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Newsletter of the Nigerian Branch of the South African Cochrane Centre
Calabar Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital

Pneumococcal Conjugate Vaccines

for Preventing Pneumonia and Pneumonia -Related Deaths in Children

Pneumonia is an acute lower respiratory tract infection that results from the inflammation of the lung tissue. It is currently the leading cause of under-five mortality worldwide, accounting for 15% of under-five deaths. Most pneumonia-related deaths occur in South Asia and sub-Saharan Africa.[1]

Bacteria and viruses are responsible for 45 – 85% of cases of childhood pneumonia. Of the bacterial agents, *Streptococcus pneumoniae* (*Strep. pneumoniae*) is a leading cause of severe pneumonia. Other causes are smoke, aspiration of feed and foreign bodies in the airway. The risk of childhood pneumonia increases with failure to breastfeed exclusively for six months, overcrowding, low birth weight and low immunization coverage. Some of the specific risk factors for pneumonia are asthma, cystic fibrosis, gastro esophageal reflux disease, sickle cell anaemia and HIV/AIDS.

Symptoms of pneumonia vary with the age of the child and the cause of the illness. The common symptoms are fever, cough, fast breathing, labored breathing and chest pain. However, with progression in disease severity, young infants may develop vomiting, refusal to feed, diarrhea, restlessness, apprehension, cyanosis (bluish discoloration of the lips and extremities) and abdominal distention. Death from pneumonia usually arises from the occurrence of life-threatening complications. These include heart failure, respiratory failure, pleural effusion (fluid in the lungs), pneumothorax (air in the lungs), lung collapse and septicaemia (bacteria multiplication in the blood). Since pneumonia in children is a rapidly progressive illness, these complications occur within a few days of onset of illness when initiation of effective treatment is delayed.

Pneumonia can be diagnosed clinically, by use of chest X-ray or by identification of specific causative agents. Since most cases of childhood pneumonia occur in developing countries where bacterial agents are quite common, prompt treatment with effective antibiotics remains a major strategy for reducing the burden of the disease. To effectively control the scourge of pneumonia in children, it is necessary to focus on strategies for preventing the illness. Vaccines prevent infants and young children from developing an illness by stimulating their immune systems to produce antibodies against the microbial agents that cause the illness (ref). Since *Strep. pneumoniae* is known to be one of the most virulent pneumonia-causing bacteria in children, the use of an effective vaccine against this organism will significantly reduce the burden of childhood pneumonia and pneumonia-related deaths in children globally.

A Cochrane Systematic review was conducted in 2009 by Lucero and associates to assess the efficacy of pneumococcal conjugate vaccine (PCV), a vaccine that is specific against *Strep. pneumoniae* infection. They reviewed 11 clinical studies that were conducted in Africa, Asia, US, Philippines and Finland. The studies aimed at determining the efficacy of PCV in preventing vaccine-serotype invasive pneumococcal disease, pneumonia and childhood death from all causes. A total of 113, 044 children aged two years and below participated in the clinical studies. Of these, 57, 015received PCV while the remaining 56, 029 did not. Those that received PCV got three doses between the sixth week and first year of life at an interval of 4 – 8 weeks between each dose. The results showed that there was an 80% reduction in occurrence of vaccine serotype invasive pneumococcal diseases, 27% reduction in occurrence of World Health Organization X-ray defined pneumonia, 6% reduction in clinical pneumonia and 11% reduction in all-cause mortality among those that received the PCV compared with those that did not. The vaccine was also shown to reduce the occurrence of pneumonia as well as death in HIV-positive children[2].

With the proven efficacy of PCV in preventing the occurrence of pneumonia and pneumonia-related deaths in young children, the Ministry of Health at country levels should consider integrating the vaccine into the routine childhood immunization schedule where that has not already been done. Implementation of effective strategies like PCV for preventing childhood morbidity and mortality will go a long way in achieving the Millennium Development Goal 4. Caregivers of children, health care providers and policy-makers should be enlightened on the benefits of PCV to child health.

REFERENCES

1. http://www.who.int/mediacentre/factsheets/fs331/en/
2. Lucero MG, Dulalia VE, Nillos LT, Williams G, Parreño RAN, Nohynek H, Riley ID, Makela H. Pneumococcal conjugate vaccines for preventing vaccine-type invasive pneumococcal disease and X-ray defined pneumonia in children less than two years of age. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD004977. DOI: 10.1002/14651858.CD004977.pub2.

EVIDENCE AT YOUR FINGERTIPS

(From the Cochrane Library)

TECHNICAL SUMMARY

Antiretroviral Interventions for Preventing Breast Milk Transmission of HIV

BACKGROUND

In 2012, approximately 260000 children under the age of 15 acquired HIV. In settings where breastfeeding is the norm, a significant number of mother-to-child transmissions (MTCTs) occur through breastfeeding. The use of antiretroviral drugs by breastfeeding HIV-infected mothers or their infants is one of the means by which MTCT of HIV through breast milk can be prevented.

OBJECTIVES

To assess the efficacy and safety of antiretroviral prophylaxis in HIV-infected women or their infants for preventing mother-to-child-transmission of HIV during breastfeeding.

MAIN RESULTS

- Seven Randomized controlled trials were included in the study. Two of these were trials that had maternal prophylaxis alone during breastfeeding, four addressed infant prophylaxis alone and one addressed both maternal and infant prophylaxis.
- Most of the trials included in the review were conducted in African countries.

MATERNAL PROPHYLAXIS ONLY

Triple ARV prophylaxis versus short ARV regimen: At twelve months (but not at six months), this trial showed

an association between the use of maternal triple-ARV prophylaxis during breastfeeding (compared with a short ARV prophylaxis regimen) and a decreased risk of HIV transmission (HR 0.40, 95% CI 0.16 to 0.96) and HIV transmission or death (HR 0.52, 95% CI 0.28 to 0.93). No difference in infant mortality was observed between the two arms (low to moderate quality evidence).

Nucleoside reverse transcriptase inhibitor (NRTI)-only regimen versus protease inhibitor containing regimen: This trial compared six months of Zidovudine, lamivudine, and lopinavir/ritonavir versus zidovudine, lamivudine, and abacavir. At six months there was no difference in risk of infant HIV infection (RR 0.21, 95% CI 0.1 to 4.3), infant mortality (RR 1.05, 95% CI 0.37 to 2.14), or infant mortality and death (RR 0.81, 95% 0.3 to 2.14) (Very low to low quality evidence).

INFANT PROPHYLAXIS ONLY

Single dose nevirapine versus infant zidovudine: In one trial which compared single dose nevirapine to six weeks of infant zidovudine the risk of HIV infection at 12 weeks was found to be greater in the zidovudine arm than in the single dose nevirapine arm in infants without evidence of HIV infection within 10 days after birth and who were breastfed (HR 2.35, 95% CI 1.07 to 5.17) (Very low quality evidence).

Six week versus six months of nevirapine: This trial compared the efficacy of a six week infant regimen of nevirapine to a six month regimen. In infants whose mothers were not using highly active antiretroviral therapy, there was no difference in risk of HIV infection among infants in the six week and six month regimen groups at twelve months (HR 0.65, 95% CI 0.33 to 1.28). (low to moderate quality evidence).

Single Dose Nevirapine plus One week Zidovudine, or Extended Nevirapine, or Extended dual Prophylaxis: This trial had three arms: a control regimen of single dose nevirapine plus one week zidovudine, control regimen plus extended dose of nevirapine, and control regimen plus extended dual prophylaxis. At 24 months, when compared with the control regimen, the extended nevirapine regimen group had a lower risk of HIV transmission (HR 0.60, 95% CI 0.46 to 0.78) and of HIV transmission or death (HR 0.71, 95% CI 0.58 to 0.87). There was, however, no statistically significant difference in infant mortality alone.

The extended dual prophylaxis nevirapine group had a lower risk of HIV transmission(HR 0.65, 95% CI 0.50 to 0.85) as well as risk of HIV transmission or death (HR 0.73, 95% CI 0.60 to 0.90) but no significant difference in infant mortality alone(HR 0.73, 95% CI 0.53 to 1.00) when compared with the control regimen.

When extended dual prophylaxis was compared with extended nevirapine regimen there was no statistically significant difference in risk of HIV transmission (HR 1.04, 95% CI 0.71 to 1.51), infant mortality (HR 0.91, 95% CI 0.61 to 1.36), or HIV transmission or death (HR 1.00, 95% CI 0.75 to 1.34) between the two arms (moderate to high quality evidence).

MATERNAL OR INFANT PROPHYLAXIS

Maternal triple Antiretroviral Regimen, extended infant nevirapine or neither intervention: Infants in the maternal prophylaxis arm whose mothers received the triple drug antiretroviral prophylaxis regimen from 2-28 weeks were at lower risk of HIV infection (RR 0.52, 95% CI 0.3 to 0.89), and HIV infection or death (RR 0.61, 95% CI 0.38 to 0.96) compared to the infants in the control group. There was, however, no statistically significant difference in risk of infant mortality alone (RR 0.67, 95% CI 0.31 to 1.45) between the groups. Infants in the extended infant nevirapine group were also found to be at a lower risk for HIV infection (RR 0.29, 95% CI 0.15 to 0.56), and HIV infection or death (RR 0.38, 95% CI 0.22 to 0.65) than infants in the control group. There was no difference in the risk of infant mortality alone in the extended infant nevirapine group compared to the control group. There was no statistically significant difference in HIV infection (RR 1.78, 95% CI 0.88 to 3.59), infant mortality (RR 1.78, 95% CI 0.48 to 2.47), and HIV infection or death (RR 1.60, 95% CI 0.91 to 2.82) between the maternal and extended infant prophylaxis groups. (Low to moderate quality evidence).

In this trial, there was an increased risk of severe adverse events among mothers with the maternal regimen (RR 2.19, 95% CI 1.2 to 4).

Authors' conclusions

Maternal and infant antiretroviral prophylaxis regimens are both effective in preventing mother-to-child transmission of HIV through breastfeeding. However there is need for research to determine how nevirapine resistance affects children who have undergone Maternal or infant antiretroviral prophylaxis but who still become infected. Research is also required on ARV resistance in mother who have taken ARV prophylaxis to prevent MTCT of HIV through breastfeeding.

White AB, Mirjahangir JF, Horvath H, Anglemyer A, Read JS. Antiretroviral interventions for preventing breast milk transmission of HIV. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD011323. DOI: 10.1002/14651858.CD011323.

PLAIN LANGUAGE SUMMARIES

Artemether injection for treating people with severe malaria

In this review, researchers from The Cochrane Collaboration examined the effects of treating people that have severe malaria with artemether injected intramuscularly, and compared it to treatment with other antimalarial drugs given intramuscularly or intravenously. After searching for relevant trials up to 9 April 2014, we included 18 randomized controlled trials that recruited 2662 adults and children and were conducted mainly in Africa and Asia.

What is severe malaria and how might artemether injection reduce deaths

Severe malaria is caused by infection with the *Plasmodium* parasite, which is transmitted to people through the bite of an infected female *Anopheles* mosquito. It is a serious medical condition and can cause vomiting, anaemia, convulsions and death. People need to be treated as quickly as possible.

Injection of artesunate is recommended by the World Health Organization (WHO) for treating adults and children that have severe malaria as trials have shown that it results in fewer deaths compared to quinine treatment. Artemether is an alternative artemisinin derivative but is only available as a pre-mixed oil-based solution for intramuscular injection. Artemether is now widely available and is used in many African countries, although it is not specifically recommended by the WHO.

What the research says

Artemether versus quinine:

For children in Africa, intramuscular artemether is probably as good as quinine at preventing deaths from severe malaria (*moderate quality evidence*). Artemether may shorten recovery time from coma by about five hours (*low quality evidence*), and may reduce the number of children with signs of brain damage at the time of hospital discharge (*low quality evidence).*

In older children (> 15 years) and adults in Asia, treatment with artemether probably results in fewer deaths than quinine (*moderate quality evidence*).

Artemether versus artesunate:

In adults from Asia, artesunate probably prevents more deaths than artemether (*moderate quality evidence*), but no trials have been conducted in young children from Africa.

Authors conclusions

Although there is a lack of direct evidence comparing artemether with artesunate, artemether is probably less effective than artesunate at preventing deaths from severe malaria. In circumstances where artesunate is not available, artemether is an alternative to quinine.

Esu E, Effa EE, Opie ON, Uwaoma A, Meremikwu MM. Artemether for severe malaria. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD010678. DOI: 10.1002/14651858.CD010678.pub2.

Repeated use of hormonal drugs right before or after sex to prevent pregnancy

Currently, no oral birth control method is approved for using only when needed, that is, at the time of sex. However, many women may want to use such a method. Our review looked at studies of different drugs taken around the sex act to find out how well the drugs worked to prevent pregnancy. We also assessed the safety of the drugs and whether women liked them.

We ran computer searches until 1 September 2014 to find relevant studies in any language. For the initial review, we also wrote to researchers to find other trials. We assessed the quality of the research methods in the studies. We used the Pearl Index to estimate the effect. The Pearl Index is the number of pregnancies for every 100 years of pill use.

We found 22 studies from the past 40 years. They included a total of 12,400 women in Europe, Asia, and the Americas. Fifteen trials studied different doses of the hormone levonorgestrel and seven looked at other hormones. These studies showed that using

some hormones right before or after sex did prevent pregnancy. Levonorgestrel seemed to work well, and was safe and accepted by thousands of women in several large trials. The most common side effects were menstrual bleeding problems. However, such bleeding issues were not always related to how often women took the pills or the total dose of the drug.

Most studies were old and many reports were not complete. However, the data had moderate quality because of the many women in these studies, the low pregnancy rates, and the consistent results. We do not know for sure whether using levonorgestrel repeatedly around the time of sex is a good and safe method of birth control. More high-quality research is needed to answer the question.

Halpern V, Raymond EG, Lopez LM. Repeated use of pre- and postcoital hormonal contraception for prevention of pregnancy. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD007595. DOI: 10.1002/14651858.CD007595.pub3.

Treatment for epilepsy in pregnant women and the development of the child

Background

For most women who have epilepsy it is important for their health that they continue their medication during pregnancy. Over the last 25 years research has shown that children exposed to these medications in the womb can be at a higher risk of having a birth defect or poorer level of development.

Research question

This review aimed to understand whether exposure to antiepileptic drugs (AEDs) during pregnancy is linked to poorer levels of ability for skills such as IQ, language and memory (neurodevelopment).

Characteristics of the studies

The review included 28 studies. Participants were women with epilepsy taking commonly used AEDs who were compared to either women without epilepsy or women who had epilepsy but who were not treated with AEDs. Comparisons were also made between children exposed to different AEDs in the womb. The evidence presented in this review was up to date to May 2014.

Results

- The evidence for younger children exposed to carbamazepine (CBZ) in the womb was conflicting, however this was likely to be due to differences in the way that these studies were carried out. In older children those exposed to CBZ were not poorer in their IQ than children who were not exposed. No link was found between the dose of CBZ and child ability.

- Both younger and older children exposed in the womb to sodium valproate (VPA) showed poorer cognitive development in comparison to children not exposed and children exposed to other AEDs. A link between dose of VPA and child ability was found in six studies; with higher doses of the drug linked to a lower IQ ability in the child. The level of this difference was likely to increase the risk of poorer educational levels.

- Children exposed to CBZ in the womb did not differ in their skills from children exposed to lamotrigine (LTG), however very few studies investigated this. There were also no differences between children exposed to phenytoin (PHT) in the womb and those exposed to CBZ or those exposed to LTG.

- There were very limited data on newer medications such as LTG, levetiracetam or topiramate.

Quality of the studies

The quality of how studies were designed varied. The more recently completed studies tended to have higher quality ratings, which suggests more reliable evidence.

Conclusions

This review found that children exposed to VPA in the womb were at an increased risk of poorer neurodevelopment scores both in infancy and when school aged. The majority of evidence indicates that exposure in the womb to CBZ is not associated with poorer neurodevelopment. Data were not available for all AEDs that are in use or for all aspects of child neurodevelopment. This means decision making for women and their doctors is difficult. Further research is needed so that women and their doctors can make decisions based on research evidence about which medication is right for them in their childbearing years.

Bromley R, Weston J, Adab N, Greenhalgh J, Sanniti A, McKay AJ, Tudur Smith C, Marson AG. Treatment for epilepsy in pregnancy: neurodevelopmental outcomes in the child. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD010236. DOI: 10.1002/14651858.CD010236.pub2.

Media Practitioners at around-table discussion with members of the Nigerian Branch of the South African Cochrane Centre

Group photo: Staff of Nigerian Branch of South African Cochrane Centre with members of the Cross River State Chapter of the Nigerian Union of Journalists.

MEDIA ROUNTABLE ON PNEUMONIA

Pneumonia is the number one killer of children under five years of age. It was for this reason that pneumonia and vaccines for pneumonia was the focus of a recent Roundtable discussion with 16 Media Practitioners in Calabar on 21st October 2014. The forum, which was hosted by the Nigerian Branch of the South African Cochrane Centre (NBofSACC), consisted of a presentation by Dr. Ekong Udoh (Senior Research Associate, NBofSACC) who gave an overview of pneumonia. In his presentation, Dr. Udoh highlighted the fact that globally, Nigeria has the second highest number of deaths from pneumonia in children under five. He also spoke about the causes of pneumonia and the three pronged approach to the control of pneumonia; namely protection against pneumonia, prevention of pneumonia and treatment of pneumonia.

Following his presentation, Mrs. Olabisi Oduwole (Research Officer, NBofSACC) spoke on pneumococcal conjugate vaccines (PCVs) for pneumonia. She highlighted evidence from a Cochrane systematic review by Lucero and colleagues, which compared PCVs to placebo or other vaccines for preventing pneumonia. She noted that PCVs were found to be effective in preventing pneumonia and blood infection due to pneumonia. Based on the findings of the review, she advocated that PCVs should be included in routine immunization regime in Nigeria.

These presentations provided the focus for a lively discussion which ensued between the media practitioners and facilitators. A number of questions were raised by the practitioners which were addressed by the facilitators. At the end of the roundtable discussion, the Chairman of the Nigerian Union of Journalists (NUJ) Cross River State Chapter, Mr. Ndoma Akpet, gave closing remarks. He acknowledged that the media roundtable is an ongoing initiative between the NBofSACC and NUJ. He thanked the Branch for holding this programme and requested that the Branch should, in addition to periodic press releases, send them information on certain issues which are peculiar problems facing Nigerians such as the use of local herbal medicines for various health challenges.

New and Updated Reviews from the Cochrane Library

The following reviews published between May and July 2014 in the Cochrane Librarywere authored or co-authored by Nigerians.

New and Updated Reviews from the Cochrane Library

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

New Reviews

- Artemether for severe malaria **by** *Ekpereonne Esu, Emmanuel E Effa, Oko N Opie, Amirahobu Uwaoma and Martin M Meremikwu.* Issue 9, 2014.

Other Recent Reviews

- 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** *Ifeanyi R Ezedunukwe , Hilary Enuh , Jay Nfonoyim and Collins U Enuh*. Issue 6, 2014.
- Antibiotic prophylaxis for preventing post-solid organ transplant tuberculosis **by** *Bappa Adamu , Aliyu Abdu, Abdullahi A Abba , Musa M Borodo and Imad M Tleyjeh.* Issue 3, 2014.
- Prophylactic versus selective blood transfusion for sickle cell disease in pregnancy **by** *Babasola O Okusanya, Olufemi T Oladapo*. Issue 12, 2013.
- Interventions for the prevention of mycobacterium avium complex in adults and children with HIV **by** *Muhammed Mubashir B Uthman, Olalekan A Uthman and Ismail Yahaya. Issue 4, 2013.*
- Home or community-based programmes for treating Malaria **by** *Charles I Okwundu, Sukrti Nagpal, Alfred Musekiwa, David Sinclair. Issue 5, 2013.*
- Interventions for HIV-associated nephropathy **by** *Ismail Yahaya, Olalekan A Uthman, Muhammed Mubashir B Uthman. Issue 1, 2013.*
- Intramuscular versus intravenous anti-D for preventing Rhesus alloimmunization during pregnancy **by** *Charles I Okwundu, Bosede B Afolabi. Issue 1, 2013*.

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Fellowships/Grants

- **EDCTP-TDR Clinical Research and Development Fellowship scheme - Call for Applications:** EDCTP/TDR are inviting applications from researchers and members of clinical research teams from low- and middle-income countries (LMIC) for the EDCTP-TDR Clinical Research and Development Fellowship scheme. Successful candidates will be placed with leading product development organisations, including pharmaceutical companies and product development partnerships – the 'host organisations'- for a period of up to 24 months. Twenty-five fellowships are available under this call. For full details please visit: http://www.edctp.org/media-centre/news/announcement/edctp-and-tdr-offer-first-joint-clinical-r-d-fellowships/ **Deadline for applications** - 30 January 2015

ANNOUNCEMENTS

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- **Complete Issue 10, 2014 is online** - The complete issue of Issue 10, 2014 is now online. Please visit www.thecochranelibrary.com
- **Chief Executive Officer's office announces appointment of new Consumer Co-ordinator** - The Cochrane CEO's Office has announced the appointment of Richard Morley as the new Consumer Co-ordinator. He will cover for Catherine McIlwain while she is on the maternity leave until February 2016.
- **23rd Annual Cochrane Colloquium** - The 23rd Annual Cochrane 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

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