

A conversation with Malaria Consortium, January 19, 2017

Participants

- Dr. Ebenezer Baba – Africa Technical Director, Malaria Consortium
- Madeleine Marasciulo – Case Management Specialist, Malaria Consortium
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Note: These notes were compiled by GiveWell and give an overview of the major points made by Dr. Baba and Ms. Marasciulo.

Summary

GiveWell spoke with Dr. Baba and Ms. Marasciulo of Malaria Consortium about Malaria Consortium's injectable artesunate programs. Conversation topics included Malaria Consortium's past work to increase access to and proper use of injectable artesunate to treat severe malaria (particularly as part of the Improving Severe Malaria Outcomes (ISMO) project) and how Malaria Consortium might use additional resources to expand its injectable artesunate work.

Facilitating the adoption of injectable artesunate treatment

When the World Health Organization (WHO)'s guidelines changed in 2012 to recommend injectable artesunate for severe malaria treatment, Malaria Consortium worked to increase the supply of artesunate (which was inadequate in many places) and build the capacity of health workers to administer it. Malaria Consortium also worked on knowledge management and evidence creation aimed at educating health workers about the benefits of the practice.

At a programmatic level, Malaria Consortium worked with in-country supply chains on the pre-qualification process for injectable artesunate and on periodic quantification processes to ensure that sufficient supplies were provided.

Comparison of artesunate and quinine

Quinine was the primary drug used for the management of severe malaria for many years, but it requires three daily doses, each dose administered by slow infusion over a period of four hours. Patients given quinine can experience major side effects including auditory and cardiac problems. Quinine also affects the insulin mechanisms within the body and increases the risk of high blood sugar, a major problem during severe malaria, especially among pregnant women and young children. Intramuscular injections of quinine have been associated with abscess formation and nerve damage.

Artesunate was recommended as the preferred treatment for adults with severe malaria by WHO in 2006. In March 2011, following a *Cochrane Infectious Disease Group Systematic Review*, results from the SEAQUAMAT (which studied mainly Asian adults) and AQUAMAT (which studied African children) studies were published in the *Lancet*. WHO now recommends injectable artesunate, either by the intravenous

or intramuscular route, as the preferred treatment of severe *falciparum* malaria in adults and children.

Injectable artesunate appears particularly effective if patients are treated early and have access to other hospital support systems such as oxygen and intravenous fluids. Artesunate also has a good safety record, with fewer side effects than quinine. However, artesunate is (1) more expensive than quinine and (2) more difficult to prepare and administer, and so requires intensive practical training and supervision. Artesunate comes as a powder that needs to be reconstituted with 5% sodium bicarbonate for two minutes and then diluted with normal saline; determining the proper amounts of these to use requires special training, repeated practice, and a calculator. The correct amount of saline also depends on the patient's weight, and lower-level health facilities do not always have a scale.

Key remaining issues

While artesunate is increasingly available, ensuring that it is used properly and that severe malaria patients receive quality care remain important issues.

Individuals with severe malaria often arrive at health centers exhibiting complications from malaria, and health center procedures often start with triage and management of these complications. Malaria Consortium works to help improve support structures in health facilities to diagnose malaria early with use of rapid diagnostic tests (RDTs), before the most serious symptoms have developed, and ensure prompt referral (especially of children and pregnant women).

There is also room to improve monitoring of health worker capacity and compliance with guidelines (e.g., whether artesunate is administered correctly, whether patients receive follow-up artemisinin-based combination therapies once they can tolerate oral medication, etc.).

There are some open questions about how to best treat severe malaria; for instance, it's not known how effective intramuscular (IM) artesunate is as a pre-referral treatment or how feasible it is for health workers in first-level health facilities to use.

Funding

Malaria Consortium is not sure how much funding for artesunate there is currently. Countries may be relying on funding from the President's Malaria Initiative or other sources such as the Global Fund to purchase artesunate.

The Improving Severe Malaria Outcomes (ISMO) project

ISMO is a multi-country program funded by UNITAID aimed to strengthen the market for severe malaria treatment through catalytic supply and demand management initiatives to increase the availability and adoption of injectable artesunate for malaria treatment. The targeted outcome of the project was to create a stable and sustainable market for quality assured injectable artesunate with two or more suppliers.

The project was led by Medicines for Malaria Venture in collaboration with Malaria Consortium and the Clinton Health Access Initiative. The three-year program covered six countries and worked with various local partners and national malaria programs. Funding for Malaria Consortium's portion was roughly \$4 million.

Malaria Consortium was responsible for implementation in Ethiopia, Nigeria, and Uganda, working to introduce injectable artesunate as a first-line treatment for severe malaria, update national treatment guidelines, and establish reliable capacity in doctors and middle- to senior-level health staff responsible for severe malaria management. It focused on care at the referral level, where most individuals with severe malaria are treated, and was largely limited to areas with facilities that had the capacity for severe malaria management.

Malaria Consortium focused on adapting guidelines, providing training, and supporting quality assurance measures to ensure commodities reached their end points in good condition.

Malaria Consortium monitored outcomes by establishing baselines in health facilities and then monitoring trends in artesunate use and incidence of severe malaria cases.

Potential for Malaria Consortium to expand its program

Malaria Consortium is unsure which countries, other than the countries involved in the ISMO project, have received training on artesunate treatment. Some country-level analyses have shown a continuing gap in artesunate use. There might be an opportunity for Malaria Consortium to expand the kind of capacity building work that it did as part of ISMO.

How Malaria Consortium might use additional resources

With additional resources to support its injectable artesunate programs, Malaria Consortium roughly estimates it might direct about:

- 40% of its efforts to improving referral and access to treatment
- 30% to improving quality of care
- 20% to ensuring access to commodities (e.g. sufficient drug stockpiles)

Improving referral and access to treatment

Patients with severe malaria typically have very serious symptoms that require intensive care which cannot be effectively managed at lower-level health facilities. However, in many cases, the nearest higher-level health facility is far away, and patients may be too sick to travel. In such cases, "pre-referral" treatment at lower-level facilities involves giving patients a fast-acting drug (such as rectal or intramuscular artesunate) that quickly lowers their parasite levels to temporarily make them well enough to transport to a higher-level facility. The length of time that pre-referral treatment with artesunate allows for a patient to travel depends on a number of factors.

With additional resources, Malaria Consortium might work to:

- Educate community members to be able to identify signs of severe malaria early in order to get sick people (especially children) to health facilities as quickly as possible.
- Test the safety and feasibility of the use of intramuscular artesunate as pre-referral treatment at lower-level health facilities.
- Create sustainable mechanisms for moving patients from lower-level facilities to hospitals and tertiary level facilities. When transportation is unavailable or a patient can't pay for it, the patient may not reach the hospital even with pre-referral care. More funding to improve the availability of transportation from local facilities to the primary point of treatment could be highly beneficial. Large organizations, like USAID and DFID, have not invested much in this.

Malaria Consortium would likely focus on rural areas where the long distance to regional hospitals creates the greatest access challenges. Malaria Consortium estimates that roughly 30%-40% of Nigeria and roughly 50-60% of Niger and Chad consist of rural areas like this that it would consider eligible for such a program.

Malaria Consortium might also try to include other vulnerable groups in its work to increase access to treatment, such as pregnant mothers with malaria. In some countries, there are cultural norms against women leaving the compounds where they live, and these women often cannot access care in a health facility when they most need it.

Improving quality of care

With additional resources, Malaria Consortium might work to improve diagnosis and treatment practices and build health worker capacity.

When treatment guidelines change, health worker behavior often takes time to change to match the new recommendations. Malaria Consortium works to change health worker behavior by educating them about why particular practices are important and providing ongoing mentoring and supervision.

For example, WHO used to recommend treating all fevers as malaria. When rapid diagnostic tests (RDTs) for malaria were developed, the WHO guidelines changed to recommend confirming malaria with an RDT test or microscopy before treatment. However, health workers often would not use an RDT, or would get a negative result but still decide to treat for malaria. Treating non-malaria fevers with antimalarials has contributed to the emergence of drug resistances.

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