Efek Doksazosin terhadap metabolisme Aminopirin pada model Perfusi Hati Tikus ex vivo = the Effect of Doxazosin on Aminopyrine metabolism in perfused rat liver

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Abstrak

ABSTRAK
Ruang Lingkup dan Cara Penelitian: Banyak senyawa diketahui dapat mempengaruhi aktivitas enzim mikrosom hati. Pengaruh doksazosin - suatu obat antihipertensi baru - terhadap aktivitas mikrosom hati belum diketahui. Untuk itu dilakukan penelitian efek pemberian doksazosin (D), i.p. terhadap kecepatan metabolisme aminopirin pada model perfusi hati tikus ex vivo, dibandingkan dengan pemberian fenobarbital (F) dan NaCl. (N). Juga dilakukan pemeriksaan pengaruh-penambahan doksazosin (FD) dan simetidin (FS) pada kelompok F.

Tiap kelompok terdiri dari 6 ekor tikus jantan galur Wistar. Perfusi dilakukan secara resirkulasi dengan larutan dapar Krebs- Henseleit sebagai cairan perfusat, yang dijenuhkan dengan campuran gas 95% 02: 002 5% (v/v). Kadar aminopirin pada cairan perfusi diperiksa dengan metode Brodie dan Axelrod. Diukur pula berat hati; kadar GPT pada serum, perfusat awal dan akhir; serta penyerapan tripan biru oleh inti sel hati. Kecepatan metabolisme aminopirin dinyatakan dengan nilai slope dari garis regresi penurunan kadar aminopirin dalam perfusat.

Hasil dan Kesimpulan: Berat badan tikus, kecepatan aliran perfusi serta nilai GPT serum, perfusat awal dan akhir dari kelima kelompok tidak berbeda bermakna. Tidak ada inti sel hati yang menyerap tripan biru pada semua sediaan histopatologik. Berat hati rata-rata kelompok D (5,78 g) tidak berbeda bermakna dengan kelompok N (5,60 g), sedangkan kelompok F (7,93 g), FS (8,03 g) dan FD (8,05 g) berbeda sangat bermakna dengan kelompok N (p <0,001). Perbandingan nilai slope yang diuji dengan i "comparison of slopes", ternyata slope kelompok D (-4,17x10) tidak berbeda dengan kelompok N (-37x10), tetapi berbeda bermakna dengan kelompok F (-8,56x10-) (p < 0,001). Slope kelompok Fl (-7,84xlO-'i berbeda bermakna dengan kelompok FS (-4,67x10) (p <0,01 tetapi tidak berbeda dengan kelompok F.

Dan hasil tersebut dapat disimpulkan bahwa doksazosin tidak bersifat induktor maupun inhibitor terhadap metabolisme aminopirin oleh enzim mikrosom hati pada percobaan perfusi hati tikus ex vivo.
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ABSTRACT
The Effects Of Doxazosin On Aminopyrine Meetabolism In Perfused Rat LiverScope and Method of Study: Several hundreds synthetic and naturally occurring compounds with diverse structures are now known to in-crease the activity of microsomal enzymes. The effect of doxazosin - a new antihypertensive agent - on microsomal enzymes activities has not yet been investigated. This study was carried out to deter-mine the effects of doxazosin (D) on microsomal enzymes compared to NaC1. (N) and phenobarbital. (F). In addition, the effect of the addition of doxazosin (FD) to F group compared to addition of cimetidine (FS)

was also evaluated.

The experiment was carried out on male rats of the Wistar strain; each group consists of 6 animals. Following treatment with the respective drugs, the livers were isolated and perfuse in a recalculating system with Krebs-Henseleit buffer, saturated with 95% 02 : 5% C02 (v/v,) at 37° C and pH 7.4. Aminopyrine was introduced into the perfusion medium, and its concentration measured at intervals during a 45-minute period by the method of Brodie and Axelrod. Additional measurements were: the liver weight; GPT activity in the serum and perfusate (initial and final); per-fusion flow rate; and try pan blue uptake by the hepatocytes.

Findings and Conclusions: There is no difference in body weight, per-fusion flow rate, and GPT activity in the serum and perfusates (initial and final) of the five groups. No trypan blue uptake by the hepatocytes was observed by microscopically analysis. There is no difference in total liver weight between the D group (5.78 g) and the N group (5.60 g), while the F group (7.83 g), FS group (8.03 g) and FD group (8.05 g) are significantly different compared to the N group ($p < 0.001$). The rate of aminipyrine, metabolism rep-resented by slope of regression line of aminopyrine decreasing content in the perfusate against the time was tested by the comparison of slopes. The slope of the D. group (-4.7x10-) i not significantly different compared to the N group (3.87x10), but is significantly different to the F group (-8.56x10) ($p < 0.01$). The slope of the FD group (-7.84x14) is significantly different compared to FS (-4.67x10-3) ($p < 0.05$), but is not significantly different compared to the F group.

Thus, it can be concluded that doxazosin is neither an inducers nor an inhibitor in the metabolism of aminopyrine by the liver microsomal enzyme in the isolated rat liver perfusion model.