English Consent Form: Randomized Trial of Aggressive Antipyretics for Malaria

MALAWI site-specific

INTRODUCTION

Your child has malaria and needs admission to the hospital for care. We are seeking your permission for your child to participate in a clinical trial of antipyretics (Panadol and Brufen) for fever reduction. Panadol and Brufen are medications commonly used for treating fevers in children, but usually children with malaria only receive Panadol and they are only given a medication for fever reduction if their fever reaches 38.5ºC or higher.

In previous research we found that children with higher fevers during their acute malarial illness had a greater risk of developing neurologic problems after they recovered from the infection and we know that in other conditions affecting the nervous system, therapies that prevent the patient from becoming febrile result in better neurologic outcomes.

PURPOSE OF THE RESEARCH

This study is therefore designed to determine if there is a reduction in fevers in the children who receive aggressive antipyretic therapy vs. routine care.

PROCEDURES AND STUDY SCHEDULE

If you choose to take part in this study, we are going to randomly assign children to one of two groups, either the 'usual care' group, or the 'aggressive antipyretic therapy' group. In the 'usual care' group, children will get treatment with Panadol if they get a temperature of 38.5ºC or higher, *and* will also get Brufen if the temperature remains high on Panadol alone. In the same 'usual care' group, children will receive inactive medication (placebo) initially and active medication only if their temperature goes above 38.5ºC. In the 'aggressive antipyretic therapy' group, children will get Panadol and Brufen immediately and then every 6 hours for 72 hours even if they do not have a temperature above 38.5ºC. We do not know if giving Panadol and Brufen immediately and together will result in less fevers. In both groups children who have a fever will receive active medication to reduce that fever. Some will receive the active medication before a fever reaches 38.5, if their temperature goes over 38.5 despite the active medication they will be given inactive medication (placebo) and a fan. We do not know if giving Panadol and Brufen immediately and together will result in less fevers. It is important to remember that all children who have a fever will receive treatment for their fever.

If you agree to allow your child to participate in this research study, your child will be assigned by chance (like flipping a coin) to receive aggressive antipyretics vs. 'usual care'. Your child will have an equal chance of being in either of the two groups. Neither you nor your child's doctor will know which group he or she is assigned to.

The medications are both in liquid form which will be given by mouth every 6 hours for the next 3 days. If your child is unable to swallow the medication, we will place a tube in your child's nose going into the stomach and the medication will be delivered through that tube until your child wakes up. Once your child is awake and able to take the medication, we will remove this tube.

All children in this study will have a small sticker placed in their armpit to measure their temperature for 3 days. All children in this study will have blood taken every 6 hours by finger pricks to check the parasite count, glucose and kidney function. The total volume of blood taken over the full course of the study will be less than 2 mls. If your child is confused or sleepy from the malaria and cannot be easily awakened, we will also place some metal discs on the head attached with glue to record your child's brain activity. This is to measure continuous electroencephalogram (EEG) activity, or the electrical activity in the brain. The EEG will allow us to know if your child is having any seizures that we cannot see by just looking at the child. Seizures can happen in the brain and not be apparent by just looking.

POTENTIAL RISKS

- If your child is in this study and they are unable to swallow, then they will have a nasogastric tube (NGT) placed so that the study medications can be given to them. If your child is not in the study, no NGT will be placed today. This tube may cause nasal or throat irritation or bleeding.

- In some cases, the NGT might be misplaced. This is very rare since the members of staff who insert the tubes are well trained. In cases where this happens, it could result in the medication going into the child's lungs and would require removal of the tube and further treatment, like suction.

- As part of the research, when your child is pricked for malaria parasite counts, we will take an extra small tube of blood (*hold up capillary tube*).This may cause minimal discomfort (pain).

- Malaria can cause problems with bleeding, poor liver function and poor kidney function. It is possible that the medications given in this clinical trial could worsen the problems caused by malaria. The Brufen could cause your child to have problems with bleeding. We will monitor for this closely and if we see any signs of problems with bleeding, we will stop the study medications. The Panadol and Brufen are generally safe medications but stomach irritation and stomach pain can result from taking these medications. These medications might also worsen problems the malaria causes to your child's liver and kidneys. We will monitor for signs that the medications are causing problems and stop treatment if needed. If your child experiences any adverse effects from the drug, we will provide care and treatment plus any other assistance as may be deemed necessary.

- The glue and metal discs for the EEG are not harmful although the glue has a strong smell and some people get mild skin irritation where the glue and electrodes are placed.

POTENTIAL BENEFITS

- The EEGs may alert us to seizures we cannot detect otherwise and will allow us to treat these seizures, which might otherwise go without treatment possibly resulting in brain injury.

- If your child is randomized to aggressive antipyretics, your child may be more comfortable during this admission since in addition to fever reduction, these medications also treat pain (e.g. the headache usually associated with malaria).

YOUR RIGHTS

- Your child's participation in this research study is entirely voluntary.

- If you do not wish for your child to participate in this clinical trial, your child will continue to be cared for here. No care will be withheld. Your child's fevers will be treated with the 'usual care' detailed above. This will include treatment with Panadol, additional treatment with Brufen if Panadol does not lower the fever

- If you agree to your child's participation now, but later decide you do not wish for your child to be part of our study, you may withdraw the child from participation at any time.

- On the side of investigators, there are no foreseen circumstances under which the principal investigator may terminate a subject's participation in the study. While your child is participating in this study, we will provide you immediately with any new findings about this study or the antipyretic medications.

PRIVACY AND CONFIDENTIALITY

- Conversations you or your child may have with any of the medical personnel will remain confidential.
- To limit the risk to your privacy, when we record data in the research file, a study ID and not your child's name will be recorded
- The information about your child from this study will be kept at Queen Elizabeth Central Hospital (QECH) or University Teaching Hospital (UTH) in locked study offices.
- For all study purposes, your child will be assigned a study identifier and information sent outside the hospital will include this identifier, not your child's name.
- The study records will be kept for a minimum of three years following the completion of the study.
- People who have access to this information include:
    - Research staff who will be reviewing your child's medical records and recording information important for the study in a research file.
    - Independent Study Monitors
    - The Research Ethics Committees at this hospital and at the University of Rochester, the Malawi Pharmacy, Medicines & Poisons Board and the US National Institutes of Health.
- By signing this consent form you are agreeing that these entities can have access to your child's records
- Your privacy will be protected to the maximum extent allowable by law.

COSTS AND COMPENSATION

- There are no anticipated costs to be incurred by individual as a direct result from participating in this study.
- If you agree for your child to be in this study, we will provide you and your child with transportation home or funds for transportation home.

CONTACT INFORMATION

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

If you have any questions about your child's participation as a subject in human research or need to contact someone about a research-related injury, you may contact the investigators in charge. Or, you may contact the Chair for the Research and Ethics Committee:

Dr. Gretchen Birbeck 0995-008069 Dr. Karl Seydel 0999-452989 Dr. Mac Mallewa 0995-835083 QECH, Blantyre Malaria Project PO Box 30096 Blantyre #3	College of Medicine Research and Ethics Committee Private Bag 360, Chichiri Blantyre 3, Malawi Tele 01874377 Fax 01874740 Email: comrec@medcol.mw

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DOCUMENTATION OF INFORMED CONSENT

"I voluntarily agree for this child to participate in this study"

Name of the child _____

Name of guardian_____

Guardian's relationship to child _____

_____ Date _____ (dd/MMM/yyyy)

Parent/guardian signature or thumbprint

I affirm that I have witnessed the above explanation to the child's guardian, and that the guardian has confirmed that s/he understands and has given consent to the child's enrollment in this study.

Name of Witness_____

Signature of Witness_____Date_____(dd/MMM/yyyy)

Name of Nurse/Doctor Obtaining Consent _____

Signature of Nurse/Doctor_____ Date _____(dd/MMM/yyyy)

STUDY ID Assigned: FCS_____

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Please accept a copy of this form to keep.