Trans R Soc Trop Med Hyg

Jul-Aug 1990;84(4):492-5.
doi: 10.1016/0035-9203(90)90010-c.

Variability in the metabolism of proguanil to the active metabolite cycloguanil in healthy Kenyan adults

W M Watkins[1], E K Mberu, C G Nevill, S A Ward, A M Breckenridge, D K Koech

Affiliation

- [1]Kenya Medical Research Institute, Nairobi.

- PMID: 2091335
- DOI: 10.1016/0035-9203(90)90010-c

Abstract

Extensive metabolizers (EM) and poor metabolizers (PM) of the malaria chemoprophylactic drug proguanil have been identified by measuring the proguanil/cycloguanil ratio in urine following a single dose of the pro-drug. The pharmacokinetic characteristics of proguanil were similar in 8 EM and 8 PM subjects, but there were significant differences between the 2 groups with respect to cycloguanil pharmacokinetics. In none of the PM subjects could cycloguanil be detected in whole blood samples at any time after proguanil dosage. Plasma cycloguanil was measureable in only 2 of 8 PM subjects, despite an analytical sensitivity in the high-performance liquid chromatographic assay of 1 ng/ml cycloguanil. A comparatively high proportion of Black Kenyan adults appear to metabolize proguanil poorly, possibly because they lack the specific mixed function oxidase which will accept proguanil as substrate.