Prevention of hypertensive disorders of pregnancy: a novel application of the polypill concept

Nearly 287.000 women die every year during pregnancy, childbirth or within 42 days after birth. Most of these deaths occur in low- and middle-income countries in Africa, Asia and South-America, and could have been prevented if women had adequate care during their pregnancy.

One of the main causes of maternal deaths is high blood pressure related diseases in pregnancy, or hypertensive disorders of pregnancy. These include pregnancy-associated high blood pressure (gestational hypertension), high blood pressure with kidney damage resulting in protein in the urine (preeclampsia), eclampsia (with fits) and HELLP-syndrome (liver, blood clotting and red blood cell problems). These disorders are on a spectrum: gestational hypertension is usually at the relative harmless side if blood pressure is does not become very high. Preeclampsia, eclampsia and HELLP-syndrome are more severe and adverse outcomes for mother and baby can often be prevented with early diagnosis of high blood pressure and start of the right treatment.

Another way to prevent severe disease is preventing it from developing in the first place. An approach from cardiovascular disease prevention is a helpful example of how this could be done effectively: a fixed dose combination pill, or polypill. In a polypill, a number of effective strategies to reduce risk are combined in a single pill. This makes it easier for people to take on a daily basis, and allows us to reduce the risk of developing disease by as much and in as many people as possible. However, for the prevention of hypertensive disorders of pregnancy, such a polypill does not exist yet.

In our review, we searched the available body of literature for effective drugs or nutrient supplements that are both safe and effective to reduce the risk of hypertensive disorders of pregnancy. Fourteen interventions were identified in our search. However, only two appeared to have a significant and robust risk-lowering effect: a low dose of aspirin (80 mg) and calcium (1-2.5 grams). They could prevent 1 to 6 out of 10 women at risk of developing hypertensive disorders of pregnancy to become ill. And the earlier women started in their pregnancies and the higher their risk to develop hypertensive disorders was, the stronger the effect appeared in the included studies. Although the evidence is not as strong for vitamin D, vitamin B12 and folic acid, also these supplements may reduce the risk of hypertensive disorders of pregnancy.

Who should take the polypill to prevent hypertensive disorders of pregnancy? We know that the higher someone’s risk, the more it makes sense to use the polypill. Unfortunately, science has not reached the point yet at which we can precisely predict who will develop gestational hypertension, preeclampsia, eclampsia or HELLP syndrome. However, we *do* know what women have higher odds of developing these disorders: women who are older during their pregnancy, pregnant for the first time, are overweight or obese, have an autoimmune disorder, have preexisting diabetes mellitus or hypertension, are pregnant with twins, or have a family member who has had

hypertensive disorders. These are also the women who may benefit from taking the polypill.

At this moment, the polypill needs to still be developed and tested in a study involving women at increased risk to see if we can move from theory to a potentially life saving intervention.

Joyce L. Browne [1], ***Kerstin Klipstein-Grobusch*** [1,2], ***Arie Franx*** [3], ***Diederick E. Grobbee*** [1]
[1]*Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands*
[2]*Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*
[3]*Department of Obstetrics and Gynecology, University Medical Center Utrecht, Utrecht, The Netherlands*

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