

## ABSTRAK

### Transplantasi Alogenik Sel Punca Sumsum Tulang Untuk Perbaikan Folikulogenesis dan Hasil Fertilisasi pada Tikus Model Kegagalan Ovarium dengan Pemberian Cisplatin

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**Pendahuluan:** Infertilitas merupakan salah satu konsekuensi kemoterapi pada wanita penderita kanker akibat efek sitotoksik yang menyebabkan kerusakan folikel akut, folikulogenesis abnormal sehingga terjadi kegagalan ovarium. Terdapat 2 faktor pertumbuhan, Growth Differentiation Factor-9 (GDF-9) dan Stem Cell Factor (SCF), yang penting untuk interaksi oosit-sel granulosa menjadi berubah sehingga mengganggu perkembangan folikel. Pada penelitian ini akan dievaluasi apakah transplantasi sel punca sumsum tulang (TSPST) mempunyai peran pada perbaikan folikulogenesis dengan memeriksa ekspresi GDF-9 dan SCF serta perkembangan folikel dengan menganalisis jumlah folikel primordial, primer, sekunder dan folikel de graaf pada tikus model kegagalan ovarium dengan pemberian cisplatin.

**Materi dan Metode:** 48 ekor tikus dibagi menjadi 3 kelompok: kontrol, cisplatin dan cisplatin+TSPST. Kegagalan ovarium dibuat dengan cara pemberian injeksi cisplatin dosis 5 mg/kg BB selama 1 minggu. TST  $2 \times 10^7$  sel disuntikkan melalui pembuluh darah ekor setelah pemberian cisplatin. Sumsum tulang diisolasi dari tulang femur tikus usia 6-12 minggu dan ditandai dengan CD44(+), CD45(-), CD105(+). Pemeriksaan imunohistokimia dikerjakan setelah TSPST untuk memeriksa GDF-9, SCF dan perkembangan folikel. Hasil ke 3 kelompok diatas dibandingkan dengan menggunakan tes Anova.

**Hasil:** Ekspresi GDF-9 ( $15.91 \pm 0.69$ ) dan SCF ( $20.26 \pm 1.14$ ) pada kelompok cisplatin+TSPST lebih tinggi dari pada kelompok cisplatin saja ( $5.33 \pm 1.76$ ) dan ( $12.27 \pm 2.88$ ) dan kelompok kontrol ( $14.53 \pm 1.42$ ) dan ( $20.22 \pm 2.14$ ) ( $p=0.000$ ). Pada kelompok cisplatin+TSPST jumlah folikel primordial ( $5.31 \pm 1.30$ ), primer ( $4.37 \pm 0.88$ ), sekunder ( $3.62 \pm 0.71$ ) dan folikel de graaf ( $2.75 \pm 0.85$ ) lebih tinggi dari kelompok cisplatin saja ( $4.31 \pm 1.19$ ), ( $3.81 \pm 1.22$ ), ( $2.87 \pm 0.95$ ) dan ( $0.37 \pm 0.69$ ), tapi lebih rendah dari kelompok kontrol ( $6.12 \pm 1.20$ ), ( $4.93 \pm 1.61$ ), ( $4.25 \pm 0.77$ ) dan ( $5.81 \pm 1.37$ ) ( $p=0.000$ ). Pengecatan label PKH tampak positif pada kelompok cisplatin+TSPST, sedangkan pada kelompok cisplatin saja hasilnya negatif.

**Kesimpulan:** Pada tikus model kegagalan ovarium, transplantasi alogenik sel punca sumsum tulang akan memperbaiki folikulogenesis. Masih diperlukan penelitian lanjutan.

**Kata kunci :** bone marrow, GDF-9, SCF, follicle, ovarian failure

**ABSTRACT****Allogeneic transplantation of bone marrow stem cell on folliculogenesis improvement and fertilization result of cisplatin-induced ovarian failure in rat**

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**Introduction:** Infertility is one of the consequence of chemotherapy in cancer patients due to its cytotoxic effect that induces acute follicular damage, abnormal folliculogenesis leading to ovarian failure. Two crucial growth factors in abnormal folliculogenesis namely Growth Differentiation Factor-9 (GDF-9) and Stem Cell Factor (SCF), which act on the oocyte-granulosa cell interaction, will be disrupted and in turn it will affect follicular development. In this study we try to evaluate whether bone marrow transplantation (BMT) has a role on oocyte-granulosa cell interaction by analyzing GDF-9 and SCF expressions and also follicular development by analyzing primordial, primary, secondary and graafian follicles of experimental cisplatin-induced ovarian failure in rat.

**Design:** Animal laboratory experimental study

**Materials and Methods:** Forty eight rats (*rattus norvegicus* strain wistar) were divided into three groups : control, cisplatin and cisplatin+BMT. Ovarian failure was induced by administration of intraperitoneal cisplatin dose 5 mg/kg body weight for 1 week. BMT  $2 \times 10^7$  cell was injected through rat tail vein after cisplatin administration. Bone marrow was isolated from rat femur 6-12 weeks of age and characterized by CD44(+), CD45(-), CD105(+). Immunohistochemistry examinations for ovarian GDF-9, SCF and follicle development evaluation were performed after 2 weeks of BMT injection. All three groups data were compared using the Anova test.

**Results:** The expressions of GDF-9 ( $15.91 \pm 0.69$ ) and SCF ( $20.26 \pm 1.14$ ) in cisplatin+BMT group were higher than those in cisplatin group: ( $5.33 \pm 1.76$ ) and ( $12.27 \pm 2.88$ ) and control group: ( $14.53 \pm 1.42$ ) and ( $20.22 \pm 2.14$ ) ( $p=0.000$ ). In cisplatin+BMT group the number of primordial ( $5.31 \pm 1.30$ ), primary ( $4.37 \pm 0.88$ ), secondary ( $3.62 \pm 0.71$ ) and graafian follicles ( $2.75 \pm 0.85$ ) were higher than those in cisplatin group: ( $4.31 \pm 1.19$ ), ( $3.81 \pm 1.22$ ), ( $2.87 \pm 0.95$ ) and ( $0.37 \pm 0.69$ ); but were lower than those in control group ( $6.12 \pm 1.20$ ), ( $4.93 \pm 1.61$ ), ( $4.25 \pm 0.77$ ) and ( $5.81 \pm 1.37$ ) ( $p=0.000$ ).

Positive PKH labeling was seen in cisplatin+BMT group, while negative result in cisplatin group.

**Conclusion:** On cisplatin-induced ovarian failure in rat, bone marrow transplantation may improve oocyte-granulosa cell interaction and follicular development. Further study is needed.

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**Key words:** bone marrow, GDF-9, SCF, follicle, ovarian failure