

Volume 6, No. 1 (Supplement)

June 2011

ISSN 1823-2140

The
National University
with an
INTERNATIONAL REACH



UNIVERSITI
KEBANGSAAN
MALAYSIA
National University of Malaysia

MEDICINE & Health

The Official Journal of The Faculty of Medicine UKM

7th Malaysia Indonesia Brunei Medical Sciences Conference "TOWARDS A HOLISTIC AND INTEGRATIVE APPROACH IN HEALTHCARE"



22nd - 24th July 2011

Equatorial Hotel, Bangi, Selangor,
MALAYSIA

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CO-ADMINISTRATION OF RITONAVIR AND PRIMAQUINE DECREASES PLASMA CONCENTRATION OF PRIMAQUINE: SINGLE- AND MULTIPLE-DOSE STUDY IN THE RATS

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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 the rats.

Methods:

In single-dose study, 30 male Spraque Dawley rats were randomly allocated to receive primaquine 12.5 mg/kgBW or primaquine 12.5 mg/kgBW + ritonavir 10 mg/kgBW or primaquine 12.5 mg/kgBW + ketokonazole 10 mg/kgBW. Ketokonazole was used as positive control for inhibitor of primaquine metabolism. In the multiple-dose study, thirty Spraque Dawley male rats were randomly allocated to receive primaquine 12.5 mg/kgBW/day or primaquine 12.5 mg/kgBW/day + ritonavir 10 mg/kgBW/day or primaquine 12.5 mg/kgBW/day + rifampicin 100 mg/kgBW/day. Rifampicin was used as a positive control for inducer of primaquine metabolism.

Results:

In the single-dose study, ketokonazole increases the area under the plasma concentration (AUC) of primaquine ($\uparrow 45.8\%$, $p < 0.000$), while the ritonavir decreases the AUC of primaquine ($\downarrow 64.6\%$, $p < 0.000$). Multiple-dose study shows that both rifampicin and ritonavir decreases the AUC of primaquine by 60.2% ($p < 0.000$) and 67.7% ($p < 0.000$), respectively.

Conclusion:

Concomitant administration of primaquine and ritonavir decreases the AUC of ritonavir. This effect could result in the insufficient concentration of primaquine as anti-relapse therapy in malaria caused by *Plasmodium vivax*, which might lead to treatment failure with primaquine.

Keywords:

Primaquine, ritonavir, drug interaction, metabolism.