PREVENTION OF PRE-ECLAMPSIA: EVIDENCE FROM RANDOMISED TRIALS AND SYSTEMATIC REVIEWS

Meher S

University of Liverpool, Liverpool, UK

Background
Development of rational strategies for prevention of pre-eclampsia remains a challenge, mainly because the cause of pre-eclampsia is uncertain. A wide range of interventions has been proposed, based either on epidemiological observations or pathophysiological disturbances seen in pre-eclampsia. Numerous randomised trials have evaluated the effectiveness of these interventions. An ongoing HTA project in the UK aims to identify all randomised trials of interventions for prevention of pre-eclampsia, and to then summarize the evidence available from these trials in Cochrane systematic reviews.

Methods
We identified randomised trials for prevention of pre-eclampsia using the Cochrane Pregnancy and Childbirth (PCG) group's trials register (up to April 2005). The PCG group's search strategy includes quarterly searches of CENTRAL, monthly searches of MEDLINE; handsearches of 30 journals and the proceedings of major conferences; and weekly current awareness search of a further 37 journals. Further searches were conducted on EMBASE (up to February 2005). We also identified existent Cochrane reviews of interventions for prevention of pre-eclampsia from The Cochrane Library 2005, issue1.

Findings
We found randomised trials evaluating 17 different types of interventions for prevention of pre-eclampsia. Topics included lifestyle changes such as rest and exercise; dietary alterations of salt and energy/protein intake; nutritional supplementation with calcium, magnesium, zinc, folate, garlic, rhubarb, fish oil and other prostaglandin precursors, and anti-oxidant vitamins and minerals; and pharmacological interventions such as aspirin, diuretics, anticoagulants, anti-hypertensive drugs, and nitric oxide. Nine of these interventions are the subject of existent Cochrane systematic reviews, and the other eight are topics for new Cochrane reviews currently under development. Results from systematic reviews show a statistically significant reduction in the risk of pre-eclampsia only with aspirin RR 0.81 (95% CI 0.75,0.88), calcium RR 0.35 (95% CI 0.20,0.60), and anti-oxidants RR 0.58 (95%CI 0.47,0.70).

Conclusions
Aspirin, calcium, and anti-oxidants appear to have a beneficial effect on the risk of pre-eclampsia and its complications. An ongoing individual patient data review of aspirin trials may guide clinical practice on which women will benefit most from aspirin. Calcium supplementation in pregnancy is the subject of a large WHO trial, and if beneficial effects are confirmed, calcium may become part of the routine antenatal care package in areas with low calcium intake. Anti-oxidants hold promise, and are being evaluated in six large trials. Results from these trials will have implications for clinical practice.