

Turning the tide against severe malaria in Africa: where are we today?

As severe malaria continues to claim lives, MMV's Hans Rietveld and Elizabeth Poll discuss the issues and what can be done

The majority of the African children who lose their lives to severe malaria each year live in remote or rural areas far from health facilities. One of the key issues is timely access to life-saving treatment. The malaria parasite multiplies rapidly in the body and if left untreated a case of uncomplicated malaria can quickly become severe and can kill within 24 hours. This is particularly the case in young children that have yet to develop any immunity to the parasite.

Since 2011, based on the results of the landmark studies AQUAMAT¹ and SEAQUAMAT² demonstrating the superiority of injectable artesunate (Inj AS) over injectable quinine (Inj quinine) for the treatment of severe malaria in African and Asian patients respectively, World Health Organization (WHO) guidelines have recommended Inj AS as the preferred medicine for treating this life-threatening condition. MMV supported the manufacturer Guilin Pharma, a Fosun Pharma company, to achieve WHO prequalification for its Inj AS formulation, Artesun[®], in November 2010. This approval represented a critical turning point, making it possible for the first time for donor funds to support procurement of Inj AS as WHO's preferred treatment for severe malaria.

In December 2018 a second Inj AS product, Larinate 60, manufactured by Ipca, received WHO prequalification with support from MMV. Having two WHO prequalified manufacturers helps provide greater assurance of adequate supply of quality product for this lifesaving drug. Figure 1 shows the African countries where Inj AS is registered. However, there are countries which, despite having registered and adopted Inj AS in their treatment guidelines, still continue to use Inj quinine widely. There is no scientific justification for continued use of Inj quinine when Inj AS is available.

Patients presenting with severe malaria need to be treated as quickly as possible with Inj AS, followed by a full oral treatment with an artemisinin combination therapy (ACT) when the patient is sufficiently well. The first point-of-care for many severe malaria patients – particularly from rural areas – is a health-care worker either at the community-level or at a primary care facility. However, most community health posts do not have access to Inj AS nor personnel trained in its administration. As a result, patients need to be referred to higher-level facilities, creating

Hans Rietveld and Elizabeth Poll, Medicines for Malaria Venture



Figure 1: African countries in which WHO-prequalified injectable artesunate is registered

delays in access to critically-needed treatment, which can result in disability or death.

In such cases, the WHO Guidelines for the treatment of malaria³ recommends the use of rectal artesunate (RAS) for pre-referral management of severe malaria. A single dose reduces the risk of death and permanent disability significantly.^{4,5} RAS starts to cure the disease and therefore 'buys time' until Inj AS can be administered. It can literally mean the difference between life and death.⁶ As such, quality-assured RAS is the most powerful intervention for severe malaria since the WHO prequalification of Inj AS.

Despite the WHO recommendation supporting the use of RAS, up until the end of 2016 no quality-assured product existed. With funding from UNITAID and building on the early work of TDR (the WHO-hosted Special Programme for Research and Training in Tropical Diseases) MMV collaborated with two Indian pharmaceutical companies, Cipla and Strides Shasun, to obtain WHO prequalification for their RAS products in 2018. Just ahead of these approvals, in 2017, the product (100 mg RAS) was also added to WHO's Model List of Essential Medicines for children, which serves as an important guide for countries to prioritise medicines for use throughout national health systems, and thereby supports wider use of the medicine.



Figure 2: African countries in which WHO-prequalified rectal artesunate is registered

RAS has been enthusiastically welcomed in a number of African countries; to date 16 countries have granted marketing authorisation for at least one of the WHO prequalified products (see Figure 2). In 2018, an estimated 1.7 million RAS products were ordered by endemic countries – more than double the volume procured in 2017 and most of these orders were for the WHO-prequalified quality-assured RAS. Furthermore, studies have demonstrated that the optimal and most cost-effective way to implement RAS is through Community Healthcare Workers.⁷

With this in mind, in Zambia, the National Malaria Elimination Centre (NMEC) and Ministry of Health together with a consortium of partners including MMV and Transaid established a programme to pilot the use of RAS at community level in one district. The initial pilot project, that ran from 2017 to 2018, reduced severe malaria fatality by 96% (from 8% to 0.25%). The success of the initial pilot was achieved through a combination of effective community engagement, a functioning drug supply chain, implementing an innovative emergency transport system for patients using bicycle ambulances and increased access to key medicines for severe malaria (RAS) and (Inj AS) (see Mervis's story, opposite page). Based on these results, the decision was taken to scale-up use of RAS nationwide. Funding from Grand Challenges Canada, the Government of Canada, MMV and Transaid (December 2018 to May 2020) is enabling scale-up in five districts.

With funding from Unitaid, MMV's work to support improved introduction and scaleup of RAS is now continuing across additional Africa continues. This work is further supported by the Community Access to Rectal Artesunate for Malaria (CARAMAL) project, led by the Clinton Health Access Initiative. The project is focused on three high-burden countries – Democratic Republic of the Congo,

Nigeria and Uganda – and is currently piloting community case management schemes and multicountry observational research to identify the operational- and health system-related factors affecting the introduction of RAS.

MMV is also working with the National Malaria Control Programme in Malawi to conduct an Information, Education and Communication (IEC) intervention study. The goal is to support the continuum of care for severe malaria from the community to the referral health centre through the introduction of a quality IEC toolkit. The study hypothesises that the toolkit will increase early presentation to the Health Surveillance Assistant (HAS, similar to Community Health Worker) for RAS pre-referral intervention, and will improve diagnosis, treatment and referral of danger signs and in turn enhance prompt compliance with referral instructions by caregivers.

In Madagascar, MMV is working with the NMCP to roll out RAS to Community Health Workers through the implementation of a RAS toolkit which has been tailored to meet the needs of the country. The objective of the toolkit is to increase awareness of severe malaria and its danger signs, improve accep-

tance and patient referral, and ultimately decrease severe malaria related morbidity and mortality. The support will initially cover the training of regional malaria officers, district malaria officers, health center chiefs and community health workers in nine regions.

In collaboration with NMCP teams in Uganda, Democratic Republic of Congo (see testimonial) and Liberia, MMV has conducted rapid assessments of severe malaria case management. The findings as well as the real-life stories and testimonials clearly demonstrate that much more progress in the fight against malaria can be achieved if countries are able to make these medicines available where and when needed. In addition, it will be critical that healthcare workers are trained on up-to-date malaria treatment guidelines and have access to training on the administration of RAS and Inj AS.

Based on these myriad in-country RAS implementation experiences, and building on lessons learned from rapid assessments of severe malaria case management conducted in Uganda, DRC and Liberia, in addition to good planning and having a well-functioning health system, the following interventions were found to be critical to the successful adoption and scale-up of RAS:

- Training and equipping health workers
- Sensitising communities
- Adding RAS to integrated Community Case Management programmes
- Strengthening referral systems
- Ensuring high-quality care at referral facilities
- Using robust quantifications and having an effective distribution network

MMV remains committed to working with partners to achieve broad availability of RAS and Inj AS, and to support training and implementation programmes as part of



Mervis's story: surviving severe malaria

Three-year-old Mervis is from Serenje District, Zambia. One evening in 2018, she fell ill and then began to have convulsions – a terrifying situation for any parent. Her mum Priscilla rushed her to the nearest Community Health Volunteer, who had been trained through an MMV-supported project and as such recognised the danger signs of severe malaria. As a result, Mervis received rectal artesunate to help “buy time” for her to be transported to a health facility for the full treatment she needed.

Photo from Transaid

the global mission to reduce mortality from malaria. We believe malaria is a disease that can and must be defeated and we are eager to work in partnership with countries to make this a reality.

References

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