

Prevention of Pre-Eclampsia - Is It Possible?

Pages with reference to book, From 25 To 26

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Pre-eclampsia (PE) and Eclampsia are serious complications of pregnancy leading to high maternal and perinatal morbidity and mortality throughout the world. Hypertensive disorders of pregnancy (HDP), mainly PE and Eclampsia, are globally among the four major causes of maternal death, comprising 12% of all deaths¹. In the United Kingdom HDP is one of the two most common causes of maternal deaths². In Pakistan, an analysis of 644 maternal deaths in hospitals of the four provinces showed hypertensive disease, mostly eclampsia, to be the second most common cause (18.6%) preceded only by haemorrhage (21%)³. In a community survey of maternal deaths in Karachi, eclampsia again was the second most common cause⁴. Data regarding maternal morbidity is not well documented. It is known however, that serious complications are directly related to the severity of the pre-eclampsia. In this issue a study of 120 cases of PE from a tertiary hospital of Karachi shows that a dangerous complication like HELLP (Haemolysis, elevated Liver Enzymes, low Platelets) was seen more often in women who had severe PE. In these women complications like seizures, disseminated intravascular coagulation (DIC) and acute renal failure were significantly higher than those who did not have HELLP syndrome. One of the risk factors identified was the 'unbooked status' i.e., lack of antenatal care. The high perinatal morbidity and mortality seen in PE is due to intrauterine growth retardation (IUGR), intrauterine death of the foetus and premature delivery. In the study referred to above however, the perinatal outcome though adverse, was not significantly so in the two groups.

What can be done to reduce this high maternal and foetal loss? Once the complications have set in, prompt and effective treatment and timely delivery will save many lives. But many a times this may be too late. Is it possible, therefore, to prevent pre-eclampsia and eclampsia? Eclampsia is almost always preventable. Good antenatal care will identify pre-eclampsia in the early stages and effective management will prevent a woman from developing complications. But what about Pre-eclampsia? This question remains unresolved, though various strategies for its prevention are being tried. PE is a multisystem disorder affecting almost all the systems of the body. Its exact aetiology is unclear though there is now an increased understanding of its pathophysiology. PE is associated with structural and occlusive changes in the spiral arteries of the uterus leading to underperfusion of the placenta. There is characteristically imbalance between Prostacyclin 12, a vasodilator and anti-platelet agent and thromboxane A₂, a vasoconstrictor and platelet aggregating agent, with decreased production of the former and increase of the latter⁵. Hence any drug or agent can alter this ratio would be helpful in preventing PE. This forms the rationale for the use of Aspirin, an anti-platelet drug, in preventing PE. Aspirin acts by irreversible acetylation of the enzyme cyclo-oxygenase thus selectively inhibiting the production of thromboxane. Beaufrils and co-workers⁶ were the first to report a beneficial effect of low dose (150 mg) aspirin and dipyridamol 300 mg in significantly reducing PE in randomised 102 women, mostly multiparous, at high risk of developing PE. This was followed by a series of small studies showing reduction of upto three-quarters in PE with low dose aspirin (60 mg)⁷. Much enthusiasm on the use of aspirin ensued. However, the randomised placebo-controlled Collaborative Low Dose Aspirin Study in Pregnancy (CLASP)⁸ carried out on 9364 women in 16 countries has not confirmed this beneficial effect. The CLASP group does not support the "routine prophylactic or therapeutic administration of anti-platelet therapy in pregnancy to all women at increased risk of PE or IUGR". Low dose aspirin may be justified, they suggest, in women where PE sets in early leading to very preterm delivery. The group recommends starting aspirin prophylactically in such cases in early second trimester. The study found aspirin to be safe for the foetus and newborn with no increased risk

of bleeding⁸. Another collaborative randomised trial of 60 mg Aspirin on 1009 women however, does not show any beneficial effect on any category of high risk women and the use of Aspirin is not advocated⁹. More large scale studies are being earned out on the role of aspirin in preventing PE and the last word has not yet been said. Another drug which shows hope is Calcium. Populations who have a high intake of Calcium in their diet have been seen to have a low incidence of PE¹⁰. Several studies of Calcium supplementation of upto 1.5 - 2G daily have shown good results¹¹. A meta-analysis of randomised control trials concluded that Calcium supplementation reduces blood pressure and the incidence of PE and hypertension during pregnancy¹². However, most of the studies included in the meta-analysis were small studies and results of larger trials are awaited. Natural oils, both of fish and plants have been tried for prophylaxis of PE. They are rich in essential fatty acids and stimulate the production of the vasodilator prostaglandins. Fish oils favourably affect the balance between prostacyclin and thromboxane. In a randomised, double blind, placebo controlled trial on women with high risk pregnancy, fish oil supplementation did not affect the frequency of proteinuric or non-proteinuric pregnancy-induced hypertension, though a small protective effect remained a possibility¹³. Other drugs including diuretics, oxidants and dietary measures like restriction of salt, weight restriction, zinc and magnesium supplementation have all been tried but none have been seen to be of benefit. Some of them, like any other therapy, have potential side effects¹⁴. The bottom line is that at present there is no effective prophylaxis against PE. Research for better understanding of the aetiology and pathophysiology of PE is ongoing, because only then can an effective strategy for prevention be planned. Meanwhile the high maternal and perinatal morbidity and mortality associated with HDP, both in the developing and developed countries, can only be prevented by effective antenatal care of pregnant women particularly those at high risk and appropriate intervention if and when required.

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