

# Regenerasi Tulang Rawan Hialin pada Defek Osteokondral Melalui Penyuntikan Intraartikular Suspensi Sel Punca CD34+ Darah Tepi Manusia, Asam Hialuronat, TGF- $\beta$ 1, IGF, FGF dan Fibronectin pada Tikus Sprague Dawley = Hyaline Cartilage Regeneration in Osteochondral Defect by Intraarticularly Injecting Human's Peripheral Blood CD34+ Stem Cell Suspension, Hyaluronic Acid, and TGF- $\beta$ 1, IGF, FGF, and Fibronectin to Sprague Dawley Rats

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Abstrak

## **ABSTRAK**

Latar Belakang: Sel punca CD34+ adalah sel punca hematopoietik yang positif terhadap penanda sel CD34 dan mempunyai potensi regenerasi. Potensinya dapat ditingkatkan dengan penambahan asam hialuronat dan faktor pertumbuhan. Tujuan penelitian adalah menghasilkan regenerasi tulang rawan hialin pada defek osteokondral sendi lutut tikus Sprague Dawley (SD) non rekayasa melalui penyuntikan intraartikular sel punca CD34+ darah tepi manusia, asam hialuronat, TGF- $\beta$ 1, IGF, FGF dan Fibronectin.

Metode: Penelitian dilakukan 3 tahap. Tahap 1: Pembuatan Model Defek, Model Intervensi, dan Uji Toksik. Tahap 2: Penyiapan Sel dan Pembuatan Suspensi. Tahap 3: Intervensi. Pada tahap intervensi, 30 tikus SD dibagi menjadi 3 kelompok dan setiap tikus dibuat defek dangkal dan dalam pada sendi lutut. Setelah luka operasi ditutup, tiap tikus diberi suspensi secara intraartikular. Kelompok kontrol diberi PBS, kelompok perlakuan 1 diberi sel CD34+, kelompok perlakuan 2 diberi sel CD34+, asam hialuronat, TGF- $\beta$ 1, IGF, FGF dan Fibronectin. Setiap kelompok dievaluasi laboratoris, radiologis, makroskopis dan mikroskopis pada minggu ke-4 dan ke-8. Hasil penelitian diuji secara statistik (Uji Manova).

Hasil : Tidak terjadi reaksi penolakan. Terjadi perbedaan bermakna antara kelompok perlakuan dengan kelompok kontrol dalam kadar Hb ( $p = 0,016$ ), Trombosit ( $p = 0,009$ ), SGPT ( $p = 0,000$ ), dan Kreatinin ( $p = 0,029$ ), namun mikroskopis hati dan ginjal normal.

Pemberian sel CD34+ tidak memperbaiki skor radiologis ( $p = 0,074$ ), namun terjadi regenerasi, skor makroskopis defek dangkal ( $p = 0,000$ ), makroskopis defek dalam ( $p = 0,000$ ), mikroskopis defek dangkal ( $p = 0,000$ ) dan mikroskopis defek dalam ( $p = 0,000$ ). Kelompok perlakuan 2 tidak berbeda dengan kelompok perlakuan 1, skor makroskopis defek dangkal ( $p = 1,000$ ), mikroskopis defek dangkal ( $p = 1,000$ ) dan defek dalam ( $p = 0,818$ ), namun perlakuan 2 lebih baik dari perlakuan 1 pada makroskopis defek dalam ( $p = 0,023$ ).

Skor defek dangkal dan defek dalam tidak berbeda bermakna pada kelompok kontrol dan perlakuan pada minggu ke-4 dan ke-8 ( $p$  makroskopis = 0,793,  $p$  mikroskopis = 0,754).

Skor minggu ke-4 dan ke-8 tidak berbeda bermakna pada kelompok kontrol dan perlakuan, pada defek

dangkal dan defek dalam (p radiologis = 0,200, p makroskopis dangkal = 0,507, makroskopis dalam = 0.350, p mikroskopis dangkal = 0,446, p mikroskopis dalam = 0,239).

Simpulan : Sel punca CD34+ darah tepi manusia dapat menghasilkan regenerasi hialin pada model defek osteokondral. Penambahan asam hialuronat dan faktor pertumbuhan tidak meningkatkan hasil regenerasi. Pembuatan mikrofraktur pada defek osteokondral tidak meningkatkan hasil regenerasi. Hasil regenerasi minggu ke- 8 tidak lebih baik dari minggu ke-4.

#### **ABSTRACT**

**Background:** CD34+ is hematopoietic stem cell that is positive to CD34 cell markers and potential for tissue regeneration. The regeneration potential for the cartilage has never been researched. The potential can be increased by adding the hyaluronic acid and growth factors. The research was aimed at producing the hyaline cartilage regeneration in the osteochondral defect of naïve Sprague Dawley (SD) rats? knee joints by intraarticularly injecting human?s peripheral blood CD34+ stem cell, hyaluronic acid and TGF- $\beta$ 1, IGF, FGF, and Fibronectin.

**Methods:** The research comprised 3 stages. Stage 1: The Development of Defect Models, Intervention Model, and Toxic Test. Stage 2: Preparation of Cells and Suspension Making. Stage 3: Intervention. During the intervention process, 30 SD rats were grouped into three groups and the superficial and deep defects were made on their knees. After the surgical wound was covered, each rat was intraarticularly injected by suspension. The control group received PBS, the treatment group 1 received CD34+ cell, the treatment group 2 was given CD34+ cell, hyaluronic acid, and TGF- $\beta$ 1, IGF, FGF, and Fibronectin. Every group was evaluated in the laboratory, radiologically, macroscopically, and microscopically on the 4th and 8th weeks. The research result was analyzed statistically (Manova Test).

**Result:** There was no rejection. There were significant differences between the treatment group and control group with respect to the Hb (p = 0.016), thrombocyte (p = 0.009), SGPT (p = 0.000), and creatinine (p = 0.029), but the liver and kidney microscopic were normal.

The administration of CD34+ cells did not improve the radiological score (p = 0.074), but there was regeneration, the macroscopic score of the superficial defect (p=0.000), macroscopic score of the deep defect (p=0.000), microscopic score of the superficial defect (p=0.000), and microscopic score of the deep defect (p=0.000). The macroscopic score of the superficial defect of the treatment group 2 was not significantly different from the results of the treatment group 1 (p=1.000), macroscopic score of the superficial defect (p=1.000), microscopic score of the superficial defect (p=1.818), and the microscopic score of the deep defect (p=0.023).

There were no significant differences between the score of the superficial defect and score of the deep defect in the control and treatment groups in the 4th and 8th weeks (p macroscopic = 0.793, p microscopic = 0.754).

There were no differences with respect to the scores in the 4th and 8th weeks in the control and treatment groups and with respect to the superficial and deep defects (p radiological = 0.200, p superficial

macroscopic = 0.507, deep macroscopic = 0.350, p superficial microscopic = 0.446, p deep microscopic = 0.239).

Conclusion: Human's peripheral blood CD34+ stem cell can produce hyaline regeneration in the osteochondral defect models. The addition of hyaluronic acid and growth factors does not improve the regeneration results. The microfracture deep in the osteochondral defect does not improve the regeneration result. The regeneration result in the 8th week is better than the result in the 4th week.</i>