

Increasing uptake of rectal artesunate to buy time against severe malaria

Medicines for Malaria Venture's Pierre Hugo and Elizabeth Poll discuss the steps being taken to increase the use of rectal artesunate as a pre-referral intervention for children with severe malaria

More than 400 000 people still die each year from malaria. The vast majority are African children living 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 exponentially in the body and if left untreated can quickly progress to severe malaria, which can kill within hours. This is particularly the case in young children without sufficient immunity.

The first point-of-care for many severe malaria patients—particularly from rural areas—is a healthcare worker either at the community-level or at a primary care facility. Those presenting with severe malaria should be treated as quickly as possible with injectable artesunate (Inj AS), followed by full oral treatment with an artemisinin combination therapy (ACT) when the patient is sufficiently well; however, most community health workers or community health posts do not have access to Inj AS or personnel trained in its administration. As a result, patients need to be referred to higher-level facilities, creating delays in access to critically-needed treatment, often resulting in disability or death.

In such cases, the World Health Organization (WHO) *Guidelines for the treatment of malaria*¹ recommend 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.^{2,3} RAS starts to cure the disease and therefore 'buys time' until Inj AS can be administered. It can mean the difference between life and death.⁴ As such, RAS is potentially the most important and powerful new intervention for severe malaria since the WHO prequalification of Inj AS.

Developing a quality product

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) Medicines for Malaria Venture (MMV) has been working with two Indian pharmaceutical companies, Cipla and Strides Shasun, to obtain WHO prequalification for their RAS products. Both companies submitted their dossiers to the WHO Prequalification of Medicines Programme in 2015.

In 2016, the Expert Review Panel (ERP) of the Global Fund issued a 12-month authorisation for procurement of Cipla's product. The authorisation allows RAS to be

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procured while awaiting WHO prequalification, and offers a landmark opportunity for donor financing to support broad uptake of this critically-needed medicine. In 2017, the product (100 mg RAS) was then 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.

Supporting correct use

As National Malaria Programmes across Africa begin to introduce RAS in their malaria management strategy, it is important that healthcare providers in remote rural community settings understand how to administer the product. MMV has worked with numerous stakeholders to develop training materials to illustrate, step-by-step, the correct use of RAS.

A key message that health workers must understand is that RAS alone is not an adequate treatment for severe malaria, but rather is an important first step in the continuum of care of severely ill children. RAS helps buy time for patients to be transferred to facilities that can then administer parenteral treatment, followed by an ACT.

With continuous feedback from WHO Global Malaria Programme, Save the Children, International Federation of Red Cross and Red Crescent Societies, Médecins Sans Frontières, President's Malaria Initiative, Clinton Health Access Initiative and Malaria Consortium, MMV worked in collaboration with a research agency to develop user-friendly training materials to support correct use of RAS and highlight the critical importance of referral. Interviews with health workers in Malawi and Senegal were conducted and revised materials incorporating lessons learned were tested daily over two weeks. This iterative process helped ensure that the final training materials will meet the needs of community health workers—the healthcare personnel most likely to administer RAS.

Optimising use

One of the first steps to create expanded access to the ERP-approved RAS product is registration in countries with high severe malaria burdens. MMV is working with partners and funders to ensure that speedy registration occurs in multiple countries, including Nigeria, DRC and Uganda.

Understanding the larger health system context in which RAS will be used—as part of severe malaria case management—is also critical. In one notable example, for several years, the Kenyan NMCP has been conducting bi-annual health facility surveys to measure improvements in the case management of febrile patients,

Administer rectal artesunate and refer

Age
For children between 6 months to less than 6 years old

Danger signs requiring rectal artesunate

If in addition to fever or history of fever, you notice one or more of these danger signs, administer rectal artesunate.

LETHARGY / UNCONSCIOUSNESS **REFUSAL TO FEED**

CONVULSIONS **REPEATED VOMITING**

Step 1: Administer rectal artesunate

Step 2: Refer

After receiving rectal artesunate suppository the child must be referred immediately to the nearest hospital or health care facility where the full required treatment for severe malaria can be provided.

Administer rectal artesunate for severe malaria: 4 steps

- 1 Prepare**
Weigh the child or put on approximate weight.
Check the dosage register to the child's age and weight.
Wash your hands.
Put on a pair of disposable gloves.
- 2 Administer**
Remove the suppository from the wrapper.
Break the suppository.
Insert the suppository into the rectum.
Cover the rectum for 1-2 minutes.
- 3 Refer**
Complete the referral form.
Where to refer?
If you transport.
- 4 Follow up**
Return to the nearest hospital or health care facility where the child will receive a full course of treatment. Rectal artesunate is only the first step of treatment.

en of reproductive age and children under five.

Exploring innovative ways to improve rural access to pre-referral management of severe malaria is another important focus. In July 2017, MMV began working with the Non-Government Organisation Transaid to conduct a pilot project in Serenje District, Central Province, Zambia to address the lack of access to quality severe malaria commodities including RAS. Drawing on the expertise of a Zambian partner Disacare, bicycle ambulances

For the complete set of training material correct administration of rectal artesunate see: <https://www.mmv.org/access/tool-kits/rectal-artesunate-tool-kit>



Bicycle ambulance with community volunteers and Emergency Transport Scheme riders

and to disseminate results via its Outpatient Quality of Care (QOC) report. In 2016, MMV, the Global Fund and the NMCP supported Kenya's MOH to expand the focus of the QOC survey to include inpatient monitoring of severe malaria case management, bringing attention to opportunities to improve outcomes in this area.

In another example within the context of understanding larger health systems, in May 2017 MMV collaborated with the Aga Khan Foundation Canada (AKFC) to conduct qualitative research in the Mopti region of Mali to understand gaps in the management of malaria for women and children under five. In line with WHO policies, the research findings will be used to strengthen malaria prevention and treatment practices in the region, with the goal of reducing malaria mortality among wom-

will also be used to strengthen the rural emergency transport systems in the intervention district while Development Data will be gathering the evidence to demonstrate proof-of-concept. The project ultimately aims to generate an evidence-based sustainable strategy for improving nationwide access to severe malaria commodities.

Conclusion

Prevention is always better than cure, especially when it comes to children and malaria. When prevention fails, timely diagnosis and early treatment with ACTs can save lives. If those precious windows of time are missed and children fall critically ill, severe malaria becomes an acute medical emergency. With each passing hour it becomes increasingly more urgent to take immediate steps to stop the disease in its tracks or to risk the death of a child. RAS is a tool designed for use in such dire circumstances, often in rural settings, when the time to access injectable treatments may be six hours or more. MMV is committed to playing its part to support the access and appropriate use of this life-saving tool and sharing the key learnings from one country to another. We work towards the day when this tool will be available to all those that need it. As part of complete malaria case management, RAS really does buy time to save lives.

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