Abstract

Background

Pre-eclampsia complicates 3-5% of pregnancies and is a leading cause of maternal, fetal and neonatal morbidity and mortality. The disease was first thought to be related primarily to poor placentation; however, it is now considered a multifactorial entity also involving alterations to the immune system, genetics, pre-existing disease and adaptation of the cardiovascular system. Maladaptation of the cardiovascular system has been described in women with pre-eclampsia and other adverse pregnancy outcomes including gestational hypertension and delivery of a small for gestational age baby. Screening for pre-eclampsia using the Fetal Medicine Foundation Model (FMF) has demonstrated the algorithm predicted early-onset pre-eclampsia in 95% of women at a 10% false positive rate, with therapeutic low dose aspirin commenced prior to 16 weeks' gestation reducing the prevalence of early-onset disease. The FMF model works less well for the prediction of late-onset disease with aspirin not shown to be significantly effective this group.

Aims

The aim of this thesis was to identify potential maternal cardiovascular indices that may make the current screening algorithm more specific for prediction of pre-eclampsia and determine whether there is potential to assess cardiovascular function as a second tier of pre-eclampsia screening. This may improve the positive predictive value of pre-eclampsia screening and better direct therapeutic intervention.

Methods

This was a prospective longitudinal study between 14 and 30 weeks' gestation investigating cardiovascular structure and function assessed by echocardiography. The study included women who were screened high-risk and low-risk for early-onset pre-eclampsia using the FMF first trimester algorithm. Cardiovascular variables were compared between women grouped by pregnancy outcome.

Results

Women screened low-risk for early-onset pre-eclampsia with a subsequent normal pregnancy outcome demonstrated an appropriate cardiovascular adaptation to pregnancy as evidenced by an increase in cardiac output and a decrease in total peripheral resistance (primarily due to an increase in heart rate). In women screened high-risk with a subsequent normal pregnancy outcome, the increase in cardiac output and concomitant decline in total peripheral resistance was observed however, these changes were not to the same degree as seen in low-risk women with a normal pregnancy outcome. Coupled with significantly higher mean arterial pressure these findings suggest high-risk women with a normal pregnancy outcome have mildly inhibited vascular tone adaptation leading to reduced cardiac output expansion during pregnancy.

The cardiovascular profile of women stratified as high-risk who developed pre-eclampsia was of low cardiac output and high total peripheral resistance prior to the symptoms and signs of late-onset disease. This finding was replicated when these variables were indexed. Cardiac output and stroke volume were lower with total peripheral resistance increased, secondary to the combination of lower cardiac output and higher mean arterial pressure. Consequently, women who developed pre-eclampsia clearly showed maladaptation of their cardiovascular system.

One of the most important findings of high-risk women who developed pre-eclampsia was that their haemodynamic profile was different to those that developed gestational hypertension. Cardiac output in women who developed gestational hypertension was in keeping with high-risk women with a normal pregnancy outcome suggesting their vascular tone was not compromised despite significantly elevated mean arterial pressure. These women appear to have better cardiovascular adaptation compared do women who developed pre-eclampsia, which facilitated a greater increase in cardiac output with gestation.

With respect to the different haemodynamic profiles of women who developed pre-eclampsia and gestational hypertension compared to high-risk women with a normal pregnancy outcome, we have identified a number of cardiovascular markers including;

cardiac output, total peripheral resistance, stroke volume index and heart rate with potential value that could improve current pre-eclampsia screening algorithms.

Conclusion

Women who develop pre-eclampsia have cardiac maladaptation that is evident from 14 weeks' gestation. Cardiac output and total peripheral resistance are the most significant cardiovascular indices that could potentially be incorporated into the current algorithm or alternatively be used as a second tier of screening at 20 weeks' gestation to improve the positive predictive value of the test.