Pregnancy Induced Hypertension — Recent Observations

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Pregnancy Induced Hypertension (PIH) still continues to be the second killer of pregnant mothers all over the world in developing countries (Anderson 1984). This complex disease continues to defeat all efforts to bring about a satisfactory and rewarding policy of management because of its poorly understood pathological basis.

In this presentation the author wishes to bring new observations under the focus of clinicians with a particular objective to find some light thrown on this complex syndrome. Instead of trying to project all under mirror of one understanding which will confuse more than help in the clarification of the jungle of piecemeal pathological observations attempt will be made in this communication to highlight the important and meaningful research findings in an attempt to help understand at least some basis of this disease.

Basic Pathology: - Currently, there are enough scientific evidences to suggest that the initial trigger to the whole sequence of events is provided by the failure of trophoblastic invasion of the spiral decidual arteriole in the placental bed. There are now ample evidences to substantiate this pathological starting episode.

Effect of Failure of Trophoblastic Invasion

1. Ischaemia — It can be easily understood that the failure of trophoblastic invasion of decidual arterioles would be likely to result in failure of continuing adequate blood supply to the placental intervillous bed. This ischaemia may now set up a situation of stress which would soon be followed by — (a) Immunological response amongst which the most important participant would be the activity of TNF alpha is the cytokine inflicts damage to the vascular endothelium and also liberates reactive oxidising species (ROS). The polymorphonuclear neutrophils (PMN) liberate adhesin molecules — $VCAM_1$ and $VCAM_2$ indicating the vascular circulating adhesin molecules responsible for adhesion of platelets. Further these PMN by their periodic burst undergo degranulation. Those granules generate highly toxic material synthesising the dangerous molecules of lactoferria followed by CD-11B, CD-18, CD62L and many other noxious substances. The PMN further induces and magnifies the TNF morbidities.

The Arena of pathology in the placental bed is now virtually a picture of stage of destruction which are poised to damage multiple organs of the patient.

The damaging effects are due to liberation of free radicals and consumption of antioxidants like superoxididismutase (Chen et al 1994) increasing the concentration of elements like hydrogen peroxide and O_3. All these are because of the subversion of mitochondrial electron liberation resulting in circulating unpaired electron — free radicals.

Having understood the basic starting damage inflicted by ischaemic placental bed, damaging effects on other tissues may now be discussed serially.

1. Endothelium: - The vascular endothelium suffers considerable damage by superoxide and lipid peroxide. The damaged endothelium becomes

hyperpermeable resulting in leakage of colloids into the extravascular space. The oncotic pressure in extra vascular space now gradually increases drawing fluid from the intravascular compartment leading to reduction of circulating blood volume and increased viscosity. This reduction of fluid in the extra vascular compartment ultimately leads to tissue oedema and precipitates crisis like pulmonary oedema which is aggravated by generalised vasospasm and rise in pulmonary capillary wedge pressure (PCWP).

Other Effects of Endothelial Damage: -

A). Reduction of prostacyclin and increase of thromboxane A_2. This change leads to slowing of circulation and favours platelet aggregation.

B). Reduction of vascular nitric oxide — Increase of endothelin-1 leading to vasospasm.

C). Liberation of serotonin and precipitating fibrinoid changes in hepatic endothelium HELLP syndrome.

Thrombosis in PIH: - PIH is a condition in which intravascular thrombosis is one of the most dreaded vascular complications. The tendency to thrombosis is because of the following factors —

A). Initiation of thrombosis may be due to factor-V Leyden mutation. In this condition this abnormal factor-V which is because of the replacement of arginine at the site of 506 of amino acid sequence by glutamine (Tan and Swiet 1998). This mutational change of genetic origin reduces the natural anticoagulant activity of protein-C and protein-S by its resistance to activation of protein-C and opposing these two natural anticoagulants in the blood making the patient highly susceptible to intravascular thrombosis.

B). The second factor responsible for thrombosis is the reduction of prostacyclin and increase to the thromboxane A_2.

C). Increased platelets aggregation due to lipid peroxide liberated after TNF alpha action.

D). Reduction of antithrombin-III which is also associated with great danger of intravascular thrombosis.

Systemic Vascular Pathology: - PIH is associated with marked vasospasm caused by (a) reduction of nitric oxide and increase of endothelin-1 action (b) serotonin liberated after platelet aggregation (c) dominance of endothelin-1.

The systemic changes characterised by the severe vasospasm may be manifest in — (a). Cranial perfusion. (b) Cardio pulmonary circulation. (c) Placental bed circulation. (d). Renal circulation.

I. Cranial Perfusion: - Headache has long be known to be the fore runner of eclamptic convulsion. Though the exact cause of headache is not clearly understood, recent advent of Doppler has solved the problem of significance of severe headache by enabling the researchers to study cranial perfusion pressure (CPP) (Belfort, 1999)

Belfort (1999) have recently made detailed study of the middle cerebral artery and its changes in preeclampsia with severe headache using the colour doppler. The summary observation of these authors reveal the relation of headache with presence of abnormal cerebral perfusion pressure (CPP). These authors have further categorised two types of cranial perfusion pressure: -

1. Hypoperfusion indicating the use of nimodipine a drug known to increase the CPP in the therapy.
2. Magnesium sulphate in cases of hyperperfusion which is known to reduce the CPP and prevent cerebral oedema. It is interesting to note that nimodipine normally increases the CPP whereas magnesium sulphate reduces the CPP.

II. Cardiopulmonary perfusion: Pulmonary oedema is one of the dreaded complication of severe preeclampsia. It is now believed that the incidence of cerebral vascular accident in (CVA) eclampsia is becoming less while the incidence of pulmonary oedema has gone up all over the world. The reduction of CVA is believed to be due to the use of antihypertensive therapy in UK (Walker 1983). The pulmonary oedema can be either of the two types: namely cardiogenic pulmonary oedema and non cardiogenic pulmonary oedema. The former is due to left ventricular failure resulting from severe

hypertension which needs to be treated on warfooting. The latter is due to the rise of extravascular oncotic pressure as a result of the migration of colloids from intra vascular to extravascular compartment. In this condition dehydration of the patient is urgently indicated.

III. Placental Bed Perfusion: - Severe preeclampsia may lead to the premature separation of the placenta with formation of retro-placental clot and dissemination of thrombotic agents released into maternal circulation. Very serious complication like disseminated intravascular coagulation may set in threatening the patient's life.

In the final part of this presentation attempt will be made to enlist some of the ingredients recovered from the preeclamptic maternal plasma which are considered to be the breakdown products of endothelium and placental bed.

1. Maternal activin and inhibin particularly maternal inhibin — A which is found in larger amounts than normal.
2. Transforming growth factor of beta family, a large group of proteins involved in stimulation of inhibition of cellular differentiation and proliferation associated with morphogenesis. These are produced by placental decidua and fetal membranes indicating disintegration.
3. The other endothelial breakdown product is fibronectin which is indicative of endothelial damage.
4. Rheological changes: The cell membrane of RBC may undergo thickening and loss of elasticity resulting in clumping of RBC in capillaries hampering tissue perfusion.

In conclusion it is hoped that the author has been able to highlight very important and salient discoveries made through research in the recent times all over the world with a promise of better survival and salvage rate of patients with PIH and severe pre eclampsia.

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