Gilead Forderprogramm Infektiologie 2012: Update

Title:
Piloting of a rapid based screening for hepatitis B in pregnancy in South Africa

Applicants:
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Background:
Hepatitis B virus (HBV) infection carries a morbidity and mortality which remains largely unappreciated. Together with chronic hepatitis C infection, chronic hepatitis B (CHB) is responsible for more deaths than either tuberculosis or malaria. Almost 240 million people worldwide are chronically infected with HBV and around 780 000 die as a direct consequence of this infection. This is despite the availability of a safe and effective vaccine for more than three decades and potent therapy for those who are infected.

In order to reduce prevalence and impact the ongoing cycle of infection, infant infection must be halted. The risk of chronic infection developing in the neonate or even young child is much greater than in the adult, 50-90% vs <5%. The WHO recommends administration of the recombinant HBV vaccine to infants within 24 hours of delivery. In much of subSaharan Africa however babies are given the first dose of HBV vaccine at 6 weeks of age. So, whilst access to vaccine has increased over the past decade, timing of vaccine administration remains at 6 weeks. This was based on data showing a low prevalence of HBeAg in pregnant African women, thought to indicate that perinatal transmission from mother to child was negligible. We and others have however shown that this is not the case. Almost 20% of pregnant women are HBeAg positive and have a 90% chance of infecting their infants and their infants developing CHB.

Birth dose vaccine will not prevent all HBV transmissions. Hepatitis B immunoglobulin (HBIG) is available in resource rich settings and is known to further reduce transmission. This is however not available in resource poor settings due to its cost. However nucleos(t)ide drugs with anti-HBV activity given in the second and third trimester of pregnancy are known to reduce HBV viral load and will reduce the risk of MTCT transmission. It is likely that with this combination of interventions it may be possible to eradicate perinatal HBV transmission.

Aim:
The aim of this study is to assess the operational feasibility of HBsAg rapid testing for pregnant women in antenatal clinics.
As a secondary aim we will assess the feasibility of the use of tenofovir for women with high HBV viral loads to prevent MTCT and administering birth dose HBV vaccination.

Progress to date:
1. Establishment of HBsAg Rapid Test

The aim of this study was to compare the performance characteristics of the Determine HBsAg Rapid test with the automated AXSYM HBsAg assay (Abbott Laboratories) and the plate based Murex HBsAg Version 3 assay (Diasorin, Saluggia). The Determine test is being used in the Gilead funded study.

This data has been presented at the University of Stellenbosch Academic Day in August 2014 – see poster attached. It will also be presented at Unipath, the South African National Congress for Pathologists in September 2014 (cf. http://www.pathconference.com).

2. Pilot Study of HBsAg Rapid Testing in Pregnant Women in South Africa

The next phase of this project was piloting HBsAg rapid testing in pregnant women and infant follow up. Ethical approval for this study was obtained from the University of Stellenbosch Health Research Ethics Committee (N13/10/132). The study is based at Tygerberg Hospital, accessing the infrastructure from the Safe Passage study, a large cohort study on maternal and child health. A study sister has been appointed and recruitment for the HBV study has commenced.

Women at the primary care community clinic in Bishop Lavis, near Cape Town, are given information about the study and if interested offered transport to Tygerberg Hospital where they are consented. Women are tested for HBsAg using the Determine Rapid Test. If HBsAg is positive a further blood is taken for laboratory confirmation of HBsAg status (Abbott Architect). Other testing includes HBeAg and antiHBe status (Abbott Architect), HBV viral load (Roche) and in-house pol/surface sequencing and where possible whole genome sequencing. They are followed up in the Hepatology Viral Hepatitis Clinic, where liver health is assessed and a decision is made about commencing tenofovir.

Results

To date 75 women have been consented and tested with the Determine HBsAg rapid test. Three tested HBsAg positive. All three were HIV negative. The HBsAg prevalence rate of 4% is similar to data from our previous studies in pregnant women in the Western Cape.

HBsAg confirmation

All three women were confirmed HBsAg positive on laboratory based ELISA testing (Abbott Architect). All three women were HBeAg negative and anti-HBe positive and all had normal AST, platelets and no evidence of chronic liver disease.

Interestingly two of the three women had HBV viral laods (VL) greater than 10,000 IU/ml and one had a viral load of 767,000 IU/ml. This is high in the context of antiHBe positivity. These two women have been offered tenofovir from the second trimester. All women had instructions for HBV birth dose to be administered to their infants in their antenatal notes.

To date only one of these women has delivered. Her baby was given HBV vaccine within 24 hours of delivery. We will review all HBsAg positive women and their infants at 6 weeks post delivery to test for markers of HBV infection.

Interim conclusion
The HBsAg rapid test is operationally simple to institute and acceptable to pregnant women. Instituting tenofovir therapy for prevention of HBV MTCT and the administration of HBV birth dose vaccine has not resulted in any major logistic issues.

3. Roll out of HBV Rapid Testing Study to Primary Care Antenatal Clinics
The third and final phase of this study is the roll out of this protocol to larger primary centres, which will allow us to assess the operational impact of rapid testing in a primary care setting.

We will roll out this study to two other sites.
i) *Michael Mapongwana Community Clinic:* We are in the final phase of discussions with Medicins Sans Frontieres (MSF) to roll out the protocol to Michael Mapongwana Community Clinic in Khayelitsha, Cape Town. This is a primary care setting and recruitment and testing will take place in the clinic. Follow up of HBsAg positive patients will also take place in the clinic. Whilst looking at the operational feasibility of HBsAg point-of-care testing in a large primary care clinic, it will also be a trial of HBV therapy in a primary care setting. All patients will have access to specialist referral if the clinician in charge deems it necessary. We have support of the Department of Health for this study and we expect recruitment to start by November 2014 and plan to recruit around 800 women from this site.

ii) *Wits Reproductive Health and HIV Institute:* We also plan to roll out this protocol to the antenatal clinic at Wits Reproductive Health and HIV Institute under the direction of Professor Helen Rees. We will have access to a large antenatal clinic which will allow us to address additional critical questions like the optimum HBV viral load for starting HBV therapy to prevent MTCT. We plan to start recruitment is January 2015 and to recruit around 1000 women.

Conclusion
This important study will provide data on the testing and management of antenatal women with CHB in South Africa. It will provide important data to support the call to test and treat women with CHB and to administer a birth dose of HBV vaccine, so offering the opportunity to eradicate HBV transmission in subSaharan Africa.