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ACTs: Efficacy, Resistance and Future Malaria Control

Emanuel Mesah*

Department of Malaria Surveillance and Control Department Ghana Center for Infectious Disease Studies, Accra, Ghana

Introduction

This systematic review and meta-analysis confirmed that artemether-lumefantrine is an effective and safe artemisinin-based combination therapy for treating uncomplicated Plasmodium falciparum malaria in pregnant women across all trimesters. The findings support its continued use, highlighting its crucial role in maternal and child health initiatives in malaria-endemic regions [1].

This study provides insights into the molecular surveillance of artemisinin and partner drug resistance markers in Plasmodium falciparum across sub-Saharan Africa. It emphasizes the importance of continuous monitoring for resistance to artemisinin-based combination therapies to inform treatment policies and prevent widespread drug failure in high-burden areas [2].

This systematic review and meta-analysis assesses the real-world effectiveness of artemisinin-based combination therapies in treating uncomplicated Plasmodium falciparum malaria in children. The findings underscore the sustained efficacy of ACTs in pediatric populations, reaffirming their critical role in malaria control strategies for this vulnerable group [3].

This review discusses the ongoing development of novel artemisinin-based combination therapies, highlighting efforts to create next-generation antimalarials that can overcome emerging drug resistance. It provides a comprehensive overview of the pipeline, emphasizing strategies to extend the lifespan of ACTs and maintain effective treatment options against malaria [4].

This article explores the molecular underpinnings of artemisinin resistance in Plasmodium falciparum, focusing on the Kelch13 propeller domain mutations. Understanding these mechanisms is crucial for designing new antimalarial drugs and optimizing existing artemisinin-based combination therapies to circumvent or delay the spread of resistance globally [5].

This article outlines the updated World Health Organization Guidelines for Malaria from 2022, which significantly emphasize the continued reliance on and strategic deployment of artemisinin-based combination therapies. It highlights policy adjustments made in response to evolving resistance patterns and aims to optimize malaria treatment and control efforts worldwide [6].

This study presents a population pharmacokinetic analysis of artemether-lumefantrine in African children suffering from uncomplicated Plasmodium falciparum malaria. Understanding drug exposure in this vulnerable group is crucial for optimizing dosing regimens of artemisinin-based combination therapies to ensure maximal efficacy and prevent the emergence of resistance [7].

This systematic review and meta-analysis evaluates the safety profiles of various artemisinin-based combination therapies in patients with uncomplicated malaria, drawing data from randomized controlled trials. The findings reinforce the generally favorable safety of ACTs, identifying common adverse events while confirming their continued suitability as first-line treatments [8].

This systematic review examines the impact of mass drug administration using dihydroartemisinin-piperaquine, an artemisinin-based combination therapy, on the malaria burden in Cambodia. It highlights the significant role of this intervention in reducing parasite prevalence and incidence, offering valuable insights for malaria elimination strategies in endemic regions [9].

This review discusses the future landscape of artemisinin-based combination therapies in the context of malaria control and eventual elimination. It addresses emerging challenges like drug resistance and highlights strategies for developing new compounds, optimizing existing regimens, and implementing robust surveillance to ensure ACTs remain effective tools against malaria [10].

Description

Artemisinin-based combination therapies (ACTs) represent the frontline defense against uncomplicated Plasmodium falciparum malaria, demonstrating consistent efficacy and safety across a wide spectrum of patient groups. For instance, artemether-lumefantrine has been systematically reviewed and confirmed as both effective and safe for treating pregnant women across all trimesters, highlighting its essential contribution to maternal and child health in regions where malaria is endemic [1]. Parallel findings affirm the sustained effectiveness of ACTs in pediatric populations, solidifying their critical role in malaria control strategies for children, a particularly vulnerable demographic [3]. The broader safety landscape of ACTs is also well-established, with comprehensive systematic reviews and meta-analyses of randomized controlled trials reinforcing their generally favorable safety profiles and confirming their continued suitability as first-line treatments for uncomplicated malaria, despite the identification of some common adverse events [8]. Understanding optimal drug exposure is also crucial, as exemplified by population pharmacokinetic analyses of artemether-lumefantrine in African children, which are vital for tailoring dosing regimens to ensure maximal efficacy and preempt the emergence of resistance in this susceptible group [7].

A persistent and growing challenge to malaria control is the emergence and spread of artemisinin resistance. Molecular surveillance efforts are paramount, providing crucial insights into resistance markers for both artemisinin and its partner drugs in Plasmodium falciparum across areas like sub-Saharan Africa. Continuous monitoring is essential to inform and adapt treatment policies, thereby preventing widespread drug failure in highly affected regions [2]. Deepening this understanding, research has focused on the molecular underpinnings of artemisinin resistance, particularly identifying mutations within the Kelch13 propeller domain.

Deciphering these mechanisms is fundamental for the rational design of new antimalarial drugs and for refining existing ACT regimens to delay or circumvent the global dissemination of resistance [5].

In response to these resistance challenges, the landscape of artemisinin-based combination therapies is continuously evolving with significant efforts directed towards the development of novel compounds. Reviews highlight the ongoing pipeline for creating next-generation antimalarials, specifically designed to overcome emerging drug resistance. The strategic focus is on extending the effective lifespan of current ACTs and ensuring a robust arsenal of treatment options remains available against malaria [4]. Looking ahead, the future of ACTs in malaria control and ultimate elimination hinges on addressing these emerging drug resistance challenges, developing new compounds, optimizing existing regimens, and implementing comprehensive surveillance systems to maintain their effectiveness as indispensable tools [10].

Policy and public health interventions play a pivotal role in the global fight against malaria. The World Health Organization's 2022 Guidelines for Malaria strongly emphasize the continued strategic deployment of artemisinin-based combination therapies. These guidelines reflect necessary policy adjustments made in light of evolving resistance patterns, all aimed at optimizing malaria treatment and control efforts globally [6]. Beyond individual patient treatment, public health strategies like mass drug administration (MDA) have shown considerable promise. A systematic review on the impact of MDA with dihydroartemisinin-piperaquine in Cambodia, for instance, demonstrated its significant role in reducing parasite prevalence and incidence. Such findings offer invaluable insights that can inform broader malaria elimination strategies in other endemic regions, reinforcing the multifaceted approach required to tackle this disease [9].

Conclusion

Artemisinin-based combination therapies (ACTs) are the cornerstone of uncomplicated Plasmodium falciparum malaria treatment, demonstrating consistent efficacy and safety across diverse populations. Studies confirm that artemether-lumefantrine is effective and safe for pregnant women across all trimesters, playing a vital role in maternal and child health in malaria-endemic areas [1]. Similarly, ACTs show sustained effectiveness in pediatric populations, underscoring their importance in treating vulnerable children [3]. A systematic review further reinforces the generally favorable safety profiles of various ACTs, confirming their suitability as first-line treatments for uncomplicated malaria, despite identifying common adverse events [8].

However, the efficacy of ACTs is continuously threatened by emerging drug resistance. Molecular surveillance efforts are crucial for monitoring artemisinin and partner drug resistance markers in Plasmodium falciparum, particularly in high-burden regions like sub-Saharan Africa, to inform treatment policies and prevent widespread drug failure [2]. The molecular basis of artemisinin resistance, specifically involving Kelch13 propeller domain mutations, is critical for understanding and designing new antimalarial drugs to circumvent resistance [5]. Given these challenges, significant efforts are underway in the development of novel ACTs, focusing on creating next-generation antimalarials that can overcome existing resistance and extend the lifespan of current therapies [4]. These strategies are essential for the future of malaria control and eventual elimination [10].

Global health organizations, such as the World Health Organization, continue to emphasize the strategic deployment of ACTs in their 2022 guidelines, adapting policies to evolving resistance patterns to optimize treatment worldwide [6]. Furthermore, optimizing dosing regimens through population pharmacokinetic analysis, especially in vulnerable groups like African children, is essential to ensure maximal efficacy and prevent further resistance emergence [7]. Interventions like mass drug administration with ACTs, as seen in Cambodia, have proven effective in reducing malaria burden, offering valuable insights for broader elimination strategies [9]. This collective body of research reinforces ACTs' critical role while highlighting the ongoing need for vigilance against resistance and continuous innovation in antimalarial development.

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Conflict of Interest

None.

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Address for Correspondence: Emanuel, Mesah, Department of Malaria Surveillance and Control Department Ghana Center for Infectious Disease Studies, Accra, Ghana, E-mail: e.mesah@gciorg.gh

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