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Interaction of erythromycin and clarithromycin with orange juice

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Abstrak

Pemberian jus jeruk dengan feksofenadin telah ditemukan menurunkan bioavailabilitas feksofenadin sampai kurang dari 30% melalui hambatan organic-anion transporting polypeptide (OATP), suatu polipeptida yang mentransport obat ke dalam sel dan terdapat pada organ-organ seperti hati, ginjal dan usus. Eritromisin dan klaritromisin adalah substrat dan penghambat CYP3A4, suatu enzim pemetabolisme obat di hati dan usus, dan P-glikoprotein (P-gp), protein yang mentransport obat ke luar dari sel. Karena terdapat tumpang tindih antara substrat dan penghambat CYP3A4, P-gp dan OATP, kami ingin meneliti apakah pemberian bersama jus jeruk lokal (jeruk Siam) akan mempengaruhi bioavailabilitas ke-2 antibakteri tersebut di atas. Kami melakukan 2 studi menyilang, satu studi untuk setiap antibakteri (500 mg), yang diberikan bersama jus jeruk (200 ml) dan bersama air pada 12-13 sukarelawan sehat per studi. Kadar serum antibakteri diukur dengan cara mikrobiologik. Rasio rata-rata (kisaran) AUC0-t dengan jus jeruk / dengan air adalah sbb.: eritromisin : total (n=13) 81.7 (9.7-193.8)%, tidak berubah (n=4) 96.4 (80.5-107.9)%, menurun (n=6) 31.9 (9.7-49.0)%, meningkat (n=3) 161.8 (134.6-193.8)%; klaritromisin : total (n=12) 91.4 (20.6-158.3)%, tidak berubah (n=5) 103.1 (80.9-123.0)%, menurun (n=4) 34.8 (20.6-64.3)%, meningkat (n=3) 147.2 (132.9-158.3)%. Disimpulkan bahwa pemberian eritromisin atau klaritromisin bersama jus jeruk Siam menghasilkan efek yang tidak konsisten terhadap bioavailabilitas ke-2 antibakteri ini pada masing-masing subyek, dengan penurunan yang besar pada hampir separuh dari subyek, meskipun secara total efeknya tidak bermakna secara statistik. (Med J Indones 2004; 14: 78-86)
<hr>Concomitant administration of orange juice with fexofenadine has been found to decrease the bioavailability of fenofenadine to less than 30% via inhibition of organic-anion transporting polypeptide (OATP), a drug uptake transporter expressed in organs such as liver, kidney and intestine. Erythromycin and clarithromycin are substrates and inhibitors of CYP3A4, a drug metabolizing enzyme in the liver and enterocytes, and P-glycoprotein (P-gp), a drug efflux transporter expressed in the same organs as OATP. Since an extensive overlap exists between substrates and inhibitors of CYP3A4, P-gp and OATP transporters, we want to study the effect of coadministration of our local orange (Siam orange) juice on the bioavailability of the above antibacterials. We conducted two 2-way cross-over randomized studies, one study for each antibacterial (500 mg), crossed between administration with orange juice (200 ml) and with water, in 12-13 healthy subjects per study. The serum concentrations of the antibacterials were assayed by microbiological method. The mean (range) ratio of AUC0-t with orange juice/with water were as follows : erythromycin : total (n=13) 81.7 (9.7-193.8)%, unchanged (n=4) 96.4 (80.5-107.9)%, decreased (n=6) 31.9 (9.7-49.0)%, increased (n=3) 161.8 (134.6-193.8)%; clarithromycin : total (n=12) 91.4 (20.6-158.3)%, unchanged (n=5) 103.1 (80.9-123.0)%, decreased (n=4) 34.8 (20.6-64.3)%, increased (n=3) 147.2 (132.9-158.3)%. It was concluded that coadministration of Siam orange juice with erythromycin or clarithromycin produced unpredictable effects on the bioavailability of these antibacterials in individual subjects, with marked decreases in almost half of the subjects, although in totals the effects were not statistically significant. (Med J Indones 2004; 14: 78-86)