SHORT REPORT: EFFECTS OF PYRONARIDINE ON GAMETOCYTES IN PATIENTS WITH ACUTE UNCOMPPLICATED FALCIPARUM MALARIA

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Abstract. The effects of pyronaridine and chloroquine on mature Plasmodium falciparum gametocytes were compared in 161 patients treated with chloroquine or pyronaridine. Neither pyronaridine nor chloroquine showed gametocytocidal activity. The relative risks of post-treatment gametocytemia after pyronaridine and chloroquine treatment in the presence of chloroquine-resistant isolates were 1.25 and 11.5, respectively, suggesting that the use of chloroquine was associated with a high risk of favoring post-therapeutic gametocytemia in chloroquine-resistant infections.
on mature data on the absence of gametocytocidal effect of chloroquine against the gametocytes of *P. falciparum*. The absence of gametocytes carried the resistant gene.

Compared with the gametocytocidal efficacy of primaquine (gametocyte clearance within 4–8 days), our data based on a small number of gametocyteemic patients suggest the absence of gametocytocidal effect of pyronaridine and chloroquine against the gametocytes of *P. falciparum*. Our data on the absence of gametocytocidal effect of chloroquine on mature *P. falciparum* gametocytes are in agreement with those of previous studies. However, our observation that chloroquine-treated patients infected with chloroquine-sensitive parasites had lower gametocytemia, compared with the patient with chloroquine-resistant parasites, is consistent with the fact that chloroquine exerts an inhibitory action against immature gametocytes.

Forty-seven (64%) of 73 patients in the pyronaridine group and 16 (21%) of 77 patients in the chloroquine group without detectable gametocytes on day 0 subsequently developed gametocytemia. The evolution of gametocytemia in these patients is summarized in Table 2. Although the mean gametocyte count did not differ significantly in patients with positive gametocyte counts (P > 0.05, by t-test), the difference in the number of gametocyte-positive patients in the treatment groups was evident on days 7 and 14. The absence of post-treatment gametocytemia in the majority of chloroquine-treated patients is in agreement with the results of a previous study. The underlying reason may be related to the activity of chloroquine against immature gametocytes, which are sequestered in deep organs during the maturation process. Subjects treated with pyronaridine were more likely to have post-treatment gametocytemia than subjects treated with chloroquine (relative risk = 3.26, 95% confidence interval [CI] = 2.16–4.91; P < 0.001), suggesting that pyronaridine has either no activity or less activity than chloroquine against immature gametocytes.

The relative risks of post-treatment gametocytemia after pyronaridine and chloroquine treatment in the presence of chloroquine-resistant isolates were 1.25 (95% CI = 0.88–1.77) and 11.5 (95% CI = 1.60–82.7), respectively. Among the pyronaridine-treated patients in whom gametocytes were detected during the post-treatment period, 26 (58%) of 45 were infected with chloroquine-resistant isolates, which corresponds to the expected proportion (50–60%) of the chloroquine-resistant isolates in Yaoundé. Fourteen of 15 isolates obtained from chloroquine-treated patients with post-therapeutic appearance of gametocytes were chloroquine-resistant. This observation agrees with other studies that have suggested that chloroquine therapy in a chloroquine-resistant endemic region may favor the survival and selection of gametocytes carrying the resistant gene. These preliminary results, which suggest that patients who are infected with chloroquine-resistant isolates are more likely to become gametocyte carriers than those who are infected with chloroquine-sensitive parasites, need to be evaluated in different patient populations under various epidemiologic conditions. Further studies are needed to establish whether post-therapeutic gametocytes are infective to mosquitoes, leading to an increased transmission of chloroquine-resistant *P. falciparum* strains.

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