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Newsletter of Cochrane Nigeria, Calabar Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital

Rapid Diagnostic Tests For Malaria – What The Evidence Says

Malaria is an important disease globally with an estimated 216 million cases and 655, 000 deaths occurring annually[1]. Most cases of malaria occur in sub-Saharan Africa with under-fives, pregnant women and people living with HIV/AIDS being the most vulnerable to the disease.

The main clinical feature of malaria is fever which is also present in diseases like typhoid, pneumonia, tuberculosis and HIV that are equally prevalent in the region. In view of the similarity in presentation of malaria with other infectious diseases, there is need for confirmatory diagnosis prior to treatment. Light microscopy is the gold standard for malaria diagnosis. Most cases of malaria morbidity and mortality occur in rural communities where facilities for standard microscopy are not available. In these areas, people with fever are presumptively treated for malaria without laboratory confirmation. Presumptive treatment can lead to over-diagnosis of malaria, indiscriminate use of antimalarials, development of drug resistance and increased risk of mortality from malaria. The artemisinin-based combination drugs are currently the most effective drugs for the treatment of malaria, and there is need to avoid development of resistance to these drugs. This is one of the reasons why the World Health Organization (WHO) recommends diagnosis of malaria confirmed by Rapid Diagnostic Tests (RDT) in places where standard microscopy is not feasible.[2]

RDTs are point of care-tests for the diagnosis of specific diseases. They are designed to provide immediate results which could either confirm or exclude a particular diagnosis and ensure prompt and accurate treatment. Rapid diagnostic tests are particularly useful in low resource settings as they are reasonably priced, simple to use and do not require electric power for operation. They are, therefore, an affordable and effective alternative to standard microscopy.

Rapid diagnostic tests for malaria detect parasite-specific antigens in a drop of fresh blood through lateral flow immunochromatography.[3] These antigens are produced by the malaria parasites and are present in the blood of infected or recently infected people.[4] Most RDTs use histidine rich protein-2 (HRP-2) or plasmodium lactate dehydrogenase (pLDH) to detect malaria parasites. Histidine rich protein-2 RDTs detect *Plasmodium falciparum (P. falciparum)* and are used mainly in sub-Saharan Africa where *P. falciparum,* the species responsible for the severe form of malaria, is most prevalent. Plasmodium lactate dehydrogenase can be used to detect *P. Falciparum* or *Plasmodium vivax* and mixed infections with *Plasmodium ovale* and *Plasmodium malariae*.

A number of Cochrane Systematic Reviews have been carried out on RDTs for malaria. Abba et al.[5] carried out a review of 74 studies to assess the diagnostic accuracy of RDTs for detecting *falciparum* parasites in people living in endemic areas. They found that although sensitivity and specificity of different RDTs varied, RDTs generally have high sensitivity and specificity and can replace or augment

microscopy in the diagnosis of *P. falciparum* malaria. In addition, they found that HRP-2 based tests were more sensitive but less specific than pLDH tests; the differences were however small.

A Cochrane Review[6] of seven trials, involving 17,505 persons, which compared algorithms incorporating RDTs with algorithms using clinical diagnosis alone, found that RDTs reduced prescribing of antimalarials by up to three-quarters. However, RDT-supported diagnosis had little or no effect on the number of participants who remained unwell four to seven days after treatment. In their review evaluating the effectiveness of home and community based management strategies for treating malaria, Okwundu et al.[7] also found that the use of RDTs in home/community based programmes reduced the over-prescription of antimalarials. RDTs did not have consistent effect on the prescription of antibiotics i.e. some trials showed higher antibiotic prescribing with RDTs while some showed lower prescribing of antibiotics when RDTs were used[6].

Another Cochrane review[8] which was carried out to assess the diagnostic accuracy of RDTs for detecting non-*falciparum* or *P. Vivax* parasitaemia in malaria endemic areas found that RDTs designed to detect *P. vivax* specifically, whether alone or as part of a mixed infection, appeared to be more accurate than older tests designed to distinguish *P. falciparum* malaria from non-falciparum malaria. These tests had a specificity of 99% and sensitivity of 95% i.e. compared to microscopy, these tests would fail to detect about 5% of *P. vivax* cases.

Based on the evidence from research, the use of RDTs should be encouraged as they have been found to be an effective alternative to microscopy, have high sensitivity and specificity, can be used with little training, are affordable and save time compared to microscopy. In addition, RDTs were found to reduce over-prescription of antimalarials which is very important for preventing development of antimalarial drug resistance.

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EVIDENCE AT YOUR FINGERTIPS

(From the Cochrane Library)

TECHNICAL SUMMARY

Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing Cesarean delivery

Background

Caesarean birth is one of the most common surgical procedures performed worldwide. Compared to vaginal birth, Caesarean birth is associated with five times the risk of developing postpartum infections. As the rates of Caesarean births continue to rise, there is a need to seek measures to reduce post partum infections in women undergoing Caesarean birth.

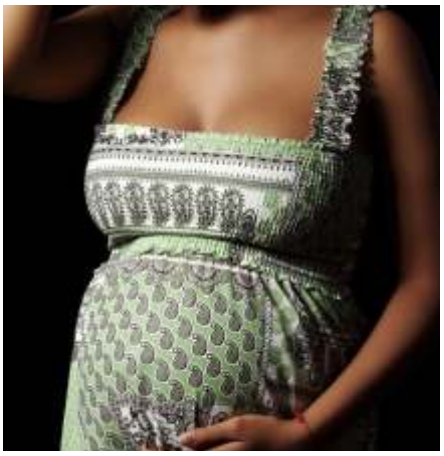
A number of recent studies have evaluated the effect of timing of prophylactic antibiotics on incidence of post partum infectious morbidity. This review seeks to assess the effectiveness of administration of prophylactic antibiotics prior to skin incision compared to administration after clamping of the umbilical cord for prevention of infectious morbidity and to assess neonatal outcomes of the intervention.

Objectives

To assess the differences in infectious morbidity for mother and neonate when prophylactic cesarean antibiotics are administered preoperatively versus after neonatal cord clamping.

Main Results

- Ten studies involving 5041 women enrolled for the primary outcome of composite infectious morbidity were included in the study.
- Six trials were conducted in developed countries and four in developing countries.
- The intervention was antibiotic administered intravenously before the incision versus after the clamping of the neonatal cord. Cefazolin was the antibiotic administered in 7 trials while ceftriaxone was administered in 3 trials.
- Primary outcomes assessed were composite maternal postpartum infectious morbidity while secondary outcomes were maternal morbidity, maternal postpartum infection, neonatal mortality, and neonatal morbidity.
- Primary Outcomes -Composite morbidity(as defined by trials): Participants who received antibiotics preoperatively showed significant reduction in composite morbidity compared to those that received antibiotics after cord clamping (risk ratio (RR) 0.57; 95% confidence interval (CI) 0.45 to 0.72, 10 trials, 5041 women, high quality evidence).
- Secondary Outcomes – Maternal: There were significant reductions in endomyometritis (RR 0.54; 95%CI 0.36 to 0.79, 10 trials, 5041women, high quality evidence); wound infection (RR 0.59; 95% CI 0.44 to 0.81, 10 trials, 041 women, high quality evidence) and length of hospital stay (mean difference (MD) -0.17; 95% CI - 0.30 to -0.04, two trials, 1342 women) in women who received antibiotics preoperatively compared to those who received antibiotics after cord clamp. There were no clear differences in occurrence of UTI/cystitis/pyelonephritis (RR 1.02; 95% CI 0.65 to 1.59, eight trials, 4001 women, moderate quality evidence); pelvic abscesses (RR 1.00; 95% CI 0.06 to 15.97, one trial, 741 women); respiratory infections (e.g. pneumonia) (RR 2.30; 95% CI 0.34 to 5.45, four trials, 1849 women, low quality evidence) or febrile illness (RR 0.93; 95% CI 0.63 to 1.35, four trials, 2650 women) in women who received antibiotics preoperatively compared to those who received after cord clamp. Maternal death was reported in one study but there was no occurrence.
- Secondary Outcomes – Neonatal: There were no clear differences between the groups for any of the neonatal outcomes: neonatal sepsis (RR 0.76; 95%CI 0.51 to 1.13, five trials, 2907 neonates, moderate quality evidence); neonatal sepsis work up (RR 0.92; 95% CI 0.69 to 1.23, four trials, 1170 neonates); infection with a resistant organism (RR 0.70; 95% CI 0.12 to 4.14, one trial, 379 neonates); infection (other) (RR 0.93; 95% CI 0.52 to 1.64, one trial, 302 neonates); ICU admission (RR 0.91; 95% CI 0.74 to 1.13, six trials, 3708 neonates);ICU length of stay (days) (MD -0.07; 95% CI-2.60 to 2.46, three trials, 1731 neonates, random-effects, Tau² = 4.07; I² = 97%); neonatal antibiotic treatment (RR 0.84; 95% CI 0.12 to 5.68, one trial, 90 neonates); and febrile illness (RR 0.67; 95% CI 0.28 to 1.62, one trial, 953 neonates). No data were available in the trials for neonatal mortality.
- Overall risk of bias for the studies was low.



Conclusion: Prophylactic Cesearean antibiotics administered preoperatively significantly reduced the occurrence of post partum maternal infections compared to administration after cord clamping especially for endomyometritis and wound infection.

There was not enough information on whether intravenous antibiotics administered preoperatively can significantly reduce occurrence of genitourinary infections, pelvic abscess, respiratory infections or febrile illness compared to administration after cord clamping. There were no adverse neonatal outcomes detected however, additional research may provide further insight into adverse effects for neonates.

Mackeen AD, Packard RE, Ota E, Berghella V, Baxter JK. Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing cesarean delivery. Cochrane Database of Systematic Reviews 2014, Issue 12. Art.No.: CD009516. DOI: 10.1002/14651858.CD009516.pub2.

PLAIN LANGUAGE SUMMARIES

Preventing occupational stress in healthcare workers

Background

Healthcare workers suffer from work-related or occupational stress. Often this is because healthcare workers face high expectations and they may not have enough time, skills and social support at work. This can lead to severe distress, burnout or physical illness. In the end, healthcare workers may be unable to provide high quality healthcare services. Stress and burnout can also be costly because affected healthcare workers take sick leave and may even change jobs.

We evaluated how well different ways to prevent healthcare workers' stress or burnout work.

Study characteristics

We included 58 studies that included altogether 7188 participants. Fiftyfour of the included studies were randomised controlled studies and four were non-randomised studies. We categorised the interventions as either cognitive-behavioural training, mental and physical relaxation, or organisational changes.

Key findings and quality of the evidence

Cognitive-behavioural interventions

According to six studies, there was low-quality evidence that cognitive-behavioural training decreased stress with about 13% when compared to no intervention and when measured at follow-up periods ranging from less than a month up to two years. It is unclear how relevant this reduction is for a person with stress. The results were similar when cognitive-behavioural training was combined with relaxation. However, in three studies, stress levels were similar after a cognitive-behavioural training course compared to other training that was not focused on stress management but on the content of care.

Mental and physical relaxation interventions

In 17 studies there was low- to moderate-quality evidence that both mental and physical relaxation led to a reduction of 23% in stress levels compared to no intervention.

Organisational interventions

Organisational interventions were aimed at changing working conditions in 20 studies, improving support or mentoring in six studies, changing content of care in four studies, improving communication skills in one study and improving work schedules in two studies. Shorter or interrupted work schedules reduced stress levels in two studies but there was no clear benefit of any of the other organisational interventions.

Conclusions

We conclude that cognitive-behavioural training as well as mental and physical relaxation all reduce stress moderately. Changing work schedules can also reduce stress, but other organisational interventions have no clear effects. We need randomised studies with at least 120 participants and preferably a single component intervention. Organisational interventions need to be better focused on addressing specific factors that cause stress.

Ruotsalainen JH, Verbeek JH, Mariné A, Serra C. Preventing occupational stress in healthcare workers. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD002892. DOI: 10.1002/14651858.CD002892.pub4.

Interventions aimed at communities for informing and/or educating about early childhood vaccination

Researchers in The Cochrane Collaboration conducted a review of the effect of informing or educating members of the community about early childhood vaccination. After searching for all relevant studies, they found two studies, published in 2007 and 2009. Their findings are summarised below.

What are interventions aimed at communities for childhood immunisation?

Childhood vaccinations can prevent illness and death, but many children do not get vaccinated. There are a number of reasons for this. One reason may be that families lack knowledge about the diseases that vaccines can prevent, how vaccinations work, or how, where or when to get their children vaccinated. People may also have concerns (or may be misinformed) about the benefits and harms of different vaccines.

Giving people information or education so that they can make informed decisions about their health is an important part of all health systems. Vaccine information and education aims to increase people's knowledge of and change their attitudes to vaccines and the diseases that these vaccines can prevent. Vaccine information or education is often given face-to-face to individual parents, for instance during home visits or at the clinic. Another Cochrane Review assessed the impact of this sort of information. But this information can also be given to larger groups in the community, for instance at public meetings and women's clubs, through television or radio programmes, or through posters and leaflets. In this review, we have looked at information or education that targeted whole communities rather than individual parents or caregivers.

The review found two studies. The first study took place in India. Here, families, teachers, children and village leaders were encouraged to attend information meetings where they were given information about childhood vaccination and could ask questions. Posters and leaflets were also distributed in the community. The second study was from Pakistan. Here, people who were considered to be trusted in the community were invited to meetings where they discussed the current rates of vaccine coverage in their community and the costs and benefits of childhood vaccination. They were also asked to develop local action plans, to share the information they had been given and continue the discussions with households in their communities.

What happens when members of the community are informed or educated about vaccines?

The studies showed that community-based information or education:

- may improve knowledge of vaccines or vaccine-preventable diseases;

- probably increases the number of children who get vaccinated (both the study in India and the study in Pakistan showed that there is probably an increase in the number of vaccinated children);

- may make little or no difference to the involvement of mothers in decision-making about vaccination;

- may change attitudes in favour of vaccination among parents with young children;

We assessed all of this evidence to be of low or moderate certainty.

The studies did not assess whether this type of information or education led to better knowledge among participants about vaccine service delivery or increased their confidence in the decision made. Nor did the studies assess how much this information and education cost or whether it led to any unintended harms.

Saeterdal I, Lewin S, Austvoll-Dahlgren A, Glenton C, Munabi-Babigumira S. Interventions aimed at communities to inform and/or educate about early childhood vaccination. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD010232. DOI: 10.1002/14651858.CD010232.pub2.

Regular antibiotics for preventing pneumococcal infection in young children with sickle cell disease

People with sickle cell disease (SCD) are especially prone to respiratory infections and blood poisoning. These infections are often caused by pneumococcal bacteria. Infections occur partly due to the spleen not working correctly, but also because damaged tissue and bone resulting from SCD can harbour bacteria. The highest risk of infection occurs in children under three years old, but the usual pneumococcal vaccines are of limited use in these patients. Therefore regular antibiotics are needed to prevent infection. As risk of infection decreases with age, there might be a time when preventative antibiotic treatment can be halted. Three trials with over 800 children are included in the review. All three trials showed a reduced rate of infection in children with sickle cell disease receiving penicillin preventatively. Two trials looked at whether treatment was effective. The third trial followed on from one of the early trials and looked at when it was safe to stop treatment. Adverse drug effects were rare and minor. However, there were problems with children keeping to the treatment schedule and with the development of antibiotic resistance. We conclude that penicillin given preventatively reduces the rate of pneumococcal infections in children with sickle cell disease under five years old. The risk of infection in older children is lower, and the follow-on trial did not show a significant increase in risk when regular penicillin was halted at five years old. Further research should look at how common and how clinically important resistant bacteria are.

Hirst C, Owusu-Ofori S. Prophylactic antibiotics for preventing pneumococcal infection in children with sickle cell disease. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD003427. DOI: 10.1002/14651858.CD003427.pub3.

Cochrane Protocol Development Workshop

The Nigerian Branch of the South African Cochrane Centre held a Cochrane Protocol Development Course at the Calabar Institute of Tropical Diseases Research and Prevention from 2-3 December 2014. Five participants from Calabar, Abuja, Nnewi and Enugu attended the workshop. The aim of the workshop was to guide authors with registered systematic review titles through the methodology of developing review protocols and the basics of conducting Cochrane style systematic reviews. The workshop comprised of group discussions, one-on-one support, didactic sessions and individual work time. The facilitators were Dr. Emmanuel Effa (Consultant Nephrologist, University of Calabar Teaching Hospital), Dr. Friday Odey (Consultant Paediatrician, University of Calabar Teaching Hospital), Mr. Ekpereonne Esu (Lecturer, Department of Public Health, University of Calabar), and Mrs. Olabisi Oduwole (Research Officer, Nigerian Branch of the South African Cochrane Centre).

Presentations were made on a number of topics including: formulating a review question, methods of a systematic review, searching for studies, risk of bias assessment, introduction to meta-analyses, overview of study Methods, critical appraisal of randomized controlled trials. There were also a number of practical sessions.

The participants said although the workshop was very intensive they had learnt a lot. They also commended the facilitators and staff of the Branch for their willingness to assist them with any challenges they had.

Cochrane Library

New and Updated Reviews from the Cochrane Library

The following reviews published recently in the Cochrane Library were authored or co-authored by Nigerians.

Updated Reviews

- Antibiotic prophylaxis during the second and third trimester to reduce adverse pregnancy outcomes and morbidity by Jadsada Thinkhamrop , G Justus Hofmeyr, Olalekan Adetoro , Pisake Lumbiganon and Erika Ota. Issue 1, 2015.
- Honey for acute cough in children by Olabisi Oduwole, Martin M Meremikwu, Angela Oyo-Ita, and Ekong E Udoh. Issue 12, 2014.

Other Recent Reviews

- Artemether for severe malaria by Ekpereonne Esu, Emmanuel E Effa, Oko N Opie, Amirahobu Uwaoma and Martin M Meremikwu. Issue 9, 2014.
- Extra fluids for breastfeeding mothers for increasing milk production by Chizoma M Ndikom, Bukola Fawole and Roslyn E Ilesanmi. Issue 6, 2014.
- Immediate postabortal insertion of intrauterine devices. Babasola O Okusanya , Olabisi Oduwole and Emmanuel E Effa. Issue 7, 2014.
- Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp by Helena Kastarinen , Tuija Oksanen , Enembe O Okokon , Vesa V Kiviniemi , Kristiina Airola , Johanna Jyrkkä , Tuomas Oravilahti , Piia K Rannanheimo and Jos H Verbeek. Issue 5, 2014
- Anticoagulation therapy versus placebo for pulmonary hypertension by

FELLOWSHIPS/GRANTS

TEG Postgraduate Training Fellowship in Medical Statistics for African Scientists: The UK Medical Research Council (MRC) is funding a fellowship to provide support for two years training in medical statistics to African Scientists. The training involves one year of study for the MSc degree in Medical Statistics at the London School of Tropical Medicine and Hygiene (LSHTM) followed by a one-year professional attachment at one of the African centres associated with the research programme of the Tropical Epidemiology Group (TEG) at LSHTM. The fellowship will provide costs for fees, stipend (£15,000 per annum) and return air travel.

For full details and eligiblility Criteria please visit: *http://www.lshtm.ac.uk/study/funding/teg_fellowship_in_medical_statistics_for_african_scientists.html*

Deadline for Applications: 30th April 2015

ANNOUNCEMENTS

- Cochrane Rebrand: Cochrane is undergoing rebranding. The rebranding includes among other things a new name, new organizational identity, new website (including the Cochrane Library), and new logos. The organization is now known simply as 'Cochrane'. The rebranding is expected to play an important role in Cochrane's *Strategy to 2020* and to enable the organization reach out and engage much more effectively with the clinicians, researchers, policy-makers and patients who use Cochrane evidence.
- Cochrane Releases List of Priority Reviews: The Cochrane Collaboration has released a list of priority review topics. The list contains over 200 review topics across review groups including new titles and reviews requiring updates that best meet the needs of healthcare and health policy decision makers.
- 23rd Annual Cochrane Colloquium - Early Bird Registration – Early Bird Registration is open for the 23rd Annual Cochrane Colloquium and will close 22 July 2015. The Colloquium will be hosted by the Austrian Cochrane Branch in Vienna, Austria from 3-7 October 2015. Colloquium theme: 'Filtering the information overload for better decisions'.
- How can we serve you better - Please feel free to contact us and let us know how we can tailor the *Info Sheet* to better meet your needs. Send your emails to cochranenigeria@yahoo.co.uk
- Rebranding of the Nigerian Branch - As part of the rebrand exercise of Cochrane, the Nigerian Branch of the South African Cochrane Centre is undergoing rebranding and shall now be called 'Cochrane Nigeria'. The branch also has a new logo and will launch a new website in a few months.

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Please visit our website: nigeria.cochrane.org
Email us at: cochranenigeria@yahoo.co.uk

Call us on:
Moriam:+234 (0)8039733998
Bisi:+234 (0) 8056071976
Emmanuel: +234 (0) 8037236919

Follow us on:

Nigerian Cochrane Branch

@cochranenigeria

Cochrane

Address:
Cochrane Nigeria Branch
Calabar Institute of Tropical Diseases Research and Prevention
University of Calabar Teaching Hospital, Moore Road
GPO Box 3134, Calabar, Cross River State

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