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PRIMAQUINE DECREASES PLASMA CONCENTRATION OF RITONAVIR: SINGLE AND MULTIPLE DOSE STUDY IN RATS

Melva L, Vivian S, Nafrialdi, Rianto S, Frans DS

Department of Pharmacology and Therapeutics, Faculty of Medicine, Universitas Indonesia

Background:

The present study was aimed to explore the effects of ritonavir and primaquine combination given as a single-dose or multiple-dose compared to ritonavir alone on ritonavir plasma concentration in rats.

Materials & Methods:

In single-dose study, 30 male Spraque Dawley rats were randomly allocated to receive ritonavir 20 mg/kgBW or ritonavir 20 mg/kgBW + primaquine 1.2 mg/kgBW or ritonavir 20 mg/kgBW + ketoconazole 10 mg/kgBW. Ketoconazole was used as a positive control for inhibitor of ritonavir metabolism.

In multiple-dose study, thirty male Spraque Dawley rats were randomly allocated to receive ritonavir 20 mg/kgBW/day or ritonavir 20 mg/kgBW/day + primaquine 1.2 mg/kgBW/day or ritonavir 20 mg/kgBW/day + rifampicin 100 mg/kgBW/day. Rifampicin was used as a positive control for inducer of ritonavir metabolism.

Results:

In the single-dose study, ketoconazole increased the area under the plasma concentration (AUC) of ritonavir ($\uparrow 114,8\%$, $p < 0.05$), while primaquine tends to decrease the AUC of ritonavir ($\downarrow 32,6\%$, $p > 0.05$). Multiple-dose study showed that rifampicin decreased the AUC of ritonavir ($\downarrow 42,8\%$, $p < 0.001$), while primaquine decreased the AUC of ritonavir plasma concentration ($\downarrow 46,6\%$, $p < 0.001$).

Conclusion:

Concomitant administration of primaquine and ritonavir decreases the AUC of ritonavir. This effect could result in the insufficient concentration of ritonavir as anti-HIV, which might lead to treatment failure with ritonavir.

Keywords:

primaquine, ritonavir, drug interaction, metabolism