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IMPROVING MATERNAL HEALTH

Improving maternal and perinatal outcomes in the hypertensive disorders of pregnancy: A vision of a community-focused approach

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ABSTRACT

The hypertensive disorders of pregnancy (HDP; pre-existing hypertension, gestational hypertension, and pre-eclampsia) remain important causes of maternal morbidity and mortality, especially in low- and middle-income countries. The paper summarizes the current state of evidence around possible technologies to support community-based improvements in maternal and perinatal outcomes for women with pre-eclampsia. Through the testing and, where proven, introduction of these technologies, we believe that HDP-related progress toward achieving Millennium Development Goal 5 can best be accelerated. The evidence and discussion are presented under the following headings: (1) prediction; (2) prevention; (3) diagnosis; (4) risk stratification; (5) decision aids; (6) treatment; (7) geographic information systems; (8) communication; and (9) community and patient education.

1. Introduction

The hypertensive disorders of pregnancy (HDP) complicate 5%–10% of pregnancies and can lead to serious maternal illness or death [1,2]. HDP include the conditions of pre-eclampsia, pre-existing hypertension, and gestational hypertension. Pre-eclampsia is the most serious of these disorders, is the second leading cause of maternal death worldwide, and results in 63 000–72 000 maternal deaths each year. Over 99% of these deaths occur in low- and middle-income countries (LMICs) [1,2]. The World Health Organization (WHO) estimates that pre-eclampsia causes the deaths of more than 500 000 fetuses and neonates annually [1,2]. The only way to cure pre-eclampsia is to deliver the placenta and fetus [1]. Pre-eclampsia-related maternal deaths result primarily from delays in diagnosis, triage, transport, and treatment [3].

The present paper provides a summary discussion of the current state of evidence around possible technologies to support community-based improvements in maternal and perinatal outcomes for women with pre-eclampsia. Any such community-level improvements must be supported through strengthened facility- and evidence-based comprehensive emergency obstetric and neonatal care (CEmONC). In this way, we believe that HDP-related progress toward achieving Millennium Development Goal 5 can best be accelerated.

The evidence and discussion are presented under the following headings: (1) prediction; (2) prevention; (3) diagnosis; (4) risk stratification; (5) decision aids; (6) treatment; (7) geographic information systems; (8) communication; and (9) community and patient education.

2. Prediction

Ideally, it would be possible to identify pregnancies destined to develop pre-eclampsia so that the manner and place of prenatal care can be adapted to accurately assigned risk.

2.1. Based upon clinical findings

There is some information from high-income countries, but the performances of individual clinical findings as predictors of pre-eclampsia fail to meet requirements for generalized implementation [1,4,5].

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Uterine artery Doppler continues to be the most useful clinical adjunct, but suffers from low sensitivity [5]. Theoretically, additional information may come from prenatal diagnostic analytes (first trimester pregnancy-associated plasma protein-A [PAPP-A]; second trimester alpha-fetoprotein [AFP], human chorionic gonadotropin [hCG], and inhibin-A), but in the large prospective analysis done as part of the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (NICHD MFM) Network antioxidant trial, data were disappointing [6,7]. For uterine artery Doppler insonation, several portable machines are available [8,9], and the technique does not require a great deal of training or expertise.

2.2. Based upon laboratory findings

Currently, there are no biomarkers that are ready for translation into day-to-day clinical practice. It may be that angiogenic and antiangiogenic factors predict early-onset pre-eclampsia (and placental intrauterine growth restriction), as these are more closely associated with failed placentation and metabolomics (especially a metabolic syndrome metabolomic profile) predict late-onset pre-eclampsia [10,11]. Despite significant differences between values 5–7 weeks before disease onset, the receiver operating characteristic (ROC) curves at 15–23 weeks have area under the ROC curves of only 0.5–0.6.

Although little has yet been published in terms of predictive ability for pre-eclampsia, preliminary first trimester data suggest that uric acid may be a very useful and inexpensive rule-out test [12]. Currently, there is a portable device for measuring salivary uric acid that might be adaptable to purpose [13].

3. Prevention

It should be remembered that the goal of pre-eclampsia prevention should be the prevention of the adverse maternal and perinatal events that cluster around that diagnosis (but also complicate both pre-existing and gestational hypertension at lower rates), rather than just the avoidance of women achieving the definition of pre-eclampsia. For example, and relevant to the options listed below, calcium supplementation acts as a mild antihypertensive in women with low dietary calcium intake. Therefore, in trials performed in low intake settings, women in the calcium arms of randomized controlled trials will less frequently develop proteinuric hypertension, but may not avoid the consequences of the pre-eclampsia disease processes that have been masked by lowering maternal blood pressure. Such an effect may have been responsible for the observed increase of HELLP syndrome in women in the calcium arm of the WHO and Calcium for PreEclampsia Prevention (CPEP) trials [14]. This apparent conflict in outcomes (fewer women diagnosed with "pre-eclampsia," but more with the complication of HELLP) can only be resolved through clinical trials with sufficient statistical power to exclude the complications of pre-eclampsia, perhaps through innovative and more efficient approaches such as stepped-wedge or Bayesian design.

3.1. Calcium

For the reasons discussed above, calcium supplementation remains controversial, but WHO has supported its use in low calcium intake areas [15].

3.2. Low dose acetyl salicylic acid

Again this intervention remains controversial, but WHO has recommended acetyl salicylic acid (ASA) for women deemed to be at high risk for the development of pre-eclampsia, especially if begun at less than 16 weeks [16].

3.3. Vitamins C and E

There is no evidence of benefit for vitamin C and E pre-eclampsia prophylaxis in pregnancy, and some concerns have been raised about perinatal harm (inconsistent between trials and not observed in the largest trial, the NICHD MFMU Network trial) [15,16].

3.4. Arginine

While randomized controlled trial data are not adequate to recommend use at this time, and arginine use was associated with more non-severe side effects, arginine remains an agent that deserves further investigation [17].

4. Diagnosis

4.1. Blood pressure

Currently, there are 4 novel technologies that may improve accessibility to accurate community-based blood pressure measurement. Semi-automated low-resource setting blood pressure measurements are likely to be more reliable than training community health workers to use a fully manual sphygmomanometer [18].

It remains unclear if such a blood pressure machine should give a digital readout, or whether, as a simplified decision aid, it should simply have a red, orange, and green light to identify severe hypertension ($\geq$160/110 mm Hg), non-severe hypertension (140–159/90–109 mm Hg), and normotension ($<$140/90 mm Hg), respectively. The device will ideally: (1) force clinical adherence; (2) cost less than or equal to US $20 per device; (3) use the battery power, display, and communication features of a mobile device such as a cell phone; (4) be combined with pulse wave measurement at the finger to improve pressure thresholds (pulse wave returns) [19,20] and provide measurements of oxygen saturation.

The current options that might be considered are: (1) battery-powered automated blood pressure machine (ABPM), with sealed battery pack (disposable); (2) solar panel-powered ABPM; (3) manual inflation cuff, with deflationary readout to a cell phone platform; and (4) pulse oximetry-measured blood pressure (or peripheral perfusion surrogate for blood pressure), using the Phone Oximeter platform [20–23].

4.2. Urine protein measurement

Currently, there are 4 active research tracks that could lead to community-level and cheaper facility access to cost-effective urinary protein estimation. The first is the Jhpiego Safety Pen that uses felt-tip pen technology to create proteinuria test strips from filter paper (http://www.popsci.com/diy/article/2011-05/2011-invention-awards-safety-pen).

Second, is microfluidics. Diagnostics For All (DFA) proposes to develop an accurate, low-cost (less than US $0.10) postage stamp-sized paper-based diagnostic to detect the proteinuria of pre-eclampsia (http://www.savinglivesatbirth.net/summaries/60).

Third, is the urinary Congo Red Dot Test that utilizes a textile dye to detect increased concentrations of misfolded urinary protein [24].

The fourth is the potential use of sensor-powered urinary protein measurement, based on existing point-of-care protein-to-creatinine ratio measurement [25].

4.3. Other hemodynamic indices

Other hemodynamic indices may add clinically useful knowledge during the assessment and surveillance of women with pre-eclampsia. While community health workers would not be expected to be able to interpret such data, such data could be automatically