Drug-drug interactions and possible clinical consequences between antimalarials and concomitant drugs prescribed for uncomplicated malaria in the Democratic Republic of the Congo

Flavien Gurba[1,2], Christian Burri[1,2], Christoph R. Meier[3,4], Andrea Kuemmerle[1,2]

[1]Swiss Tropical and Public Health Institute, Basel, Switzerland

[2]University of Basel, Basel, Switzerland

[3]Clinical Pharmacy and Epidemiology, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland

[4]Hospital Pharmacy, University Hospital of Basel, Basel, Switzerland

Introduction

Malaria is a worldwide disease and the most spread parasitic infection. Nowadays it occurs particularly in tropical areas and is a major public health problem for several countries especially for the Democratic Republic of the Congo. The parasite, a protozoon from Plasmodium species, is transmitted through the bite of an infected female Anopheles mosquito and causes malaria. The guidelines of the WHO recommend artemisinin combination therapies (ACTs) to treat malaria. Antimalarials are often simultaneously administered with concomitant drugs to treat the unspecific symptoms or concomitant diseases. It is known that antimalarials may cause drug-drug interactions (DDIs) with some other drugs such as antibiotics, analgesics and antivirals. The goal of this thesis was to determine the prevalence of DDIs and to describe the possible clinical consequences of DDIs between antimalarials and concomitant drugs.

Method

A database containing 2'300 patient files was shared by the Clinical Pharmacology and Pharmacovigilance Unit of the University of Kinshasa. Data was collected retrospectively for the purpose of a drug utilization study carried out in Democratic Republic of the Congo from January to March 2014. Patient files with diagnosis of uncomplicated malaria were included in this study whereas severe malaria cases and no malaria diagnosis cases were excluded. An algorithm was developed to assess all drug pairs occurring at least once in the database for their DDI potential. Drug pairs were classified as demonstrated DDI, potential DDI, safely use together or unknown. Data analysis was descriptive.

Results

A total of 2'300 patient files were included in the analysis. The age median was 10 years. Only 52% of patients were diagnosed positive before the antimalarial was given and a majority of patients were not followed-up after treatment (84% of patients). ACTs were only used in 58% of cases. Analgesic, antibiotic and supplements were the three most frequently prescribed concomitant drugs classes (53% of all prescriptions). Each patient received an average of 3.45 concomitant drugs (median = 3). The most frequently observed drug pair was the combination of ASAQ with paracetamol (26% of patients). Half of the patients (51%) present at least one potential or demonstrated DDI. The most frequent possible clinical consequences of DDI were QT-elongation (30% of patients), decrease in antimalarial exposure (9%) and increase in antimalarial exposure (8%).

Discussion and conclusion

Malaria is a major health problem in tropical areas. The potential and demonstrated DDIs observed within this database and their possible clinical consequences might add an additional burden to public health. Some actions might improve the appropriate therapeutic management of malaria cases by giving safe drug combinations and avoiding combinations at risk for DDIs: encourage health staff to follow the guidelines of the WHO, awareness program on the field with the healthcare staff, establishment of instruction sheet/algorithm informing about the combinations to avoid or to promote, establishment of an application on computer or smartphone allowing healthcare staff to choose the appropriate drug combinations. All these options may permit to treat correctly and safely the patients, to reduce the burden of malaria and to improve the malaria control.