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THE RISE IN THE MORBIDITY AND THE MORTALITY OF MALARIA IS A GLOBAL THREAT: EVIDENCE FROM MULTIPLE ANTIMALARIAL DRUG RESISTANCE

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Abstract

Antimalarial multidrug resistance is a major global public health problem and the main reason for the erosion of efficacious treatments. The spread of malaria globally has been attributed to emergence of falciparum strains that are insusceptible to antimalarials, which medical experts blamed on the development of monotherapy (single-pill form). This research paper examines the policies of the pharmaceutical industry that account for antimalarial resistance. Further, it focuses on malaria as a threat to global health, and the parasite's increasing resistance to antimalarial drugs. Strategies are also suggested for international collective action for containment of drug resistance to malaria as well as solutions to some of the problems that confront the pharmaceutical industry.

This paper noted that the pharmaceutical companies' policies today promote early resistance to antimalarials, and thus treatment failures. Combination therapy, a new approach to making antimalarial drugs including artemisinin and other antimalarials, is particularly effective in slowing development and the spread of resistance, and reducing the death toll in the endemic areas. This objective is achievable only if it gains adequate support from international organizations such as the World Health Organization (W.H.O.), political leaders around the globe and other stakeholders.

Malaria, an infectious disease, is a global threat and therefore requires a global response and control. An estimated 350 – 500 million clinical cases of malaria occur worldwide, and greater than 90% of them are reported in Africa (Center for Disease Control and Preventive [CDC], 2004). Out of these, at least two million deaths are recorded annually, mostly among children less than 5 years and pregnant women. The rapid spread of the debilitating disease around the world is mainly attributed to Plasmodium falciparum strains that are now resistant to most of the antimalarial drugs that have been developed. At the end of 2004, over 3.2 billion people lived in areas at risk of malaria transmission in more than 107 countries and territories (CDC, 2004). Economists believe that malaria is responsible for a growth penalty of up to 1.3% per year in some endemic countries, such as those in Africa (CDC, 2004). With globalization booming, this disaster can lead to a substantial difference in gross domestic product (GDP) between nations with and without malaria and severely impede the economic growth and productivity of the entire world.

Drug options for treatment of malaria are becoming increasingly difficult and limited as a result of growing falciparum strains becoming resistant to antimalarial drugs. This has become a global problem. Globalization with concomitant international travel increases the risk of countries importing diseases such as malaria, an infectious disease that travels faster and further than ever before. This stems from many factors, but currently health experts blame pharmaceutical companies. The companies' development of antimalarial drugs in a single-pill form, instead of combination therapy, results in early antimalarial drug resistance. The proponents blame drug insusceptibility on the development of substandard and counterfeit drugs by the pharmaceutical companies. On the other hand, the critics attribute drug resistance to inappropriate use or prescription of antimalarials by clinicians to patients. Also, the inability of the medical technologists to identify the species of the plasmodium in cross-infection in endemic regions is a major problem. In addition, the availability of antmalarial drugs from roadside stalls and hawkers who have little or no knowledge of dosage regimens, especially in poor countries where drug regulation is weak, is also a cause of drug resistance.

The rapid spread of antimalarial drug resistance over the past few decades globally has necessitated an increased monitoring of pharmaceutical companies, and for which the W.H.O. has taken the lead. The high morbidity and mortality rate worldwide calls for a new policy to be implemented. Also, the pharmaceutical industry is developing few new malarial drugs, so there is an urgent need to take action to preserve the effectiveness of the available drugs, for example, artemisinin. Furthermore, political leaders and health policy makers in malaria-endemic regions especially in Africa are alarmed over the death toll of the disease; hence the need to find alternative treatments.

Since most malaria-endemic countries are generally poor, pharmaceutical companies have argued that research and development of drugs are very expensive and a risky activity if their investment would not be recouped before the patent period has ended. The public-private partnership collaboration and incentives to boost the pharmaceutical industry are inadequate.

The question this research paper considers is, do the policies of pharmaceutical companies lead to antimalarial drug resistance? With booming globalization, antimalarial drug resistance is a major public health challenge and the principal reason for treatment options to avert morbidity and mortality worldwide. This paper will therefore focus on the policies of pharmaceutical companies to address the following:

1. Malaria as a global threat.
2. Why does the parasite become resistant to antimalarial drugs?
3. What are some of the problems that confront the pharmaceutical industry?
4. Mechanisms for containment of antimalarial resistance.
5. How can these problems be addressed?

Malaria as a Global Threat

In malaria-endemic regions globally, the disease has become difficult to combat because the parasite developed resistance to chloroquine, the most common and cheapest antimalarial drug. This has become a global threat because drug resistance promotes transmission of malaria to new areas, as well as to regions where the disease has been eradicated. According to Smolinski, Hamburg and Lederberg (2003), malaria cases diagnosed in the United States and its territories were imported from Africa, Asia and the Americas and a similar trend occurs in Western Europe (p. 31). Spielman et al, (2002) noted, “Malaria can impose a substantial economic burden on firms operating in endemic regions due to direct health care costs as well as opportunity costs due to loss of productivity” (p. 14). According to them, malarious areas of the globe are attractive for international travel and commerce due to the following: oil and gas, mining resources, unique agriculture products, tourism and cheap and abundant labor, etc.

Malaria imposes heavy burdens on the establishment of industry in the poor Third World countries. And the school of thought that economic globalization is the solution to poverty failed in some areas of the world due to infectious malaria.

Why Does the Parasite Become Resistant to Antimalarial Drugs?

According to the laws of Darwinian evolution, antimalarial drug use creates a selection pressure on microorganisms (parasites) by which weak ones are killed, but stronger ones might adapt and survive. It means that after sometime antimalarial resistance is inevitable as the parasites mutate and adapt. However, antimalarial resistance can be delayed with appropriate drug strategy. White (1999) has explained, “Antimalarial drug resistance usually arises when the arising mutant parasites are selected by antimalarial drug concentrations that are not sufficient to reduce the susceptible population, but less inhibit or do not inhibit multiplication of the parasites" (p. 739).

The pharmaceutical companies developed many antimalarial drugs in single-pill form that are effective to kill all stages of the parasites in the blood, and these are less expensive compare to combination therapy. Indeed, single-pill kills the parasite and cheaper, yet a drug developed in "monotherapy encourages resistance, " said Dr. Kochi, the chief of the World Health Organization's global malaria program, McNeil Jr., 2006a, para. 17). Consequently, Dr Kochi stopped 18 pharmaceutical companies from selling artemisinin in single-pill form.

The antimalarial drug, chloroquine was the first ever known drug to lose its prophylactic and therapeutic armamentarium, and it rapidly spread to other regions of the world. In the words of John and Petri Jr. (2006), "resistance to chloroquine often is associated with resistance to other antimalarials," which leads to multidrug resistance (p. 100). In order for antimalarials to remain effective long enough we must contain resistance, so Dr. Kochi asked the pharmaceutical companies to make drugs in combination form (McNeil Jr., 2006a). This is not in the interest of the pharmaceutical companies because of the cost involved. For instance when drug companies were to standardize TB drugs for patients for 6 months worth of pills, tuberculosis hospital and makers of BCG vaccine were "very unhappy" (McNeil Jr., 2006a).

Reidenberg and Conner (2001) cited studies showing that many pharmaceutical companies developed substandard and counterfeit drugs intentionally "to deceive the sick and profit them" (p. 4). Spielman et al, (2002) reported, "Diverse substandard and counterfeit drugs have been aggressively infused into the market of Africa," because most of these developing nations "lack the infrastructure required for quality assurance of imported drugs" (p. 14). Reidenberg and Conner define a substandard drug product as one that does not meet the official specifications for what it is claimed to be (p. 4). These imitation drugs are the ones which parasites quickly develop resistance to. Reidenberg and Conner (2002) cited examples of substandard and counterfeit medicine as follows: studies conducted on chloroquine efficacy revealed that some tablets had less than 50% labeled chloroquine. In like manner, a W.H.O. study on quality of drugs in Cameroon, Madagascar and Chad found that "12 of 157 major antibiotics formulations contained none of the labeled antibiotic." Likewise, in Australia 41 companies were charged with 577 crimes involving counterfeit drugs over a period of 5 years (1992 – 1997), and out these 34 were convicted of crime during the time" (pp. 5, 6, 8).

The rate of development of antimalarial resistance is accelerated by the use and misuse of antimalarials. White (1999) reported drug resistance could be induced if patients are inadequately treated for malaria infections. He also pointed out that resistance occurs with insufficient medication "as a result of inappropriate prescribing, poor compliance or, occasionally, because of unusual pharmacokinetic properties of the drug" (p. 745). In many countries, other factors responsible for resistance are self-medication without laboratory diagnosis, over-the-counter prescribing and drugs sold in roadside stalls with no knowledge of dosage regimens.

What Are Some of the Problems that Confront Pharmaceutical Companies?

The pharmaceutical companies have not done much to develop malaria drugs. What they have done is not enough, for numerous economic issues complicate efforts in drug development, production and deployment. The pharmaceutical industry argues that to research and develop antimalarial drugs requires substantial capital and time. Today, for example, as Smolinski et al. (2003) have explained, the cost to devise a new drug or vaccine is about $500 million, which is only the cost for "discovery". In addition to charges for "development and clinical evaluation," the total cost will be about $1 billion (p. 187). Smolinski et al have further noted that there is no assurance that the antimalarial drug "will remain effective" until the company recoups the investment before the "patent has ended" (p. 191). Similarly, researchers Trouiller et al (2002) pointed out that lack of research and development into diseases of the poor (such as malaria) is justified by the high price of new chemical entities.

As Martin (2006) has stated, “Research and development for diseases in the poorest countries is sorely lacking and innovative mechanisms to provide incentives for the pharmaceutical industry to develop drugs which are in the global public interest.” He said public-private partnerships have made an effort to boost the industry, but are still inadequate (para. 2). In contrast, Trouiller et al (2002) explained, “Developed countries offer viable market incentives for research and development through individual purchasing power and purchasing through government-run health insurance programs,” whereas developing countries lack such incentives. They provide the following statistics: “In Europe, these mechanisms cover two-thirds of drug cost for 80 – 100% of the population as opposed to 35% in Latin America and less than 8% in Africa” (para. 14).

Fidler (n.d.) reported that pharmaceutical companies “fear that their research and development (R&D) efforts can be undermined by loss of intellectual property right.” He explained that the insecurity patent rights “deters pharmaceutical companies from R&D activities on new drugs” (p. 8). According to Fidler (n.d.), “While the World Trade Organization (WTO) Agreement on Trade-Related Aspect of Intellectual Property Rights offers pharmaceutical companies better international legal rules on patent protection, the loss of patented agents remain a concern” (p. 8).

Mechanisms for Containment of Antimalarial Resistance

As McNeil Jr. (2006a) has noted, “The war on malaria - in theory more winnable than the war on AIDS because a cure exists – is instead being lost, Dr. Kochi says” (para. 11). McNeil Jr. further explained that Dr. Kochi said after the chloroquine efficacy was lost the pharmaceutical companies began to develop artemisinin, the only effective antimalarial in single-pill form. He said if artemisinin were also lost, it would take another 10 or more years to discover a good drug. McNeil Jr. (2006b) also reported that Dr.

Kochi then asked 18 pharmaceutical companies to make artemisinin in combination with other antimalarials, because "combination therapy not only attacks a disease more effectively, but slows the emergence of microbes resistant to drugs" (McNeil Jr., 2006a, para 5). White (1999) also pointed out that "the concept of resistance" is inevitable but it can be delayed by the use of combinations in treatment. White (1999) has noted this was effectively applied in treatment of TB, cancers and HIV infection and better results achieved. White further explained the concept of combination using artemisinin and its derivatives with other antimalarials, such as mefloquine, yielded good results. Similarly, researchers Price et al have explained, "It accelerated recoveries, increased cure rates, reduced transmissibility and appears also to have delayed the development of resistance and reduced the incidence of disease" (as cited in White, 1999, p. 746).

Smith and Coast (2002) wrote that since antimalarial resistance cannot be completely eliminated, then the aim is to contain resistance. They explained that containment of resistance reduced morbidity and mortality and further spread of resistance to the drug. Smith and Coast further said to achieve the aim of antimalarial resistance we have to tackle it efficiently by international collective action rather than by nations acting individually. The following are global collective strategies: "Surveillance of antimalarial resistance and the tracking of antimlarial consumption; use of mechanisms that encourage research and development of new antimalarials and alternative treatments; and adoption of measures ensuring appropriate and rational use of existing antimalarials" (Smith & Coast, 2002).

How Can These Problems be Addressed?

One of the major factors contributing to the spread and reemergence of malaria is globalization. People globalize for a number of reasons, including international travel and commerce, economic necessity, conflicts, tourism, and natural disasters. However, most of these factors only affect the poor, many of whom live in or near malarious areas. Today, the situation is different;

malaria is a serious global threat and a decline in its control would make it pandemic.

Identifying and understanding the influence of globalization can improve prevention measures and malaria control programs begun by W.H.O. In this regard, it is paramount to find in-depth global solutions, involving international, national and regional collective action. Smith and Coast (2002) noted, "Transmission can only occur once resistance has emerged," therefore we have to prevent emergence of antimalarial resistance. This is the rationale behind the W.H.O.'s strategy to ask the pharmaceutical companies to develop combination therapy in avoidance of drug resistance. Nevertheless, this is achievable only if other hurdles and obstacles are overcome, such as providing the pharmaceutical companies with patent incentives for innovation. But, the W.H.O. has little say over the research agenda. Additional support from charities, foundations, and philanthropic institutions would be critical to its success.

The global collective action against antimalarial resistance with good policies and regulations for the pharmaceutical industry without the strong support from the government and political leaders will be ineffective. For example, McNeil Jr. (2006a) reported that Republican Senator Tom Coburn said, "A million people are going to die this year. What's more important, having a politically correct strategy or a public health strategy that works?" (para. 32). Senator Coburn supports Dr. Kochi's policies to combat malaria. In addition, he reiterates the importance of using tax monies on drugs and nets rather than consultants.

If the mechanisms and protocols put in place to standardize antimalarial drugs are followed by the pharmaceutical industry, next is to delay the efficacy of the drugs. These issues rest on the medical professionals, patients and the drug retailers. These groups should also adhere to policies and regulations laid down by the W.H.O. that encourage more rational and appropriate use of the drugs. In all, it should be complete with regular health education.

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