Acta Tropica 179 (2018) 25–35

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Pharmaceutical interactions between antiretroviral and antimalarial drugs used in chemoprophylaxis

Andreas Erich Zautner[a], Ottmar Herchenröder[b], Awatef El Moussi[c], Norbert Georg Schwarz[d], Dorothea Franziska Wiemer[e], Uwe Groß[a], Hagen Frickmann[e,f,*]

[a] Institute for Medical Microbiology, University Medicine Göttingen, Kreuzbergring 57, 37075 Göttingen, Germany
[b] Institute for Experimental Gene Therapy and Cancer Research, University Medicine Rostock, Schillingallee 69, 18057, Rostock, Germany
[c] Unit Virology, Microbiology Laboratory, Charles Nicolle University Hospital,Boulevard du 9-Avril 1938, 1006, Tunis, Tunisia
[d] Infectious Disease Epidemiology, Bernhard Nocht Institute for Tropical Medicine Hamburg, Bernhard Nocht Str. 74, 20359 Hamburg, Germany, Germany
[e] Department of Microbiology and Hospital Hygiene, Tropical Microbiology and Entomology Unit, Bundeswehr Hospital Hamburg, Bernhard Nocht Str. 74, 20359, Hamburg, Germany
[f] Institute for Medical Microbiology, Virology and Hygiene, University Medicine Rostock, Schillingallee 70, 18057, Rostock, Germany

ARTICLE INFO

Keywords:
HIV
Malaria
Drug interactions
Resistance
Therapy
Prophylaxis
Tropics

ABSTRACT

Human immunodeficiency virus (HIV) is the causative agent of the Acquired Immunodeficiency Syndrome (AIDS). The pandemic is believed to have originated within the Northern Congo basin covering large parts of the Democratic Republic of Congo, the Republic of Congo, the Central African Republic, Cameroon and Gabon. Although over decades, HIV-1 has spread throughout the World leaving no country unaffected, sub-Saharan Africa remains the region with more than 80% of all infected individuals. The HIV-2 epidemic has largely remained restricted to West Africa along the Upper Guinean forests. Co-incident with these regions of highest HIV distribution is a part of the malaria belt and therefore, co-infections are common. In this review we carve out the consequences of HIV transmission prevention and synchronous malaria prophylaxis during occupational or leisure travelling activities within this World region. In particular, we elaborate on considering pre-existing drug resistances of both, the malaria parasites and the immunodeficiency viruses, when determining a combination for prophylactic and, if necessary, post-expositional measures with a focus on the compatibility of both medications.

1. Introduction

The choice of appropriate antivirals for HIV postexpositional prophylaxis (PEP) or preexpositional prophylaxis (PreP) can be challenging in case of complex local situations with high resistance rates against various classes of anti-retroviral drugs (Salou et al., 2016). This is particularly the case in tropical Africa, where resistance of HIV is a frequent phenomenon (Kasang et al., 2011; Salou et al., 2016; TenoRes Study Group, 2016). Although during leisure travel in areas of high HIV endemicity unprotected casual sexual encounters are the most likely reason for an HIV PEP or PrEP requirement, other indications may occasionally play a role and may make pharmaceutical HIV prevention necessary. For healthcare professionals, needlestick injuries or comparable inoculation of infectious body fluids of HIV-infected patients pose other infection risks (Wicker et al., 2007). Less frequent risks on travel comprise forceful inoculations of infectious body fluids (Frickmann et al., 2013), e.g., during military conflicts or due to sexual assaults.

In areas where antimalarial chemoprophylaxis on travel is recommended or where therapy of acute malaria may become necessary, compatibility of antivirals and antimalarial drugs has to be considered. If local resistance has to be kept in mind as well, the decision on the optimum combination can become quite challenging. To highlight the associated aspects, this narrative review summarizes indications for antimalarial chemoprophylaxis or immediate treatment of suspected malaria, describes requirements for HIV PEP or PrEP during professional or leisure travelling activities and puts a focus on the global distribution of HIV resistance as well as on the migration-associated spread of virus subtypes and resistance. Finally, considerations on compatibility of antiviral drugs and antimalarial drugs complete the overview.

* Corresponding author at: Department of Microbiology and Hospital Hygiene, Tropical Microbiology and Entomology Unit, Bundeswehr Hospital Hamburg, Bernhard Nocht Str. 74, D-20359 Hamburg, Germany.
E-mail address: Frickmann@bnitm.de (H. Frickmann).

https://doi.org/10.1016/j.actatropica.2017.12.021
Received 31 July 2017; Received in revised form 8 December 2017; Accepted 17 December 2017
Available online 19 December 2017
0001-706X/

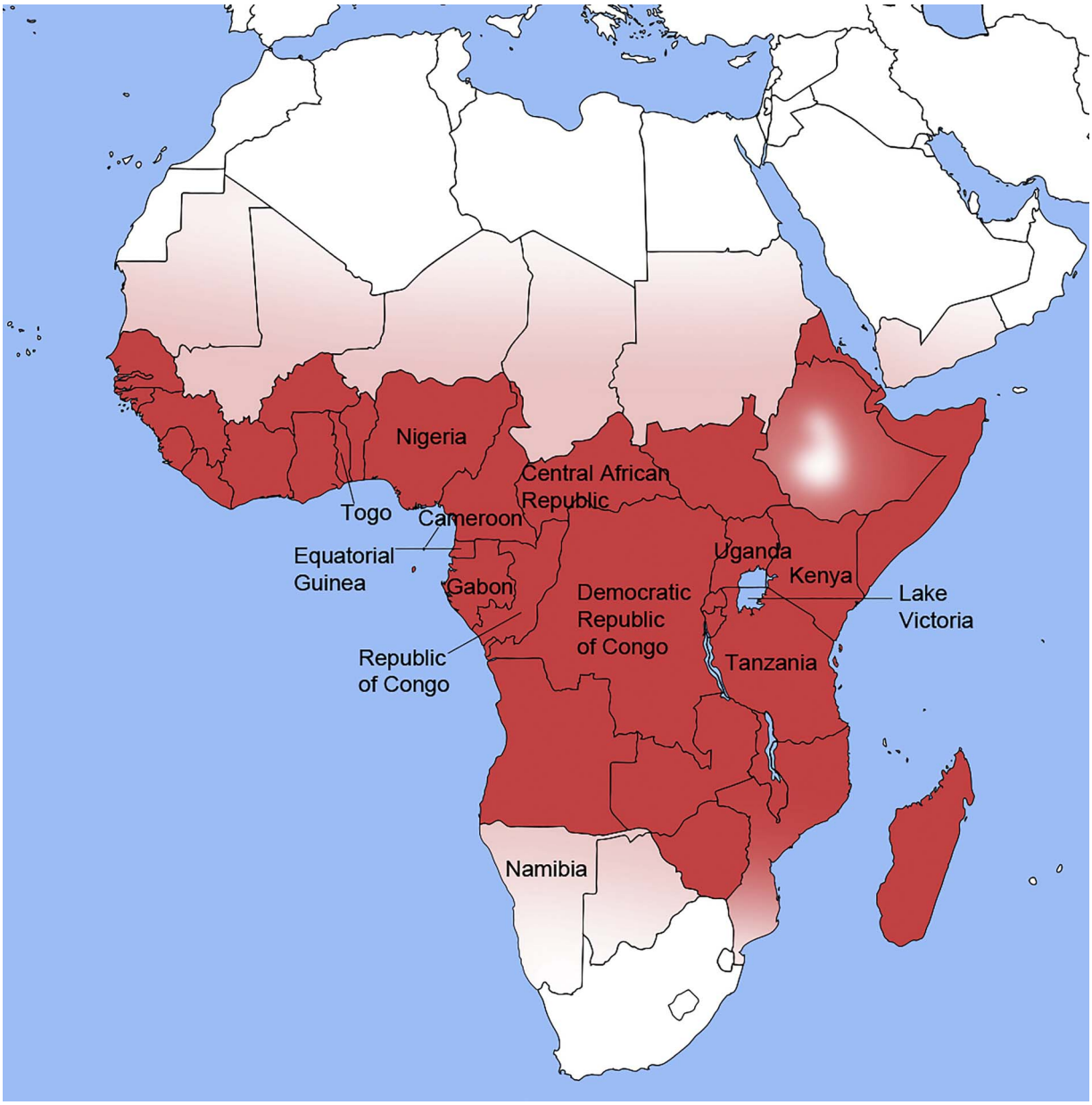

Fig. 1. Map of Africa indicating areas with widespread (red) or regional (faint red) malaria risks. Names are indicated for countries mentioned. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article. In the print version, red is shown as dark grey and faint red as faint grey.)

2. Chemoprophylaxis versus emergency treatment-prevention and treatment of malaria during travel

According to WHO, in 2015, 91 countries and areas throughout the World still had ongoing malaria transmissions. Amongst those, the areas with the highest burden are located in Sub-Saharan Africa (Fig. 1). More than 10,000 out of over 125 million international travellers become infected with malaria each year and *Plasmodium falciparum* (*Pf*) is the predominant parasite (WHO, 2017a). Prevention of malaria for travellers consists of the ABCDE scheme: Awareness, bite prevention, chemoprophylaxis, (immediate) diagnosis and stand-by emergency treatment (SBET) and lastly, environmental precautions (WHO, 2017b).

Awareness includes knowledge of the region where malaria is endemic, as well as information about the incubation period, the possibility of delayed onset and predominant symptoms. Vector control is crucial, due to the simple fact that without a mosquito bite, there is no malaria. Insecticide treated mosquito nets and indoor residual spraying are the main actions that can be taken locally. For travellers, the use of repellents and reasonable clothing are recommended, with the latter possibly being insecticide treated. Connected therewith is the advice to avoid environments prone to be mosquito breeding areas and hence, to keep housing areas and surroundings free of breeding sites. Outdoor activities between dusk and dawn should be minimized (WHO, 2017b).

Most travellers rely on chemoprophylaxis and SBET. Looking at guidelines issued by national institutions as the CDC (Centers for Disease Control and Prevention, USA), the ACMP (Advisory Committee on Malaria Prevention, UK), the SIMET (Società Italiana di Medicina Tropicale, Italy), the CMVI (Comité des maladies liées aux voyages et des maladies d'importation, France), the DTG (Deutsche Tropenmedizinische Gesellschaft, Germany) and the BfG (Bundesamt für Gesundheit, Switzerland) the recommendations vary when compared with those of the WHO. In particular, advices about who should use which chemoprophylaxis under which circumstances in a given setting seem to be ambiguous. The decision makers have to consider the incidence of malaria in the respective country, i.e., cases of *Pf* malaria