Antihypertensive Agents: Which One?

An optimal antihypertensive regime for the management of pre-eclampsia in low-resource settings would:

- Use oral drugs that are widely available
- Effectively and efficiently reduce blood pressure
- Reduce blood pressure in a controlled and predictable manner so as not to destabilize the fetal condition
- Be cerebro-protective, maintaining a normal cerebro-perfusion pressure and pulse pressure.

A number of oral strategies have been suggested, yet definitive trial data comparing oral regimens do not exist. Evidence of the relative risks and benefits of different oral regimens will help develop guidance for antihypertensive use in pregnancy, especially where multiple drugs are available.

PRE-EMPT is collaborating with Gynuity Health Projects to conduct an RCT titled: A comparison of four oral antihypertensive regimes for management of acute hypertension in pregnancy. The primary aim of the trial is to determine the efficacy of oral labetalol, oral nifedipine, oral methyldopa, and nifedipine plus oral propranolol for management of hypertension in pregnant women. The secondary aims are to assess adverse outcomes and necessity for additional hypertensive treatment among women in the four study arms, and to assess maternal and fetal outcomes among women in the four study arms.

The trial will be conducted in India and will start in the autumn of 2011. The results will provide evidence to inform the decision for which antihypertensive agent to use in the intervention package for the CLIP definitive trial.
PRE-EMPT NEWSLETTER: ISSUE 2; JULY, 2011

**CAP (Calcium And Pre-eclampsia) Trial (PI: Justus Hofmeyr)**

This RCT will provide pre-pregnancy and early pregnancy calcium supplementation for women with low calcium intake and at high risk for pre-eclampsia. The goal of this study is to determine whether or not supplementation prevents both the occurrence and consequences of pre-eclampsia.

The final Ethics committee approval has been received from both Walter Sisulu University the Eastern Cape Department of Health. The case record forms have been circulated through the WHO forms committee and finalized. The WHO team are in the process of setting up a web-based randomization system, which will allocate appropriate follow-up tablet packs for each woman, as well as setting up OpenClinica for online data entry. The randomized tablet bottle labels have been prepared by WHO, shipped and received by the manufacturer in Johannesburg.

Sub-contracts have been signed by the Universities of Cape Town and Zimbabwe. In East London, a team of field workers have been developing a database of women with previous pre-eclampsia, who are potentially suitable for screening and enrolment. So far, 110 women have been contacted who would be eligible now, and 398 who are likely to be eligible in the future (i.e. when contraception discontinued). Recruitment is ready to begin as soon as the trial tablets are received. Two hundred posters have been printed to be used for advertising the trial, and are being put up in hospitals and clinics. Also, 2000 flyers will be posted to women not contactable by phone (450 posted so far). Pilot studies at Universities of Cape Town and Zimbabwe have also reassured the respective PI’s that the enrolment targets will be met.

We wish to acknowledge the ongoing commitment of our collaborators, and valuable support from the team at WHO.

**miniPIERS Development & Validation (PI: Peter von Dadelszen)**

The PIERS models were developed to aid in case identification/diagnosis and risk stratification, and, therefore, accelerated triage and transport to centers where women will receive effective and evidence-based treatment to avert the adverse maternal and perinatal consequences of pre-eclampsia.

All 6 countries are now collecting data and have reported recruitment of 843 cases. Four of six participating countries have uploaded data to the Coordinating Centre for a total of 535 cases. Of the 535 cases entered in the database - we have an outcome rate of 21% at any time and 11.9% within 48hrs.

Since the last newsletter site visits were conducted in Sao Paulo, Brazil, Cape Town, South Africa, and Kampala, Uganda.

Interim analysis to determine differences between sites and clean data is underway, and initial results will be reported in the next newsletter.

**Community-Level Interventions for Pre-eclampsia (CLIP) (PI: Peter von Dadelszen)**

CLIP will test the impact of a community-level package of care to reduce adverse maternal and perinatal outcomes related to pre-eclampsia. The package will include miniPIERS screening, diagnostic and triage tools, an oral antihypertensive and a loading dose of MgSO4 to prevent the seizures of eclampsia in women with severe hypertension or to treat seizures in women with eclampsia.

A second visit was conducted in Pakistan in May, 2011 to eye witness the health centres in Hyderabad and Matiari, to finalize the study sites and to identify the potential strategies to uptake of the CLIP package.

A meeting was also arranged to investigate the feasibility of local manufacture of MgSO4 injections in a form which would be easily dispensable with strict quality control criteria. The visit concluded with the debriefing and finalization of work plan outlines, timelines and deliverables and budget.

An exploratory site visit was also conducted in Uganda in May, 2011 to eye witness the health centres in Fort Portal and Masaka, determine the infrastructure and scope of practice of the Village Health Teams (VHT’s), and determine the logistics of Uganda as a site for consideration for the CLIP project.
Global Pregnancy CoLaboratory (PI: Jim Roberts)

The Global Pregnancy CoLaboratory has short-term goals to bring together cohorts with data and biological samples from around the world to study the pregnancy disorder, preeclampsia. Currently such data and biological sample collections exist primarily in developed countries. Thus, a longer-term goal of the effort is to introduce such data and collections into low and middle income countries and also to extend the target of the research to all pregnancy adverse outcomes.

The members of the group held an organizational meeting in Oxford in April. At this meeting several policies were established and the project begun. We currently have membership from nearly 20 cohorts with data and biological samples from more than 100,000 pregnancies.

We have had the first teleconference of the Executive Committee and are hiring a database manager to assist the group in assembling necessary data to a central location. Several members of the group are working on identifying necessary fields for this database. The group is working closely with the GAPPS program to coordinate activities and to use as much as possible a database, which they are establishing. Templates for membership have been developed and we have had our first request for new membership that will be voted on at the first teleconference of the Steering Committee in July. We are working with Objective 1 to try to add a biological collection and storage component to this study being done in South Africa and Zimbabwe.

Plans are in progress for the first Global Pregnancy CoLaboratory application for external funding.

Pre-Eclampsia Knowledge Translation (PI: Matthews Mathai)

The knowledge translation working group will focus on updating the WHO pre-eclampsia guidelines and preparing for their active implementation. In addition, support will be given for the Preeclampsia Foundation to develop and strengthen its online presence in low and middle-income countries.

The draft guidelines have been submitted to WHO's Guidelines Review Committee. These will be reviewed, hopefully this month. Assuming the decision is favorable and no major modifications are requested, we will start the publication process. Publication is anticipated by the end of summer.

Other General Updates

Website
The PRE-EMPT website is nearing completion.

The home page will include a slideshow of the pictures of all sites and a summary of the PRE-EMPT Project. A page will be dedicated to each objective which will include a description, updates and pictures. The website will have a members only section, which includes the geographic locations of all sites and the associated team members. A discussion board will be displayed and accessible to all users once logged in. The last section of the PRE-EMPT website will provide useful links and resources.

PRE-EMPT Meeting
The PRE-EMPT Meeting will be held in Vancouver, Canada 2-4 November at the beautiful Fairmont Waterfront. The first day of meetings will review results from the miniPIERS model development and validation study and finalize the model for publication and use in CLIP. The second day will highlight the interim results of the CLIP feasibility study in Pakistan and an African site as well as review the CLIP Pilot RCT protocol. The final day will bring together the PRE-EMPT Technical Advisory Group to discuss each objective’s progress and plans for the upcoming year. We are very excited to host many of our international collaborators in Vancouver and take advantage of their expertise to further this exciting project!
Publications of Interest...


Advocacy organisations as partners in pre-eclampsia progress: patient involvement improves outcomes


Optimal maternal and neonatal health requires the expertise of maternity-care providers who base their decisions on solid research. Optimal care, however, also requires active patient participation, which is best accomplished through advocacy organisations that represent the perspective of diverse patient populations. Patients who come together under the auspices of a patient advocacy organisation, sometimes called consumer groups, can have a unique and powerful voice to advance the goals (or overcome the inertia) of the healthcare system. For preeclampsia, a condition that still carries the burden of no cure and seriously adverse or deadly outcomes, all three components - care providers, researchers and patients - are required to realize progress. In this chapter, we briefly describe the effect of preeclampsia on women, discuss the role of patient advocacy organisations, and propose a six-point call to action that can serve as a compass for patients to collaborate with practitioners, investigators, funders, non-governmental organisations, and policy makers on a set of articulated and comprehensive goals.

Passionate about Pre-Eclampsia? Lend Your Voice to the Chorus for Change

The International Society for the Study of Hypertension in Pregnancy (ISSHP) convenes its next World Congress in Geneva 9-13 July, 2012. Patient groups from around the world are collaborating with ISSHP, the World Health Organization, and other professional societies to launch a Global Preeclampsia Awareness Day in conjunction with this biennial scientific meeting. This global initiative is intended to call attention to the gross negligence of countries, research communities and health systems to the issue of pre-eclampsia, while creating an opportunity to shine a spotlight on the opportunity for progress.

Pre-eclampsia contributes enormously to the unacceptable levels of maternal and perinatal mortality and morbidity around the world and has long suffered without a unified voice advocating for progress. This global initiative encourages investigators, care providers, NGOs, and patients to unify around a collective call-to-action, raising much needed attention to the issue.

Upcoming Activities

- **miniPIERS on the Move, Development xChange**, **JULY 27-28**
- **PRE-EMPT and LOGIC Meeting, London**, **SEPT 14**
- **miniPIERS, CLIP & TAG Meeting, Vancouver**, **NOV 02-04**