

Primaquine decreased plasma concentration of ritonavir: single- and repeated-dose study in Sprague Dawley rats

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Abstrak

Latar belakang: Penelitian ini dilakukan untuk meneliti pengaruh pemberian ritonavir dan primaquin bersamaan, yang diberikan dalam dosis tunggal atau dosis berulang pada konsentrasi plasma ritonavir pada tikus. Metode: Pada studi dengan pemberian dosis tunggal, 30 tikus Sprague Dawley jantan secara acak diberikan ritonavir 20 mg/kgBB atau ritonavir 20 mg/kgBB + primaquin 1,2 mg/kgBB atau ritonavir 20 mg/kgBB + ketokonazol 10 mg/kgBB. Ketokonazol digunakan sebagai kontrol positif penghambat metabolisme ritonavir. Pada studi dengan pemberian dosis berulang, 30 tikus Sprague Dawley secara acak diberikan ritonavir 20 mg/kgBB/hari atau ritonavir 20 mg/kgBB/hari + primaquine 1,2 mg/kgBB/hari atau ritonavir 20 mg/kgBB/hari + rifampisin 100 mg/kgBB/day. Rifampisin digunakan sebagai kontrol positif penginduksi metabolisme ritonavir. Hasil: Pada pemberian dosis tunggal, ketokonazol meningkatkan area dibawah kurva kadar plasma (AUC) ritonavir (↑114,8%, $p < 0.05$), sedangkan primaquin cenderung menurunkan AUC ritonavir (↓32,6%, $p > 0.05$). Pemberian dosis berulang menunjukkan bahwa rifampisin menurunkan AUC ritonavir (↓42,8%, $p < 0.001$), dan primaquin menurunkan AUC ritonavir (↓ 46,6%, $p < 0.001$). Kesimpulan: Pemberian primaquin dan ritonavir bersamaan dapat menurunkan AUC ritonavir. Hal ini dapat menyebabkan konsentrasi ritonavir sebagai anti-HIV tidak mencukupi, sehingga dapat menyebabkan kegagalan terapi dengan ritonavir.

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Abstract

Background: The present study was aimed to explore the effects of ritonavir and primaquine combination given as a single dose or repeated-dose compared to ritonavir alone on ritonavir plasma concentration in the rats. Methods: In single-dose study, 30 male Sprague Dawley rats were randomly allocated to receive ritonavir 20 mg/kg BW or ritonavir 20 mg/kg BW + primaquine 1.2 mg/kg BW or ritonavir 20 mg/kg BW + ketokonazole 10 mg/kg BW. Ketokonazole was used as positive control of ritonavir metabolism inhibitor. In the repeated-dose study, thirty Sprague Dawley male rats were randomly allocated to receive ritonavir 20 mg/kg BW/day or ritonavir 20 mg/kg BW/day + primaquine 1.2 mg/kg BW/day or ritonavir 20 mg/kg BW/day + rifampicin 100 mg/kg BW/day. Rifampicin was used as a positive control of ritonavir metabolism inducer. Results: In the single-dose study, ketokonazole increased the area under the plasma concentration (AUC) of ritonavir (↑114.8%, $p < 0.05$), while primaquine tended to decrease the AUC of ritonavir (↓ 32.6%, $p > 0.05$). Repeated-dose study showed that rifampicin decreases the AUC of ritonavir (↓ 42.8%, $p < 0.001$), and primaquine decreased the AUC of ritonavir plasma concentration (↓ 46.6%, $p < 0.001$). Conclusion: Concomitant administration of primaquine and ritonavir decreases the AUC of ritonavir. This effect may result in the insufficient concentration of ritonavir as anti-HIV, which may lead to treatment failure with ritonavir.