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

officiated by
Y.B Datuk Rosnah Haji Abdul Rashid Shirlin
Deputy Minister of Health 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 Sprague 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 Sprague 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 (↑45.8%, p<0.000), while the ritonavir decreases the AUC of primaquine (↓ 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.