

## ABSTRAK

### **LUARAN FUNGSIONAL DAN PEMULIHAN ANATOMIS BERBASIS MAGNETIC RESONANCE IMAGING (MRI) PASKA TRANSPLANTASI SEL PUNCA MESENKIMAL PADA PASIEN CEDERA MEDULA SPINALIS KRONIS PASKA TRAUMA SECARA INTRATEKAL DENGAN PENANDA MINIOPEN LAMINOTOMY**

**Latar Belakang:** Cedera medula spinalis kronis paska trauma merupakan kondisi yang dapat menyebabkan disabilitas berat permanen. Cedera ini akan berdampak signifikan terhadap penurunan kualitas hidup pasien, dengan insidensi tertinggi pada populasi usia muda dan produktif. Berbagai pendekatan tatalaksana meliputi medikamentosa, pembedahan dan terapi rehabilitasi telah dikembangkan namun hasilnya tidak memuaskan. Transplantasi sel punca mesenkimal dapat menjadi terapi harapan untuk memperbaiki fungsi neurologis melalui regenerasi sel-sel neural dan myelin.

**Tujuan:** Penelitian ini bertujuan mengetahui efektivitas dan keamanan pemberian sel punca mesenkimal otologus asal sumsum tulang dan alogenik asal tali pusat pada pasien cedera medula spinalis kronis paska trauma, dengan teknik injeksi intratekal dan miniopen laminotomy, serta mengetahui perubahan gambaran MRI di area lesi paska transplantasi.

**Metode:** Penelitian ini merupakan kohort prospektif yang dilakukan di RSUP Dr. Sardjito Yogyakarta pada rentang waktu Maret 2017 hingga Juli 2022. Terdapat 9 pasien dengan cedera medula spinalis kronis paska trauma yang diberikan sel punca mesenkimal, yakni 7 pasien diberikan sel punca otologus asal sumsum tulang, dan 2 pasien diberikan sel punca alogenik asal tali pusat. Tiap pasien menerima 3 kali injeksi (terdiri atas injeksi inisial, booster pertama, dan booster kedua) dengan dosis total 80 juta sel. Teknik transplantasi yang digunakan yaitu injeksi intratekal dengan prosedur miniopen laminotomy sebagai penanda. Parameter luaran fungsional kemudian dievaluasi, meliputi lingkaran paha dan betis, *visual analogue score* (VAS), fungsi sensorik, motorik dan AIS (*ASIA Impairment Scale*) menggunakan sistem skor *American Spinal Injury Association* (ASIA), fungsi otonom, dan kualitas hidup menggunakan *Barthel Index* (BI), *Karnofsky Performance Scale* (KPS), dan perubahan gambaran MRI hingga 1 tahun sesudah injeksi.

**Hasil:** Pasien memperlihatkan perbaikan parameter luaran fungsional yang dievaluasi yang dibandingkan antara sebelum dan sesudah transplantasi. Sebanyak 7 pasien (77,78%) mengalami peningkatan lingkaran paha ( $p < 0,05$ ), 6 pasien (66,67%) mengalami peningkatan lingkaran betis ( $p > 0,05$ ), 6 pasien (66,67%) mengalami perbaikan VAS dan nyeri neuropatik ( $p > 0,05$ ), pada penilaian skor ASIA didapatkan 7 pasien (77,78%) mengalami perbaikan fungsi sensorik ( $p < 0,05$ ), 5 pasien (55,56%) mengalami peningkatan motorik ( $p < 0,05$ ), dan 7 pasien (77,78%) mengalami peningkatan AIS ( $p < 0,05$ ), 8 pasien (88,89%) mengalami perbaikan

fungsi otonom ( $p<0,05$ ), 7 pasien (77,78%) mengalami peningkatan BI ( $p<0,05$ ), dan 6 pasien (66,67%) mengalami perbaikan KPS ( $p>0,05$ ). Pada evaluasi MRI didapatkan 8 pasien (88,89%) mengalami penurunan volume lesi di medula spinalis ( $p<0,05$ ), dan didapatkan korelasi antara penurunan volume lesi terhadap perbaikan fungsi motorik. Tidak didapatkan efek samping paska pemberian sel punca pada semua pasien yang diamati selama periode tindak lanjut.

**Simpulan:** Transplantasi sel punca mesenkimal dengan teknik injeksi intratekal dan miniopen laminotomy aman untuk diberikan dan dapat memperbaiki fungsi neurologis dan kualitas hidup pada pasien cedera medula spinalis kronis paska trauma. Perubahan pada gambaran MRI memiliki hubungan dengan perbaikan luaran fungsional pasien.

**Kata Kunci:** cedera medula spinalis, sel punca mesenkimal, otologus, alogenik, *miniopen laminotomy*, intratekal

## ABSTRACT

### **FUNCTIONAL OUTCOME AND MRI-BASED ANATOMICAL RECOVERY FOLLOWING INTRATECHAL TRANSPLANTATION OF MESENCHYMAL STEM CELLS IN POST-TRAUMATIC CHRONIC SPINAL CORD INJURY WITH MINIOPEN LAMINOTOMY AS A MARKER**

**Background:** Complete-type post-traumatic chronic spinal cord injury is a challenging condition which can result in irreversible severe disability. The injury significantly impacts the quality of life, and the highest incidence are in young- and active-age population. Various treatment including medication, surgery and rehabilitation therapy have been performed, but the therapeutic effects and the outcomes remain unsatisfactory. Mesenchymal stem cells transplantation has become a promising treatment to improve neurological functions by generating neural cells and myelin producing cells.

**Aim:** The aim of this study is to evaluate the functional outcome and safety aspects in patients with post-traumatic chronic spinal cord injury treated with autologous bone marrow mesenchymal stem cells (ABMSC) and allogeneic umbilical cord mesenchymal stem cells (AUMSC), using miniopen laminotomy and intrathecal injection technique, and also evaluate the changes in the MRI images after the transplantation.

**Material and Method:** The design was prospective study conducted in Sardjito General Hospital Yogyakarta from March 2017 to July 2022. There are 9 patients with post-traumatic chronic spinal cord injury administered mesenchymal stem cells, 7 patients were administered ABMSC and 2 patients were administered AUMSC. Each patient were conducted 3 injections (initial injection, first booster injection and second booster injection) with the total dose of 80 million cells. The technique of transplantation was intrathecal injection with miniopen laminotomy procedure acts as a marker. The functional outcome parameters were evaluated, including lower extremity diameter, visual analogue score, sensory and motor function and AIS (ASIA Impairment Scale) using American Spinal Injury Association (ASIA) scoring system, autonomic function, and quality of life (QoL) using Barthel Index (BI) and Karnofsky Performance Scale (KPS), and MRI evaluation until 1 year after the treatment.

**Result:** The patients showed improvements in the functional outcome parameters which evaluated and compared between pre- and one year post-treatment. In thigh circumference 7 patients (77,78%) had improvement ( $p < 0,05$ ), 6 patients (66,67%) had improvement in calf circumference ( $p > 0,05$ ), 6 patients (66,67%) had improvement in VAS and neuropathic pain ( $p > 0,05$ ), 8 patients (88.89%) had improvement in autonomic function ( $p < 0.05$ ). In the ASIA score measurement, 7 patients (77.78%) had improvement in sensory function ( $p < 0.05$ ), 5 patients (55.56%) had motor improvement ( $p < 0.05$ ), and 7 patients (77,78%) had an

*increase in AIS ( $p < 0.05$ ). In the QoL assessment, 7 patients (77.78%) had an increase in BI ( $p < 0.05$ ), and 6 patients (66.67%) had KPS improvement ( $p > 0.05$ ). On MRI evaluation, 8 patients (88.89%) had decreased spinal cord lesion volume ( $p < 0.05$ ), and there was a correlation between decreased lesion volume and motor function improvement. There were no adverse effects in all patients observed during the follow-up period.*

**Conclusion:** *Mesenchymal stem cells transplantation with intrathecal injection technique and miniopen laminotomy was safe and promising as a possible hope to improve neurological functions and quality of life in post-traumatic chronic spinal cord injury patients. Changes in the lesion volume on MRI images have been associated with motor improvement in the functional outcome.*

**Keywords:** *spinal cord injury, mesenchymal stem cells, autologous, allogeneic, miniopen laminotomy, intrathecal*