INTISARI

Latar Belakang: Siklofosfamid merupakan salah satu agen kemoterapi yang banyak digunakan dan terbukti efektif untuk pengobatan kanker. Namun demikian, siklofosfamid memiliki efek gonadotoksik yang dapat merusak folikel ovarium. Mekanisme efek gonadotoksik siklofosfamid terdiri dari 2 mekanisme dominan yaitu peningkatan atresia folikel dan rekrutmen folikel primordial. Inflamasi merupakan mekanisme lain yang terjadi saat paparan siklofosfamid. IL-6 merupakan sitokin yang diekspresikan ketika terjadi inflamasi. Respon inflamasi pada folikel ovarium berpotensi berpengaruh terhadap atresia dan rekrutmen pada folikel.

Tujuan: Penelitian bertujuan untuk mengetahui pengaruh siklofosfamid terhadap ekspresi mRNA IL-6, jumlah folikel atretik dan jumlah folikel rekrutmen serta hubungan antara ekspresi mRNA IL-6 dengan kedua folikel tersebut. Selain itu, penelitian ini juga menguj dosis serta frekuensi injeksi siklofosfamid yang paling optimal dalam menimbulkan kerusakan folikel.

Metode: Sampel ovarium mencit dari 3 kelompok perlakuan injeksi siklofosfamid (dosis 50 mg/kg selama 14 kali, dosis 120 mg/kg sebanyak 1 kali dan dosis 120 mg/kg sebanyak 2 kali selama 14 hari) dan 1 kelompok kontrol (*normal saline* 50 mg/kg sebanyak 14 kali selama 14 hari) dikoleksi. Ovarium kanan mencit dibuat sediaan histologi untuk pengamatan jumlah folikel total, folikel atretik, folikel primordial dan folikel *growing* (primer, sekunder dan antral) sedangkan ovarium kiri untuk analisis ekspresi mRNA IL-6 dengan metode qPCR.

Hasil: Ekspresi mRNA IL-6 tertinggi terdapat pada kelompok mencit dosis 3 yang diinjeksi siklofosfamid dosis 120 mg/kg sebanyak 2 kali selama 14 hari. Perbedaan signifikan pada folikel atretik dan rekrutmen terdapat pada mencit kelompok dosis 3. Ekspresi mRNA IL-6 dengan folikel atretik dan rekrutmen tidak memiliki hubungan korelasi. Dosis 120 mg/kg dengan frekuensi 2 kali injeksi selama 14 hari memiliki penurunan jumlah folikel total tertinggi dengan perbedaan signifikan pada jumlah folikel primordial dibandingkan dengan kelompok kontrol

Kesimpulan: Injeksi siklofosfamid tidak berpengaruh signifikan terhadap ekspresi mRNA IL-6 namun berpengaruh signifikan pada jumlah folikel atretik dan folikel rekrutmen. Ekspresi mRNA IL-6 dengan jumlah folikel atretik dan folikel rekrutmen tidak memiliki korelasi. Regimen siklofosfamid paling optimal dalam merusak folikel adalah dosis 120 mg/kg dengan 2 kali injeksi selama 14 hari

Kata kunci: siklofosfamid, folikel, inflamasi, atretik, rekrutmen

ABSTRACT

Background: Cyclophosphamide is one of the most widely used chemotherapeutic agents and has proven effective in cancer treatment. However, it possesses gonadotoxic effects that can damage ovarian follicles. The gonadotoxic mechanism of cyclophosphamide mainly involves two dominant pathways: increased follicular atresia and premature recruitment of primordial follicles. Inflammation is another mechanism that occurs upon cyclophosphamide exposure. Interleukin-6 (IL-6) is a cytokine expressed during inflammatory responses. The inflammatory response in ovarian follicles may influence both follicular atresia and recruitment.

Objective: This study aimed to evaluate the effect of cyclophosphamide on IL-6 mRNA expression, the number of atretic and recruited follicles, and to analyze the relationship between IL-6 expression and both follicular parameters. In addition, this study examined the optimal dose and injection frequency of cyclophosphamide that most effectively induces follicular damage.

Methods: Ovarian samples were collected from mice assigned to three cyclophosphamide treatment groups (50 mg/kg daily for 14 days, 120 mg/kg single injection, and 120 mg/kg twice weekly injections in 14 days) and one control group (normal saline 50 mg/kg daily for 14 days). The right ovaries were processed for histological examination to assess the total, atretic, primordial, and growing (primary, secondary and antral) follicle counts, while the left ovaries were used to analyze IL-6 mRNA expression using quantitative PCR (qPCR).

Results: The highest IL-6 mRNA expression was found in the mice receiving 120 mg/kg cyclophosphamide twice within 14 days. Significant differences in atretic and recruited follicles were also observed in this group. IL-6 mRNA expression and both follicular atresia and recruitment had no correlation. The regimen of 120 mg/kg administered twice resulted in the lowest decrease in total follicles and showed a significant reduction in primordial follicles compared with controls.

Conclusion: Cyclophosphamide administration did not significantly affect IL-6 mRNA expression but significantly increased follicular atresia and recruitment. IL-6 mRNA expression showed no correlation with either parameter. The most damaging regimen for ovarian follicles was 120 mg/kg administered twice in 14 days.

Keywords: cyclophosphamide, follicle, inflammation, atresia, recruitment