Perbandingan kadar teofilin dalam plasma antara tablet teofilin sediaan lepas lambat uniphyllin Continus 300-400 mg dengan sediaan biasa 150 mg

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Abstrak

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Ruang Lingkup dan Cara Penelitian: Dengan berkembangnya teknologi formulasi obat dan juga kemajuan di bidang pengobatan, telah dibuat teofilin dalam bentuk sediaan lepas lambat (SLLB). Hal ini menguntungkan bagi pasien, karena selain kepatuhan dapat ditingkatkan kadar obat dalam darah dapat terkendali dengan baik.

Bioavailabilitas dan bioekivalensi obat SLLB perlu diketahui dengan baik. Untuk teofilin hal ini terutama karena, disamping indeks terapi sempit juga adanya perbedaan antar individu dalam parameter farmakokinetik. Oleh sebab itu telah dilakukan penelitian terhadap tablet Uniphyllin® Continus® yang merupakan teofilin bentuk SLLB baru dibandingkan dengan teofilin sediaan biasa.

Penelitian dilakukan terhadap 13 sukarelawan sehat, pria dewasa. Minggu I diberikan teofilin sediaan biasa selama 3 hari, 4x150 mg/hari (9 dosis). Pada minggu II diberikan sediaan lepas lambat selama 3 hari, 2 x 300-400 mg/hari (5 dosis). Pada hari ke-3 dalam keadaan puasa, sebelum dan sesudah makan obat, diambil darah dari vena kubiti. Pada sediaan biasa darah diambil pada jam 0; 0,5; 1; 1,5; 2; 2,5; 3; 6; 9; dan 11. Pada sediaan lepas lambat darah diambil pada jam 0; 2; 3; 4; 5; 7; 9; 12; 15 dan 24. Kadar teofilin plasma diukur dengan metoda enzyme immunoassay-turbidimetry (ACA IV). Dari kadar yang didapat dihitung berbagai parameter farmakokinetik.

Hasil dan Kesimpulan: Data farmakokinetik diperoleh dari 12 subyek (satu subyek dibatalkan berhubung efek samping yang berat), sebagai berikut : Cmax tablet sediaan lepas lambat (SLLB) 12,17 μg/mL dan pada sediaan biasa (SBS) 15,75 μg/mL, kedua nilai Cmax berbeda bermakna (p < 0,01). Cmin pada SLLB 8,10 μg/mL dan pada SBS 10,39 µg/mL, kedua nilai berbeda bermakna (p <0,01). Nilai tmax SLLB adalah pada jam ke-4 sedang pada SBS pada jam ke-1,13; keduanya berbeda sangat bermakna (p<0,001). Hasil indeks fluktuasi (IF) antara SLLB dan SBS tidak berbeda (p >0,05; IF SLLB = 0,42 dan IF SBS = 0,44).

Dari data farmakokinetik terlihat tablet Uniphyllin® Continus® merupakan suatu sediaan lepas lambat. Variabilitas parameter antar subyek disebabkan oleh variabilitas metabolisme obat, sehingga menimbulkan fluktuasi kadar obat. Oleh karena itu, pada kondlsi tertentu sebaiknya penggunaan teofilin diikuti dengan pemeriksaan kadar obat dalam darah.
<hr><i>ABSTRACT
Comparative Study Of Plasma Concentration Of Theophylline Using Sustained Released Tablet Uniphyllin® Continus® 300-400 Mg With Plain Capsules Of Theophylline150 MgScope and Method of

Study: Advances in drug formulation and therapeutics make it possible to produce various controlled-release (CR) theophylline preparations. Such dosage form has been advocated to be more advantageous than the conventional form as it may in-crease patient?s compliance, and the plasma concentration of the drug to be more controllable.

The bioavailability and bioequivalence of sustained released drugs should be carefully observed. This is particularly important for theophylline, because not only it has a narrow margin of safety but also the capacity to metabolize the drug varies markedly between individuals. Uniphyllin® Continus®, a controlled release theophylline preparation, is to be marketed soon here. The aim of the present study is to confirm its controlled release characteristics compared with a conventional release (CVR) dosage form.

Thirteen healthy Indonesian volunteers participated in this study. They were given 150 mg of CVR theophylline 4 times daily for 9 dosages. Venous blood samples were taken at 0; 0.5; 1; 1.5; 2; 2.5; 3; 6; 9 and 11 hours after the last dosage. After a wash-out period of two weeks, the subjects took the CR tablets twice daily for 5 dosages. Subjects with body weights less than 70 kg were given 300 mg tablets, and heavier subjects were given 400 mg tablets. Blood samples were drawn at 0; 2; 3; 4; 5; 7; 9; 12; 15 and 24 hours. Plasma theophylline concentration was determined by enzyme immunoassay-turbidimetric method (ACA IV, Dupont).

Findings and Conclusions: Data was analyzed from 12 subjects (one subject dropped due to serious adverse reactions). The mean of peak concentrations (Cmax) of the CR and CVR dosage forms were 12.17 and 15.75, μg/mL, respectively ($p < 0.01$). Trough concentrations (Cmin) of the CR and CVR forms were 8.10 and 10.39 µg/mL, respectively ($p < 0.01$). The time to attain Cmax (tmax) for the CR and CVR forms were 4 and 1.13 hours, respectively ($p < 0.001$). The fluctuation index (FI) of the CR and CVR forms were 0.42 and 0.44, respectively; which are not significantly different.

The pharmacokinetic data show that Uniphyllin® Continus® tablet is a slow sustain released tablet. Variability between subjects caused by variability in drug metabolism produce fluctuations in the plasma concentration of the drug.</i>