Prudent use can make artemisinins sustainable

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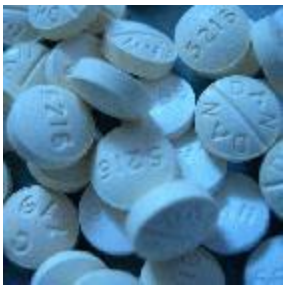

Since its introduction in the 1950s, chloroquine has been the mainstay of malaria treatment worldwide. Costing only a few cents a dose, its fever-fighting qualities have also been valuable for unrelated illnesses.

Over time, malaria parasites have become resistant to the drug, and this resistance has been amplified by widespread use. Now, except for pockets of South Asia and West Africa, the drug is largely ineffective against *Plasmodium falciparum* — the parasite that causes severe malaria.

Quinine: chloroquine, which is derived from this plant is becoming increasingly ineffective against malaria

Photo Credit (Wikipedia)

Many countries have turned to another drug, sulfadoxine-pyrimethamine, but malaria parasites have rapidly become resistant to this too. Mutant genes that enable the malaria parasites to resist sulfadoxine-pyrimethamine were first reported in the 1980s in South-East Asia, and are now widespread in many parts of the world.

This resistance may have arisen because the drug remains in the body for a long time after treatment. The longer a drug stays in the body, the more chance there is that parasites will become resistant to it. This is because the drug gradually kills off all except for resistant parasites. If a high proportion of parasites are drug-resistant, there is a good chance that those parasites will pass on their resistance genes to their offspring.

As malaria epidemics raged through many poor countries — seemingly unstoppable — new hope came in the 1990s in the form of a new class of drugs derived from *Artemesia annua* (the sweet wormwood plant). The malaria parasite is not yet resistant to these highly effective drugs, and public health agencies worldwide, especially the World Health Organization (WHO), have been championing their use.

But, despite their promise, artemisinins need to be used prudently to ensure that they can be used to treat malaria for decades to come.

Using artemisinin in combination

Practitioners of traditional Chinese medicine have used artemisinin for centuries to treat malaria. Since its adaptation to Western medicine, combinations of artemisinin with other drugs have proven extremely effective in treating the disease. However, if malaria parasites were to become resistant to these artemisinin, it would have devastating effects on tackling malaria epidemics.

To make this less likely to happen, the WHO says artemisinin should be used in combination with an antimalarial drug that works in an unrelated way.

The idea behind this recommendation is that a single genetic mutation in a malaria parasite could make it resistant to either component of the treatment, but not both.

But, because of the high cost of artemisinin combination therapies (ACTs), these guidelines are not always followed. Artemisinin is still sold on its own in many countries (this was this official treatment policy in Vietnam during the 1990s), and could compromise the effectiveness of the drug's use globally.

Artemisia annua

Photo Credit (Lawrence Berkley National Laboratory)

Subsidising treatment

Last year, a panel of economists and public health professionals, set up by the US-based Institute of Medicine, said the use of artemisinin on its own could only be discouraged through a combination of official policy and economic incentives.

In their report, the panel called for a globally administered subsidy for ACTs. They recommended that combination therapies be sold to both governments and private wholesalers at the same price as artemisinin alone — about US$0.10 per treatment course. Globally, this would cost donors and development agencies US$150-200 million each year.

As the number of malaria cases should fall the more ACTs are used, the cost of the subsidy should also decrease over time.

The panel also recommended introducing ACTs immediately, rather than first using sulfadoxine-pyrimethamine and then moving to ACTs.

There were two reasons for this. First, introducing sulfadoxine-pyrimethamine, to which resistance would be likely to emerge in a few years, would result in disease and deaths that could be averted by using ACTs straight away.

Second, the continued use of artemisinin on its own, or alongside sulfadoxine-pyrimethamine, would greatly speed up resistance to artemisinin combinations when they were eventually introduced.

Preventing resistance

Researchers have used economic and mathematical models to assess whether a large subsidy for ACTs would increase their use enough to accelerate the emergence of resistance to the combination.

In other words, could the benefits of subsidies be outweighed by expedited resistance to ACTs?

The answer turns out to be 'no'. The researchers say subsidies are likely to prolong the life of artemisinin and the drugs it is combined with (by discouraging use of artemisinin on its own) even if overall ACT use were to increase significantly in response to the subsidy. But crucially, this would happen only if subsidies were introduced without delay.

A delay would permit continued use of artemisinin or another drug on its own, which could lead to the emergence of low-level resistance. This resistance would then be magnified with the introduction of a full subsidy program.

Subsidising a single artemisinin-based combination throughout the world could result in much faster emergence of resistance than if two or three different combinations were used.

The reason is probability. Using just one combination worldwide gives the malaria parasite more chance to become resistant to that combination.

Using different combinations, preferably in the same country, but at least in the same region, reduces the probability of resistance.

If, in theory, we were able to treat every single malaria patient with a completely unique drug or combination, the likelihood of resistance developing to each of these drugs would be extremely small.

Sustainable treatment for the future

Artemisinin drugs offer great hope. The effectiveness of antimalarial drugs is a global public good, and particularly valuable to malaria-ridden regions that are also the poorest in the world.

Already, about a dozen countries in sub-Saharan Africa and South-East Asia have adopted ACTs as the first-line treatment for malaria. But inappropriate drug use in neighboring countries reduces the incentive of any country to deploy drug regimens that could be rapidly undermined by resistance originating outside their borders. Therefore, globally coordinated action is key to protect the effectiveness of these drugs.

If we are smart in how we use ACTs, there is a real promise of achieving a sustainable malaria treatment strategy for the 21st century.

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Read more about this topic in the SciDev.Net policy brief 'Treating malaria with artemisinin combinations: challenges for policymakers'

Further reading

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