The WHO's Need to Address Insecticide Resistance in Malaria Vectors

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ABSTRACT

Since 2000, incidence and mortality rates attributable to malaria have declined significantly. However, this decline may be short-lived due to the emergence of insecticide-resistant malaria vectors caused by the overuse of indoor residual spraying (IRS) and insecticide treated nets (ITNs). This policy paper will discuss the emergence, causes, and implications of vector resistance and will propose solutions to prevent a future public health crisis.

RÉSUMÉ

Depuis 2000, l'incidence et les taux de mortalité attribuables au paludisme ont diminué significativement. Toutefois, ce déclin risque d'être de courte durée en raison de l'émergence de vecteurs du paludisme résistants aux insecticides, causée par la surutilisation de la pulvérisation intradomiciliaire (PID) et de moustiquaires imprégnées d'insecticides (MII). Cet article de politique discutera de l'émergence, des causes et des implications de la résistance des vecteurs, et proposera des solutions dans le but de prévenir une éventuelle crise sanitaire.

INTRODUCTION

Malaria has long been a disease that has caused much suffering and death in the developing world. In 2015 alone, there were a total of 214 million cases of malaria, with 438,000 resulting deaths – the majority being children from Sub-Saharan Africa [1]. The economic consequences of malaria have also been significant. As an example, the management of endemic malaria has cost some Sub-Saharan countries approximately US$300 million annually since the year 2000 [1,2]. In addition, estimates from 2010 suggest that malaria has caused a 1.3% decrease in gross domestic product and has accounted for up to 40% of public health expenditure in these countries [1,2]. That being said, current indicators and trends are demonstrating that the worst of the disease may now be behind us. Funding for malaria control, prevention, and treatment has reached US $2.5 billion, resulting in 1.2 billion fewer cases and 6.2 million fewer deaths since 2000, predominantly in Sub-Saharan Africa [1]. These advances have led to a cautious optimism that malaria may one day be brought down to negligible levels. However, the emergence of insecticide-resistant malaria vectors, in part due to policies and recommendations promoting the widespread use of selected insecticides, has threatened these successes. The following policy paper seeks to highlight the shortcomings of the malaria prevention policies enforced by the World Heath Organization (WHO), while providing potential strategies to mitigate the development of resistance and prevent a future public health crisis.

CURRENT APPROACHES AND PITFALLS

Two of the most widely used prevention methods promoted by the WHO include insecticide treated nets (ITNs) and indoor residual spraying (IRS) [1]. ITNs are a primary intervention for effective malaria prevention and control as they act as both a physical and chemical barrier; physically separating humans from vectors and killing vectors via the insecticide coating found on the nets [3,4]. In the case of IRS, insecticide is sprayed on walls and roofs of buildings to kill mosquitoes when they land on such surfaces [3]. Together, ITNs and IRS work to decrease malaria vector density, and in turn lower the potential for human-vector contact. The WHO attributes much of the decline in malaria seen over the past 15 years to the growing use of both interventions [1].

ITNs and IRS both use a limited range of insecticides in their formulations, and are therefore at increased risk for the development of insecticide resistant malaria mosquito vectors resulting from overuse [1,5]. Since 2010, 60 of 78 reporting countries have discovered vector resistance to at least one insecticide type, while 49 reported resistance to two or more insecticide classes [1,5]. Furthermore, resistance has been discovered within all major mosquito vector species in Sub-Saharan Africa and Asia [6-7].

Currently, there are four classes of insecticides available for use in controlling malaria-carrying mosquitoes: organochlorines, organophosphates, carbamates and pyrethroids [8]. However, the WHO has only approved the pyrethroid class of insecticides for use in ITNs, while IRS is mainly pyrethroid-based due to proven effectiveness and cost [8-11]. Unfortunately, the extensive use of pyrethroids has promoted mutations in vectors, specifically affecting voltage-gated channels

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which results in insecticide target site insensitivity [1,8,12-13]. As voltage-gated channels are a conserved target for many other insecticides, cross-resistance among various insecticide classes may be conferred in this manner [8,11,14].

The implications of developing resistance are profound, as evidence suggests that loss of pyrethroid insecticide efficacy would result in a 55% decline in malaria control, resulting in an additional 120,000 deaths annually [11]. As an example, malaria vector resistance has already been implicated in the failure of an IRS vector control program in a community in South Africa [11]. Experts suggest that other control programs may have failed due to resistance, although they have likely gone unreported due to the difficulty of teasing out the causes of such failures [11]. The WHO has acknowledged this problem within their Global Plan for Insecticide Resistance Management (GPIRM) [11]. They have stated that resistance has the potential to become a “major public health problem,” having already reported increased rates of resistance [1-2].

STRATEGIES TO ADDRESS RESISTANCE

Although the implementation of ITN and IRS control measures over the past few decades has been impressive, the concurrent acknowledgement and awareness of the vector resistance is only just starting to affect WHO policy. The GPIRM was an important first step in acknowledging the risk of resistance development, and the potential implications of such a public health crisis. However, it is imperative that this plan be put into action, while additional resources and research be implemented and conducted to stop the development of resistance.

At present, the WHO has proposed a few strategies to control resistance development. In particular, they have highlighted the need to introduce insecticide mixtures which could be applied to both ITNs and IRS, in turn killing more vectors [11]. With regards to controlling resistance due to IRS, the WHO recommends additive spraying of pyrethroid-based insecticide, while non-pyrethroids are to be used on a rotational basis because of cost and availability [1,15]. Unfortunately, the risk associated with increased vector resistance is greater when using IRS in comparison to ITNs, as IRS forces a much greater amount of insecticide to be sprayed into the environment, thereby placing strong selective pressure on mosquito populations [14]. As for ITNs, the WHO has no major recommendations to deter the development of resistance as they remain exclusively pyrethroid-based [1,8]. Inevitably, the insecticide of an ITN becomes ineffective through washing and degradation over time, resulting in less effective bed nets which promotes the development of resistant vectors [16]. Ultimately, recent studies within endemic areas have found the effectiveness of ITNs and IRS in vector killing to be lowered by 80%. This estimate of resistance may be underreported, however, given that this phenomenon has only just begun to emerge in many parts of the world [6,17].

PROPOSED CHANGES

Currently the WHO recommends only the use of the pyrethroid class of insecticides in ITNs [9]. As such, the development of alternative insecticides for use in ITNs would be highly beneficial. Various studies have demonstrated that non-pyrethroid insecticides are equally effective in killing mosquitoes, although not all have been adequately studied as a singular insecticide component for this application [15,18]. Conversely, IRS insecticides are not solely pyrethroid-based, although the majority of IRS use this insecticide due to known effectiveness and lower cost [1]. As such, the WHO should work to support countries in using an IRS insecticide rotation, which employs additional insecticides in combination with pyrethroids, thereby preventing resistance selection pressures in vectors [11]. Furthermore, the WHO should also place more attention and resources on the development of bed nets and sprays that incorporate multiple types of insecticides. A similar therapeutic combination strategy, known as artemisinin combination therapy (ACT), has been successfully applied in the prevention of malarial parasite resistance to anti-malarial treatments [2]. Recently, the WHO approved a combination ITN, which included both a pyrethroid insecticide and piperonyl butoxide (a non-insecticide) as a synergist to promote insecticide activity [19,20]. By expanding research and development into the range of pesticides used in bed nets, resistance associated with extensive use of a single class of pesticides may be avoided.

Presently, ITNs that are available in most of the global south are either conventional or long-lasting insecticide nets (LLIN). LLINs are manufactured to maintain their biological efficacy for a minimum of 3 years or 20 washes, as insecticides are incorporated and bound to the individual fibres of the net [4]. Conversely, conventional ITNs are dipped into an insecticide solution – and thus the insecticide is not built into the net, requiring retreatment a minimum of once per year [4]. As previously mentioned, conventional ITNs begin to demonstrate decreased potency within one year of use, thereby promoting the survival and selection of insecticide resistant mosquitoes [21]. As such, the WHO should continue in their support of LLIN use, but should also actively replace and improve existing conventional ITNs that are being used in households.

In conjunction with these interventions, the WHO would benefit from improving surveillance, monitoring and diagnostic measures to prevent malaria resurgence and the development of resistance. Research has already suggested that resistance rates are underreported, potentially reducing the effectiveness of future interventions [6]. Although the WHO has created a global insecticide resistance database to track trends internationally, the organization has acknowledged that many countries do not carry out adequate monitoring for vector resistance [22]. Furthermore, the timely reporting of monitoring data is an additional concern limiting the utility of such databases [22]. Improvement in assessments of planning, processes, outcome and impact will allow for the measurement of indicators and trends, and will help establish whether goals and targets are being met – thus informing future policy decisions and recommendations, and informing public health actions [23].

CONCLUSION

Malaria incidence and mortality rates have been steadily declining for over a decade throughout malaria endemic countries [1]. However, these successes may be short-lived if the WHO does not significantly increase its efforts to prevent widespread malaria vector resistance to available insecticides. Although the desire to reduce current malaria incidence through extensive use of ITNs and IRS is admirable, the WHO must also recognize that such policies and recommendations may contribute to the resurgence of malaria due to widespread insecticide resistance. Therefore, the WHO should be proactive in ensuring that the reductions seen in malaria incidence and mortality are sustained, preventing a resurgence of malaria through resistance control. The WHO still has time to modify their policies and recommendations, as well as support alternative interventions, research and development against resistance. Otherwise, insecticide resistance in vectors has the potential to become a public health crisis which may erase decades of tremendous success fighting malaria.

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