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 (↑114,8%, p<0.05), while primaquine tends to decrease the AUC of ritonavir (↓ 32.6%, p>0.05). Multiple-dose study showed that rifampicin decreased the AUC of ritonavir (↓ 42,8%, p<0.001), while 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 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