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Efek Implantasi Sel Punca Mesenkimal (Spm) Tali Pusat, Sekretom Spm Adiposa, Dan Granul Hidroksi-Apatit Terhadap Artrodesis Sendi Pergelangan Kaki Pada Model Artritis Tikus Dengan Diabetes Melitus = Effect of Umbilical Cord Mesenchymal Stem Cell (MSC) Application, Adipose Tissue Secretome, and Hydroxyapatite Granule for A Successful Ankle Arthrodesis in Diabetic Arthritic Rat Model

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Abstrak

Diabetes melitus (DM) menyebabkan gangguan saraf autonom, sensorik, dan motorik, terutama di kaki dan pergelangan kaki yang menyebabkan perubahan postur kaki dan deformitas. Artritis pergelangan kaki penyandang DM mengakibatkan gangguan fungsional sehingga artrodesis merupakan suatu opsi tata laksana pembedahan. Sayangnya, gangguan metabolik DM mengakibatkan komplikasi yang tak jarang yakni non-union. Terapi sel dan derivatnya merupakan opsi terapi regeneratif untuk meningkatkan kesembuhan tulang. Pembuatan model artritis hewan DM dengan injeksi streptozotosin (STZ), diet tinggi lemak (HFD), dan injeksi complete freud adjuvant (CFA) dilanjutkan studi eksperimental in vivo dengan fokus hasil augmentasi fusi dengan granul hidroksiapatit (HA), sel punca mesenkimal asal tali pusat (SPM-TP), dan sekretom jaringan adiposa (JA). Sebanyak 16 sampel kaki dibagi menjadi 3 kelompok: kontrol negatif (kelompok 1), kontrol positif yang diberikan autologous bone graft (kelompok 2), dan perlakuan yang diberikan HA, SPM-TP, dan sekretom-JA (kelompok 3). Dilakukan evaluasi parameter klinis, radiologis, profil histomorfometris, dan ekspresi biomarker di subjek model artritis DM tikus Sprague Dawley (SD). Status DM tercapai setelah induksi STZ dengan rerata kadar glukosa 421 ± 27,16 mg/dL. Kelompok artritis menunjukkan perubahan diameter ankle yang bermakna dibanding kontrol serta perubahan radiologis sendi pergelangan kaki. Artritis berat (skor 3) ditemukan di mayoritas (80%) sampel kelompok 1 yang merupakan kontrol negatif (hanya induksi DM). Kelompok perlakuan menunjukkan skor artritis terendah serta osifikasi di sisi anterior tibiotalar. Terdapat perbedaan bermakna osteokalsin (p = 0,017) dan gen chordin (p = 0,003) antara ketiga kelompok.
Simpulan: Model artritis DM pada tikus SD berhasil dibuat dengan injeksi STZ dan HFD serta induksi artritis kronik dengan injeksi CFA di sendi pergelangan kaki selama 4 minggu. Pemberian SPM-TP, sekretom JA, dan granul HA menunjukkan skor artritis yang lebih rendah. Namun, pemberian ketiga bahan tersebut tidak menghasilkan gambaran fusi yang lebih baik, serta tidak meningkatkan kadar osteokalsin, namun menghasilkan jumlah chordin (protein inhibisi BMP) yang lebih kecil dibandingkan baku standar.
.....Diabetes mellitus (DM) can cause disturbances in the autonomic, sensory, and motor nerves, particularly in the feet and ankles, eventually leading to changes in foot posture and specific deformities. The advancement of management using stem cells and their secretome has shown promising outcomes. A model of DM arthritis can be created by inducing experimental animals with streptozotocin (STZ). In the DM arthritis model, the evaluation of ankle arthrodesis augmented with umbilical cord mesenchymal stem cell (MSC-Uc) and adipose tissue secretome (Secretome-AD) can be carried out to observe the existing outcomes.
This study is divided into two stages wherein the first stage involves creating an arthritis model in DM

animals. The study utilizes a pretest-posttest design to measure clinical and laboratory parameters before and after treatment. Subsequently, the second stage involves an in vivo experimental study focusing on the outcomes of fusion augmentation with MSC-Uc, secretom-AD, and HA granule. The second stage of the study includes assessments using single-blinding methods for clinical, radiological, histomorphometric profile, and biomarker expression in the SD rat model of DM arthritis.

DM status was achieved after STZ injection, with an average glucose level of 421 ± 27.16 mg/dL. The final diameter averages in groups 1 – 3, which were not induced with arthritis (9.64 ± 0.49 mm), significantly differed from group 4 (12.50 ± 0.87 mm, $p = 0.003$) and 5 (11.85 ± 0.74 mm, $p = 0.037$). The arthritis groups showed radiological changes in the ankle joint. After modeling, there was a significant increase in fasting blood glucose compared to pre-modeling measurements. Severe arthritis (score 3) was found in the majority (80%) of samples in group 1, which served as the negative control (DM induction only). Anova test results for the IHC parameter showed significant differences ($p = 0.017$) in osteocalcin and chordin gene ($p = 0.003$) among the three groups.

Conclusion: A model of DM arthritis in SD rats was successfully created by STZ and HFD induction, followed by the induction of chronic arthritis with CFA injection in the ankle joint for 4 weeks. The administration of MSC-Uc, secretome-AD, and HA granule indicated lower arthritis scores. However, the administration of these three substances did not produce a better fusion picture, nor did it increase osteocalcin levels, but it resulted in a smaller amount of chordin (BMP inhibition protein) compared to the standard.