinding aneurisma intrakranial dengan cara menumbuhkan kembali lapisan tunika muskularis. Penelitian-penelitian Mesenchymal Stem Cells (MSC) pada hewan coba berhasil menumbuhkan otot polos vaskular pada aneurisma aorta dan arteri karotis. Diharapkan MSC dapat berperan dalam pembentukan tunika muskularis pada aneurisma intrakranial. Penelitian ini bertujuan menganalisis hubungan pertumbuhan tunika muskularis aneurisma intrakranial pada hewan coba dengan perlakuan pemberian Bone Marrow Mesenchymal Stem Cells (BM MSC) dan manipulasi tekanan darah tikus, dengan penanda SM-actin dan calponin.
Sebanyak 40 tikus Wistar diinduksi aneurisma selama 16 minggu. Modifikasi penurunan tekanan darah dan pemberian BM MSC pada minggu ke16, 18. Tikus dialokasi random ke dalam empat kelompok, yaitu hipertensi tanpa BMMSC, normotensi tanpa BMMSC, hipertensi dengan BMMSC, dan normotensi dengan BM MSC. Pada akhir minggu ke18 dilakukan nekropsi untuk pemeriksaan histopatologi, ekspresi SM-actin dan calponin terhadap aneurisma intrakranial, serta penilaian histopatologi pembuluh darah ekstrakranial.
Sebanyak 27 tikus memenuhi kriteria sampel dengan 62 aneurisma intrakranial. Pada kelompok dengan pemberian BMMSC didapatkan 8 (53,33%) aneurisma memberikan ekspresi SMα-actin (p = 0,014; OR = 14,86) dan 8 (70,00%) ekspresi calponin (p = 0,008; OR = 7,78). Terdapat 4 (57,14%) aneurisma dengan ekspresi SMα-actin (p = 0,070, OR = 2,33) dan 7 (87,5%) dengan ekspresi calponin (p = 0,01, OR = 42,00) pada kelompok normotensi dengan pemberian BM MSC. Pada keempat kelompok tidak didapatkan perbedaan luas dan tebal tunika media arteri karotis (p = 0,616 dan p = 0,222) dan arteri iliaka (p = 0,452 dan p = 0,325).
Pemberian BMMSC berhubungan dengan ekspresi SMα-actin dan calponin positif pada dinding aneurisma, menunjukkan pertumbuhan tunika muskularis. Faktor tekanan darah berhubungan dengan ekspresi calponin namun tidak berhubungan dengan ekspresi SMα-actin. Pemberian BM MSC tidak memberikan efek terhadap tunika media pembuluh darah ekstrakranial.
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Saccular intracranial aneurysm is a weak arterial wall caused by degeneration of tunica muscularis. There is still no research focused on strengthening intracranial aneurysm wall by restoring or regenerating tunica muscularis. The mesenchymal stem cells research in animal model had successfully regenerate vascular smooth muscle in abdominal aorta and carotid artery aneurysm. MSC is expected to have a role in regeneration of tunica muscularis in intracranial aneurysm.
The objective of this study is to analyze the association between regeneration of tunica muscularis in intracranial aneurysm by BM MSC administration and blood pressure manipulation with SMα-actin

dan calponin marker.
Forty male Winstar rats were subjected to intracranial aneurysm induction for sixteen weeks. Then, the rats were randomly assigned into four groups, which were hypertension, normalized blood pressure, bone marrow mesenchymal stem cells BM MSC administration and hypertension group, and normalized blood pressure and BM MSC administration group. At the end of 18th week, all rats were sacrificed and evaluated for histopathology, immunohistochemistry (SMα-actin dan calponin), and extracranial artery structure.
Twenty-seven rats with 62 aneurysms were eligible for sample criteria. Eight (53.3%) and fourteen (70.0%) aneurysms in group with BM MSC administration expressed SMα-actin (p = 0.014, OR = 14.86) and calponin (p = 0.008, OR = 7.78). In normotension and BM MSC administration group there were 4 (57.1%) aneurysm with SMα-actin expression (p = 0.070, OR = 2.33) and 7 (87.5%) with calponin expression (p = 0.01, OR = 42.00). There were no significant differences of wall area and thickness of carotid artery (p = 0,616 and p = 0,222) and iliac artery (p = 0.452 and p = 0.325) among four groups.
In conclusion BM MSC administration was associated with SMα-actin and calponin expression on aneurysm wall, indicating regeneration of tunica muscularis. BM MSC administration was related to tunica muscularis regeneration, Blood pressure manipulation and BM MSC administration was related to calponin expression but was not related to SMα-actin expression. No effect of BM MSC administration was found on extracranial arteries.