ABSTRAK

Infeksi Tuberkulosis (TB), komplikasi yang cukup banyak mengenai pasien LES di daerah endemis TB. Isoniazid (INH), obat anti tuberkulosis yang direkomendasikan sebagai terapi pencegahan pada kelompok rentan TB, tetapi penggunaannya pada kelompok LES masih kontroversi, karena efek samping dari INH dikhawatirkan dapat memperburuk kondisi LES, perubahan profil farmakokinetik INH dan variabilitas individu dapat menjadi faktor dari timbulnya efek samping. Hepatotoksisitas akibat INH dikaitkan dengan proses metabolisme dan peran beberapa gen yang terkait, diantaranya adalah polimorfisme *CYP2E1* (prediktor hepatotoksisitas) yang hasilnya masih variatif. **Tujuan penelitian** Diperlukan penelitian profil farmakokinetik (PK) INH C_{maks} dan AUC_{0-8} dengan menilai konsentrasi obat dalam plasma, serta profil farmakogenetik (PG) dari gen yang terlibat, yaitu proporsi gen *CYP2E1* pada kelompok LES yang menerima terapi INH. **Desain penelitian** Penelitian deskriptif observasional dengan teknik *purposive sampling* yang dilakukan pada pasien rawat jalan LES dewasa di Rumah Sakit Hasan Sadikin Bandung, periode Desember 2022 – Agustus 2023. **Tahapan penelitian** Kriteria inklusi adalah LES dalam keadaan remisi, non TB. Kriteria eksklusi adalah alergi INH, gangguan hati dan ginjal, pasien hamil atau menyusui, komorbid lain, dan keganasan. Data PK diambil dari 6 titik waktu pengambilan darah (0, 1, 2, 3, 4, dan 8 jam setelah minum INH). DNA diisolasi untuk pemeriksaan polimorfisme gen *CYP2E1*. **Hasil**: 20 subjek yang memenuhi kriteria inklusi dilakukan pemeriksaan farmakokinetik setelah 10 hari minum INH preventif 5 mg/KgBB dalam keadaan perut kosong. Nilai C_{maks} 8,63 (2,55 – 18,27) μg/mL dan AUC_{0-8} 25,14 (8,59 – 58,6) μg/h.mL menunjukkan hasil yang cukup untuk memberikan prospek protektif tanpa ada efek samping meski dibarengi penggunaan obat LES. Distribusi dari genotipe *CYP2E1* rs2031920 (CC 70%, CT 30%), rs3813867 (GG 70%, GC 30%) dan rs2515641 (CC 65%, CT 30%, CA5%) mayoritas adalah *wild type* homozigot yang tidak berhubungan dengan C_{maks} dan AUC_{0-8} INH. **Kesimpulan**: Secara gambaran farmakokinetik, pemakaian INH preventif 300mg/hari pada LES cukup memberikan prospek perlindungan dari TB.

Kata Kunci : *CYP2E1,* Farmakokinetik, Isoniazid, Lupus, Tuberkulosis

ABSTRACT

Tuberculosis (TB) infection is a common complication in SLE patients in TB-endemic areas. Isoniazid (INH), is an anti-tuberculosis drug recommended as preventive therapy in TB susceptible groups, but its use in SLE groups is still controversial; because the side effects of INH are feared to worsen the condition of SLE, changes in the pharmacokinetic profile of INH and individual variability can be a factor in the onset of side effects. Hepatotoxicity due to INH is associated with metabolic processes and the role of several related genes, including the CYP2E1 polymorphism (predictor of hepatotoxicity) whose results are still varied. A study of the pharmacokinetic (PK) profile of INH Cmax and AUC0-8 by assessing plasma drug concentrations, as well as the pharmacogenetic (PG) profile of the genes involved, namely the proportion of the CYP2E1 gene in the SLE group receiving INH therapy is needed. ***Research design****: Descriptive observational study with purposive sampling technique conducted on adult SLE outpatients at Hasan Sadikin Hospital Bandung, period December 2022 - August 2023. Inclusion criteria were SLE in remission; and non-TB. Exclusion criteria were INH allergy, liver and kidney disorders, pregnant or lactating patients, other comorbidities, and malignancy. PK data was collected from 6 blood collection time points (0, 1, 2, 3, 4, and 8 hours after taking INH). DNA was isolated for CYP2E1 gene polymorphism testing.* ***Results:*** *20 subjects who met the inclusion criteria underwent pharmacokinetic examination after 10 days of preventive INH 5 mg/KgBB on an empty stomach. The C_{max} value of 8.63 (2.55 – 18.27) µg/mL and AUC_{0-8} of 25.14 (8.59 – 58.6) µg/h.mL showed sufficient results to provide a protective prospect without any side effects despite the use of SLE drugs. The distribution of CYP2E1 rs2031920 (CC 70%, CT 30%), rs3813867 (GG 70%, GC 30%), and rs2515641 (CC 65%, CT 30%, CA5%) genotypes were mostly homozygous wild type which was not associated with C_{max} and AUC_{0-8} of INH.* ***Conclusion:*** *In terms of pharmacokinetic features, preventive INH use of 300mg/day in SLE is sufficient to provide the prospect of protection from TB.*

Keywords*: CYP2E1, Pharmacokinetics, Isoniazid, Lupus, Tuberculosis*