

EFEK REGENERATIF EKSTRAK MEDIA PENUMBUH SEL PUNCA MESENKIMAL (EMPSPM) PADA PANKREAS TIKUS PUTIH (*Rattus norvegicus*) GALUR WISTAR DIABETES DENGAN INDUKSI ALOKSAN

Oleh
Ida Fitriana
14/373764/PKH/520

Manajemen terapi diabetes mellitus (DM) yang dapat meregenerasi sel β pankreas dengan memiliki resiko kecil masih menjadi tantangan bagi para peneliti. Penelitian ini bertujuan untuk mengetahui aktifitas ekstrak media penumbuh sel punca mesenkimal (EMPSPM) dalam meregenerasi secara struktural dan fungsional sel β pankreas tikus wistar DM dengan induksi aloksan.

Tikus dibagi menjadi tiga kelompok yaitu kelompok EMPSPM, kelompok DM, dan kelompok normal, masing-masing 16 ekor. Kondisi DM dibuat dengan induksi dosis tunggal 125 mg/kg BB aloksan dalam NaCl 0,9% secara intramuskular (IM). Terapi DM menggunakan 0,1 ml/kg BB EMPSPM secara IM diberikan selama 4x dengan selang waktu 7 hari. Pengamatan dilakukan pada hari ke-8 (sebelum induksi aloksan), hari ke-13 (hari ke-5 sesudah induksi aloksan), hari ke-20, 27, 34, dan 41 (1 minggu setelah aplikasi EMPSPM). Setiap pengamatan dilakukan penimbangan berat badan (BB) dan diambil 3 ekor tikus untuk koleksi sampel darah dan dietanasi untuk koleksi sampel pankreas. Sampel darah digunakan untuk mengukur kadar glukosa dengan glukometer dan kadar insulin dengan ELISA. Sampel pankreas diproses dengan teknik parafin, kemudian dilakukan pewarnaan Hematoksilin-eosin dan imunohistokimia. Data kuantitatif berupa BB, kadar glukosa, morfometri insula Langerhans (IL) (jumlah, luas area, diameter), sel imunoreaktif insulin (IRI), dan kadar insulin dianalisa secara statistik, sedangkan data kualitatif berupa struktur pankreas dianalisa secara deskriptif.

Pada hari ke-13, diketahui bahwa induksi DM dengan aloksan dapat menurunkan berat badan, meningkatkan kadar glukosa darah, dan menurunkan kadar insulin darah kelompok EMPSPM dan DM dibandingkan dengan kelompok normal. Aloksan juga merusak stuktur histologi pankreas baik jaringan asinus maupun IL pada semua bagian (pars gastrik, limfa, dan duodenal), memperkecil luas area dan diameter IL, dan berkurangnya jumlah IL.

Hari ke-20, proses regrenerasi secara struktural oleh EMPSPM mulai teramati, berupa perbaikan struktur pankreas, terbentuknya IL, peningkatan diameter, dan luas area IL, serta sel IRI. EMPSPM juga menaikkan BB tikus diabetes dibandingkan dengan kelompok DM. Hari ke 27, secara fungsional EMPSPM menurunkan kadar glukosa darah, meningkatkan BB, dan menaikkan kadar insulin darah, sedangkan regenerasi pankreas kelompok DM baru mulai teramati. EMPSPM bereaksi optimal pada hari ke-34, ditemukan peningkatan jumlah IL ukuran kecil dan sel IRI terbanyak, berturut-turut pada pars limfa, gastrik, dan duodenal. Secara fungsional, EMPSPM juga menurunkan kadar glukosa darah dan menaikkan BB. Hari ke-41, EMPSPM signifikan menurunkan kadar glukosa dan menaikkan kadar insulin darah. Berdasarkan hasil tersebut, disimpulkan bahwa kelompok EMPSPM dapat meregenerasi secara stuktural dan fungsional pankreas tikus DM lebih cepat dibandingkan dengan kelompok DM serta meregenerasi secara optimal pada hari ke-34.

Kata kunci : EMPSPM, regenerasi, sel beta pankreas, diabetes, aloksan

REGENERATIVE EFFECT OF MESENCHYMAL STEM CELL-CONDITIONED MEDIUM (MSC-CM-) ON THE TYPE 1 DIABETIC PANCREAS OF WISTAR RATS (*Rattus norvegicus*)

by
Ida Fitriana
14/373764/PKH/520

Therapy management of diabetes mellitus (DM) to regenerate the pancreatic β cells with low risk still a challenge for researchers. The objective of this study was to investigate the roles of mesenchymal stem cell conditioned medium (MSC-CM) in the pancreatic β cells regeneration of diabetic Wistar rats, structurally and functionally.

Rats were assigned into 3 groups, MSC-CM treated group, DM group, and normal group (n=16 each), respectively. DM was induced by intramuscular injection of alloxan at the dose rate of 125 mg/kg body weight in NaCl 0,9%. Diabetic rats were treated with intramuscular injection of MSC-CM at the dose rate 0,1 ml/kg body weight, 4 times with 7 days interval injection. Body weight was measured before each collection of the pancreatic sample. Blood and pancreatic samples from 3 rats were collected on the day of 8 (a day before alloxan-induction), day of 13 (5 days after alloxan-induction), day of 20, 27, 34 and 41 (a week after each MSC-CM-treatment), respectively. Blood samples were used to measure glucose concentration by using glucometric and insulin concentration by using ELISA. Pancreatic samples were processed with paraffin-embedded method and visualized by using hematoxyllin-eosine stain and immunohistochemistry method. The data of body weight, glucose concentration, islets of Langerhans (IL) morphometry (number, area, diameter), insulin immunoreactive cells (IIC), and insulin concentration were analyzed quantitatively, while the structure of pancreas were analyzed qualitatively.

On the day of 13, diabetic condition was achieved as indicated by the loss of body weight, increase of glucose concentration, and decrease of blood insulin concentration in DM group compared to normal group. Histologically diabetic condition was shown by the damage of islets and IL (pars gastric, pars lien and pars duodeal), the diminution of IL area and diameter, and the reduction on the number of IL. On the day of 20, the regeneration of the pancreatic tissue in MSC-CM treated group was begin observed, as indicated by the formation of IL, the enlarged of IL area and diameter, the increasing on the number of IIC, and the increasing of body weight. On the day of 27, MSC-CM shown the decreasing of glucose concentration, the increasing of body weight, and the increasing of insulin concentration, indicated the return of IL function. Optimal effect of MSC-CM was observed in the day of 34, as indicated by the great number of small IL and great number of IIC on the pars lien, pars gastric and pars duodenal, the decreasing of glucose concentration, and the increasing of body weight. On the day of 41, the significant decreasing of glucose and the significant increasing of insulin were observed in the MSC-CM treated group. Taken together, the study concluded that MSC-CM accelerate the structural and functional regeneration of the alloxan-induced diabetic pancreas and the optimal effect of MSC-CM was achieved on the day of 34.

Keyword : MSC-CM, regeneration, pancreatic β cell, diabetic, alloxan