

ONCOTIC THERAPY IN MANAGEMENT OF PREECLAMPSIA

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Oncotic therapy for preeclampsia (PE) along with antihypertensive agents has a clear pathophysiologic basis. PE is a vasospastic disorder characterized by hyperdynamic circulation with increased peripheral, uterine and umbilical arterial resistance, and decreased circulating blood volume, hemoconcentration and decreased colloid-osmotic plasma pressure (hypovolemia), with a high risk of intravascular thrombosis. These lead to vasoconstriction, uteroplacental hypoperfusion, hyperviscosity plasma volume hemoconcentration and constriction (hematocrit > 0,38), with erythrocyte deformability and increased platelet aggregation, resulting in and increased systemic vascular resistance.

Oncotic therapy in PE is aimed at improving and maintaining uteroplacental and maternal tissue perfusion, isovolemic hemodilution and thromboprophylaxis, thus reducing the risk of hypotension and fetal distress.

In severe PE, a reduced plasma colloid-osmotic pressure has been described in prepartal but not in postpartal period, thus oncotic therapy being contraindicated in the puerperium. An aggressive fluid treatment is associated with a risk of pulmonary or cerebral edema. Crystalloid solutions such as Ringer's lactate should be infused at a rate of 75 mL/h, and colloid solutions (e.g., hydroxyethyl starch-HAES) at a rate of 500 mL over more than 4 h. Intravascular administration of colloid solutions increases intravascular colloid-osmotic pressure and binds water in the intravascular space, thus leading to hypervolemic hemodilution.

Hypovolemia/hemoconcentration with oliguria and central venous pressure (CVP) <4 cm H₂O is an indication for oncotic therapy to achieve a target CVP of 4-8 cm H₂O.

Dextran 40000 and 70000, 6% and 6 / 10% HAES, 3% gelatine, and 5% albumin are used as oncotics. The combined electrolyte solution of Ringer's lactate (Hartmann's solution) has a similar but much shorter effect, whereas gelatine has not been used in clinical practice anymore.

There are relatively few recent literature reports of clinical studies of oncotic therapy for PE (Table 1). Belfort et al. advise minimal volume expansion in severe PE with decreased cardiac index and increased vascular resistance due to reduced plasma volume, however, with continuous hemodynamic monitoring. Rafferty et al. suggest aggressive antepartum vasodilative and intravenous fluid therapy. Henderson et al. employed invasive approach to measure hemodynamic parameters in 15 postpartum women with severe pregnancy induced hypertension. They found a hyperdynamic pulmonary/cardiac function with the development of pulmonary edema at high pulmonary capillary pressure due to decreased colloid-oncotic plasma pressure and consequential capillary hyperpermeability, thus they do not recommend postpartum oncotic therapy. Using Swan-Ganz thermodilution catheter, Groenendijk et al. recorded low cardiac index, low pulmonary capillary pressure and high systemic vascular resistance in pregnant women with PE. Vasodilative therapy with dihydralazine resulted in systemic vascular resistance reduction with stable pulmonary capillary pressure, whereas intravascular

expansion had no effect on blood pressure values with a decrease in systemic vascular resistance.

Normalization of fetal and maternal hemodynamics by combined therapy with antihypertensives and plasma expanders (500 mL dextran) was demonstrated by simultaneous cerebroumbilical ratio Doppler sonography and uterine artery sonography. Heillman et al. suggest therapy with volume expanders (10% HAES) for hypertension induced IUGR, whereas Hubner and Sander indicate hypervolemic hemodilution in order to maintain and improve uteroplacental and maternal perfusion in IUGR. They infused 500 mL of 10% HAES with 500 mL Ringer's lactate over 10 days in pregnant women with hemoconcentration (Htc >0.38) and IUGR, and found a correlation of maternal hematocrit decrease, normalization of Doppler parameters of cerebroumbilical circulation, fetal aorta and uterine artery with fetal growth up to 36th week of gestation, whereafter the results obtained turned unfavorable indicating abortion. In our study, we observed a decrease in hematocrit and fibrinogen; a nonsignificant platelet count decrease; and a statistically significant diastolic pressure and URI reduction. Upon administration of HAES in IUGR and PE women with hemoconcentration, Heilmann recorded a significant reduction in the incidence of IUGR (52% vs 34%), with favorable hemorheological parameters, i.e. increase in cardiac output and decrease in Htc, erythrocyte aggregation and plasma viscosity, thus suggesting HAES as a safe and efficient colloid substance for plasma expansion in pregnancy. No maternal complications have been reported with this protocol of HAES infusion. Alfireviæ et al. administer albumin by rapid infusion as a preload (500 mL over 20 min) in severe PE. Hydralazine and albumin are coadministered if median arterial pressure is >140 mm Hg. The authors advise that caution be exercised on intravascular volume load with colloid and crystalloid solutions in order to maintain normal function of the heart, kidneys and placental perfusion, with a minimal risk of water overdosing and pulmonary edema. After albumin preload, crystalloid fluid 85 mL/h (Ringer's lactate) is prescribed if 4-h diuresis is >100 mL. If diuresis is <100 mL/4 h and CVP >8 cm H₂O, 100 mL colloid are administered in rapid infusion over 10 min; if CVP <8 cm H₂O persists, a maximum of 500 mL colloid are given. Considering their "dry regimen", the authors agree that the total amount of colloid fluid should not exceed 1000 mL. In one of his studies, Heilmann investigated the effects of hemodilution therapy with 10% HAES on coagulation and other rheological maternal and fetal parameters in IUGR and PE. The favorable hemodilution effect of HAES in 36 study women manifested as a decrease of hematocrit from 40.4% to 36%, fibrinogen from 3.9 to 3.6, platelet count from 220 to 202, factor VIIIIR from 160 to 140, while aPTT from 31 to 22 sec. and uric acid concentration from 4.4 to 4.5. Light microscopy revealed a vacuolized trophoblast and placental stromal cells. Differences in the values of umbilical hemoglobin and hematocrit as compared with the control group were statistically significant, whereas differences in birth mass and umbilical pH did not reach statistical significance. Belfort et al. investigated Doppler sonography parameters of acute intravasal volume expansion with 100 mL dextran 70 and infusion of 80 mg verapamil in 200 mL NaCl in severe PE. The women were monitored by use of Swan-Ganz catheter and Doppler sonography of uteroplacental and fetal circulation. They found a statistically significant decrease of systemic vascular resistance, and an increase in cardiac index, pulmonary capillary pressure and oxygenation index at birth. The rate of maternal tachycardia was statistically nonsignificant with dextran and significant with verapamil, while fetal heart rate showed nonsignificant changes.

Doppler sonography revealed no significant changes of uteroplacental and umbilical circulation, thus the authors conclude the acute volume expansion and antihypertensive therapy with verapamil to be efficient in lowering hypertension in PE without any adverse effects on uteroplacental circulation but with a favorable effect on maternal hemodynamics.

Consistently with our study, most other authors suggest careful oncotic treatment along with antihypertensive therapy, thus improving the hemorheological parameters of uteroplacental, maternal and fetal circulation. A continuation of the present study may hopefully demonstrate a more favorable perinatal outcome in both neonates