

FARMAKOKINETIKA GLIMEPIRIDE PADA SUBJEK LAKI-LAKI DEWASA SEHAT USIA 18–40 TAHUN RAS MONGOLOID DI INDONESIA

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INTISARI

Latar belakang: Peningkatan prevalensi diabetes mellitus tipe 2 (DMT2) semakin pesat di negara-negara berpenghasilan rendah dan menengah, termasuk di Indonesia. DMT2 adalah penyebab utama dari kebutaan, gagal ginjal, serangan jantung, stroke, dan amputasi tungkai bawah. Pendekatan tatalaksana DMT2 terdiri dari diet sehat, aktivitas fisik teratur, mempertahankan berat badan normal, menghindari penggunaan tembakau, dan pengobatan farmakoterapi. Beberapa orang dengan DMT2 perlu mengonsumsi obat untuk mengontrol kadar gula darah. Hal ini termasuk injeksi insulin atau obat antidiabetes oral. Glimepiride merupakan salah satu anggota sulfonilurea yang memicu pelepasan insulin dari sel β pancreas. Dibandingkan sulfonilurea golongan pertama dan kedua, glimepiride memiliki insidensi hipoglikemia yang lebih rendah. Hipoglikemia dapat terjadi pada pasien dengan kadar glimepiride tinggi. Kadar glimepiride dalam tubuh dipengaruhi oleh metabolisme tubuh terhadap obat, yang utamanya dilakukan oleh enzim CYP2C9. Terdapat variasi pada gen pengode enzim metabolisme ini yang berbeda-beda di setiap ras. Berdasarkan deskripsi di atas, diperlukan evaluasi terhadap profil glimepirida pada subjek Indonesia ras Mongoloid.

Tujuan: Mengetahui profil farmakokinetika (C_{max} , T_{max} , $T_{1/2}$, dan AUC) obat glimepiride pada subjek laki-laki dewasa sehat usia 18–40 tahun ras Mongoloid di Indonesia.

Metode: Pada penelitian ini, evaluasi profil farmakokinetika dilakukan dengan metode studi deskriptif. Subjek penelitian ini adalah buku laporan penelitian glimepiride pada subjek Indonesia laki-laki dewasa sehat usia 18-40 tahun oleh Departemen Farmakologi Klinik Fakultas Kedokteran Universitas Gadjah Mada (FK UGM) pada tahun 2007 dengan kode nomor 175/LPO/VI/06. Kriteria inklusi dan eksklusi tidak diterapkan karena hanya ada satu laporan penelitian farmakokinetika glimepiride tablet 4 mg di Departemen Farmakologi dan Terapi FK UGM. Data yang diambil berupa tabel demografi dan kadar obat di dalam darah, lalu dilakukan pengukuran profil farmakokinetika. Kemudian, dilakukan analisis data farmakokinetika menggunakan prinsip rata-rata dengan simpangan baku. Dilakukan analisis hubungan farmakokinetika dengan penggunaan di klinik menggunakan data-data sekunder yang ada di pustaka. Parameter studi terdiri atas C_{max} , T_{max} , $T_{1/2}$, dan AUC.

Hasil: Berdasarkan hasil penelitian farmakokinetika glimepiride 4 mg pada subjek laki-laki Indonesia sehat usia 18-40 tahun ras Mongoloid, didapatkan waktu untuk mencapai kadar puncak (T_{max}) adalah $1,53 \pm 0,32$ jam. Kadar puncak glimepiride dalam darah (C_{max}) adalah $474,23 \pm 61,85$ ng/mL. Area di bawah kurva kadar plasma glimepiride dibandingkan waktu dari jam ke-0 hingga jam ke-48 (AUC_{0-48}) adalah $4742,64 \pm 1154,89$ ng/mL.jam. Area di bawah kurva kadar plasma glimepiride dibandingkan waktu 0-~ jam ($AUC_{0-\infty}$) adalah $4745,94 \pm 1157,1$ ng/mL.jam. Waktu paruh/eliminasi *half-life* ($T_{1/2}$) adalah $7,06 \pm 12,42$ jam.

Kesimpulan: Pemberian glimepiride 4 mg pada subjek Indonesia efektif. Namun, tetap perlu dilakukan penyesuaian dosis bagi setiap pasien diabetes mellitus tipe 2 agar mencapai rentang terapi yang paling sesuai untuk mencapai target terapi dan menghindari efek samping obat.

Kata kunci: Glimpiride, diabetes mellitus tipe 2, farmakokinetika, Indonesia.

PHARMACOKINETICS OF GLIMEPIRIDE IN HEALTHY ADULT MALE SUBJECTS AGED 18-40 YEARS OF MONGOLOID RACE IN INDONESIA

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ABSTRACT

Background: The prevalence of type 2 diabetes mellitus (T2DM) is increasing rapidly in low- and middle- income countries, including Indonesia. T2DM is the leading cause of blindness, kidney failure, heart attack, stroke, and lower limb amputation. The management approach for T2DM consists of a healthy diet, regular physical activity, maintaining normal body weight, avoiding tobacco use, and pharmacotherapy. Some people with T2DM need to take medication to control their blood sugar levels. This includes insulin injections or oral antidiabetic drugs. Glimepiride is a member of the sulfonylureas that triggers the release of insulin from pancreatic β cells. Compared to the first and second classes of sulfonylureas, glimepiride has a lower incidence of hypoglycemia. Hypoglycemia can occur in patients with high glimepiride levels. Glimepiride levels in the body are influenced by the body's metabolism of drugs, which is mainly carried out by the CYP2C9 enzyme. There are variations in the genes encoding this metabolic enzyme that differ in each race. Based on the description above, an evaluation of the glimepiride profile in Indonesian Mongoloid subjects is needed.

Objective: To determine the pharmacokinetic profile (C_{max} , T_{max} , $T_{1/2}$, dan AUC) of glimepiride in healthy adult male subjects aged 18–40 years of Mongoloid race in Indonesia.

Methods: In this study, the evaluation of the pharmacokinetic profile of glimepiride was conducted using a descriptive study method. The subject of this study was research report book on glimepiride in healthy adult Indonesian male subjects aged 18-40 years by the Department of Clinical Pharmacology, Faculty of Medicine, Universitas Gadjah Mada (FK UGM) in 2007 with code number 175/LPO/VI/06. Inclusion and exclusion criteria were not applied because there was only one pharmacokinetic research report on glimepiride 4 mg tablets at the Department of Pharmacology and Therapeutics, FK UGM. The data taken were in the form of demographic tables and drug levels in the blood, then pharmacokinetic profile measurements were carried out. Then, pharmacokinetic data analysis was carried out using the principle of average with standard deviation. An analysis of the relationship between pharmacokinetics and clinical use was carried out using secondary data available in the literature. The study parameters consisted of C_{max} , T_{max} , $T_{1/2}$, dan AUC.

Results: Based on the results of the pharmacokinetic study of glimepiride 4 mg in healthy Indonesian male subjects aged 18-40 years of Mongoloid race, the time to reach peak levels (T_{max}) was 1.53 ± 0.32 hours. The peak level of glimepiride in the blood (C_{max}) was 474.23 ± 61.85 ng/mL. The area under the curve of plasma glimepiride levels compared to time from 0 to 48 hours (AUC_{0-48}) was 4742.64 ± 1154.89 ng/mL.hour. The area under the curve of plasma glimepiride levels compared to time 0-∞ hours ($AUC_{0-\infty}$) was 4745.94 ± 1157.1 ng/mL.hour. The elimination half-life ($T_{1/2}$) was 7.06 ± 12.42 hours.

Conclusion: The administration of 4 mg glimepiride in Indonesian subjects is effective. However, dose adjustments are still needed for each type 2 diabetes mellitus patient to achieve the most appropriate therapeutic range to achieve therapeutic targets and avoid drug side effects.

Keywords: Glimepiride, type 2 diabetes mellitus, pharmacokinetics, Indonesia.