

**THE EFFECT OF ADHERENCE ON THE EFFICACY OF
ARTEMETHER-LUMEFANTRINE (COARTEM) IN THE
TREATMENT OF UNCOMPLICATED PLASMODIUM
FALCIPARUM MALARIA IN BANGLADESH:
A RANDOMIZED CONTROLLED TRIAL**

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A randomized controlled trial with non-inferiority design was carried out in Bandarban Hill Tract District, Bangladesh to compare the efficacy of artemether-lumefantrine between Directly Observed Treatment (DOT) group with that of Non Directly Observed Treatment (NDOT) group of uncomplicated *P. falciparum* malaria. The study also measured the adherence and risk factors of adherence/nonadherence in the NDOT group and compared the efficacy of the drug between adherent and nonadherent patients. The patients (n=320) were followed for 42 days following WHO protocol. The DOT group (n=160) were admitted in the hospital for 3 days and for NDOT group (n=160) drug was provided to be taken at home. The Kaplan-Meier curves for the "Intention to treat" analysis without correction for reinfection by PCR showed similar survival function on day 42 as 97.2% (95% CI 92.7 – 98.9%). Log-rank analysis for survival function showed no significant difference between the study groups (Kaplan-Meier, Log Rank, $p = 0.98$). Per protocol analysis after PCR adjustment showed 99.3% ACPR on D28 and D42 in NDOT group and 100% ACPR on D28 and D42 in DOT group. Statistical significant difference of ACPR was not found between the groups on D28 and D42 (RR 0.99, 95% CI 0.00 – 38.15, $P = 0.49$). Adherence was measured by tablet count and verbal response and 93% patients (95% CI 88.0 – 96.5) were found adherent. Some reasons of nonadherence and adherence were identified. No risk factors were found to be significantly associated with nonadherence. Efficacy of the drug (without PCR correction) was found higher in adherent than nonadherent patients. Median plasma lumefantrine concentration in the NDOT and DOT groups were not different both on D7 (NDOT: 670.83; DOT: 860.33; $P=0.56$) and on D28 (NDOT: 90.11; DOT: 91.88; $P=0.81$). Median plasma lumefantrine concentration was found higher for adherent than for nonadherent patient and for patients who took fatty meal with medicine than for patients who did not take fatty meal on D7 and D28 but the difference were not significant ($P>.05$). Patients who had the lower D7 plasma lumefantrine concentration (>280 ng/ml) had higher risk of reinfection (RR 5.63, $P=0.027$). Population genotyping showed diversity in all 3 genetic markers (MSP1, MSP 2 and GLURP). The study concluded that NDOT is as good as DOT with high efficacy of artemether-lumefantrine and adherence to the drug is fairly high.

KEY WORDS: UNCOMPLICATED PLASMODIUM FALCIPARUM MALARIA/EFFICACY/ADHERENCE/ARTEMETHER-LUMEFANTRINE/BANGLADESH**115 P.**