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HRP2 and HRP3 and the Performance of Diagnostic Tests for Malaria

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Description

As mentioned in the recently published article, currently, there is little evidence to document the true extent of HRP mutations worldwide. In countries where malaria is endemic, it is necessary to evaluate the genetic variability of the HRP2 and HRP3 genes in order to determine which mutations are present in each country with a view to improving the diagnosis and interpretation of the results obtained by Rapid Tests (RDT) and molecular factors, which could reduce the occurrence of false negatives and, in the medium and long term, improve malaria management programs and interventions [1].

As recommended by the WHO, malaria treatment should be based on a diagnosis of the parasite. The use of rapid detection tests is a fundamental part of this strategy as it provides a protein-based diagnosis of the parasite that is complementary to microscopy of adequate quality. The number of diagnostic tests and the scale of their use have increased rapidly in recent years, however, the limitations of comparative studies in the field, as well as the heterogeneous nature of transmission and epidemiological characteristics of malaria have restricted the availability of good quality performance data necessary to make evidence-based decisions and extrapolate the results of field studies to different populations where this disease is a true public health problem [2-4].

In the last decade, different strategies have been used to control malaria, such as the use of mosquito nets with long-lasting insecticidal action, residual fumigation of interior spaces with insecticides and combined treatment based on artemisinin. Efforts have also been made to expand the coverage and implementation of the aforementioned strategies, which is likely to reduce the burden of infection in countries where these tools are established adequately however, this is not possible in endemic countries where poverty is a major factor.

Despite the WHO's recommendations for the diagnosis of malaria infections is confirmed in the laboratory in all cases before starting the treatment, the diagnosis is often based on the clinical symptoms, which for endemic regions can be a confusing factor since several febrile "malaria-like" diseases are present in these areas. It is well described that microscopy is the gold standard of diagnosis as long as its quality is maintained; however, in endemic regions with high indices of poverty, the need for trained personnel, reagents and adequate equipment limits its availability and accessibility. For this reason, rapid diagnostic tests, accurate and accessible are increasingly important and it is necessary to ensure that these are effective, reliable and that they specifically detect the proteins of the majority of Plasmodium species that transmit malaria in humans [1,4].

In recent years, RDT, which detect specific antigens (proteins) Plasmodium in the whole blood of people infected, have emerged as an attractive option to microscopy. Rapid screening tests currently manufactured come in different presentations (test strip, cassette or card) and contain antibodies bound to specific antigens, such as protein rich in histidine 2 (HRP2) (specific for P. falciparum), the specific lactate dehydrogenase Plasmodium species (pLDH) or aldolase (specific of all major Plasmodium species: P. falciparum, P. vivax, P. malariae, P. ovale [5].

For an RDT to be useful for the diagnosis of malaria it must have a high sensitivity for ensure that all malaria infections are detected clinically significant; a high specificity to allow surveillance of the low prevalence of malaria and high stability, to allow its transport and conservation in environmental conditions in the regions in which malaria is endemic. Many publications on RDT show high variability in performance, probably due to inadequate quality of improper manufacture, storage and handling, poor preparation and interpretation, and sometimes poor methods, analysis and reporting of studies. In general, diagnostic tests either by microscopy or by RDTs up to a level of 200 parasites /µl will reliably detect reliable almost all clinically relevant infections in regions where malaria is endemic. It should also be taken into account that the clinical sensitivity of a RDT to detect malaria is highly dependent on local conditions, including parasite density in the target population, therefore it will vary between populations with different degrees of transmission [5-7].

Finally is important to mention that the performance of HRP2/3-based RDTs may be affected by factors including antigenic variability of the target proteins, persistence of the antigen in the bloodstream after deworming, and parasite density below detection threshold of RDTs. The existence of parasites lacking pfhrp2/3 may affect the accuracy of RDT in a broader range of malaria endemic regions and would have significant [8-12].

Conclusion

Implications for RDT implementation, clinical case management, and malaria control efforts, so it is essential that robust studies be carried out to establish the real rate of polymorphisms of these proteins in each region to minimize the false negatives that lead to underdiagnosis of malaria and severe disease and even death in patients who are infected but test negative do not receive antimalarial treatment

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