ABSTRACT

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PLACENTAL ABRUPTION Studies on incidence, risk factors and potential predictive biomarkers

Placental abruption, one of the most significant causes of perinatal mortality and maternal morbidity, occurs in 0.5-1% of pregnancies. Its etiology is unknown, but defective trophoblastic invasion of the spiral arteries and consequent poor vascularization may play a role. The aim of this study was to define the prepregnancy risk factors of placental abruption, to define the risk factors during the index pregnancy, and to describe the clinical presentation of placental abruption. We also wanted to find a biochemical marker for predicting placental abruption early in pregnancy.

Among women delivering at the University Hospital of Helsinki in 1997-2001 (n=46,742), 198 women with placental abruption and 396 control women were identified. The overall incidence of placental abruption was 0.42%. The prepregnancy risk factors were smoking (OR 1.7; 95% CI 1.1, 2.7), uterine malformation (OR 8.1; 1.7, 40), previous cesarean section (OR 1.7; 1.1, 2.8), and history of placental abruption (OR 4.5; 1.1, 18). The risk factors during the index pregnancy were maternal (adjusted OR 1.8; 95% CI 1.1, 2.9) and paternal smoking (2.2; 1.3, 3.6), use of alcohol (2.2; 1.1, 4.4), placenta previa (5.7; 1.4, 23.1), preeclampsia (2.7; 1.3, 5.6) and chorioamnionitis (3.3; 1.0, 10.0). Vaginal bleeding (70%), abdominal pain (51%), bloody amniotic fluid (50%) and fetal heart rate abnormalities (69%) were the most common clinical manifestations of placental abruption. Retroplacental blood clot was seen by ultrasound in 15% of the cases. Neither bleeding nor pain was present in 19% of the cases. Overall, 59% went into preterm labor (OR 12.9; 95% CI 8.3, 19.8), and 91% were delivered by cesarean section (34.7; 20.0, 60.1). Of the newborns, 25% were growth restricted. The perinatal mortality rate was 9.2% (OR 10.1; 95% CI 3.4, 30.1).

We then tested selected biochemical markers for prediction of placental abruption. The median of the maternal serum alpha-fetoprotein (MSAFP) multiples of median (MoM) (1.21) was significantly higher in the abruption group (n=57) than in the control group (n=108) (1.07) (p=0.004) at 15-16 gestational weeks. In multivariate analysis, elevated MSAFP remained as an independent risk factor for placental abruption, adjusting for parity ≥ 3, smoking, previous placental abruption, preeclampsia, bleeding in II or III trimester, and placenta previa. MSAFP ≥ 1.5 MoM had a sensitivity of 29% and a false positive rate of 10%. The levels of the maternal serum free beta human chorionic gonadotrophin MoM did not differ between the cases and the controls. None of the angiogenic factors (soluble endoglin, soluble fms-

like tyrosine kinase 1, or placental growth factor) showed any difference between the cases (n=42) and the controls (n=50) in the second trimester. The levels of C-reactive protein (CRP) showed no difference between the cases (n=181) and the controls (n=261) (median 2.35 mg/l [interquartile range {IQR} 1.09-5.93] versus 2.28 mg/l [IQR 0.92-5.01], not significant) when tested in the first trimester (mean 10.4 gestational weeks). *Chlamydia pneumoniae* specific immunoglobulin G (IgG) and immunoglobulin A (IgA) as well as *C. trachomatis* specific IgG, IgA and chlamydial heat-shock protein 60 antibody rates were similar between the groups.

In conclusion, although univariate analysis identified many prepregnancy risk factors for placental abruption, only smoking, uterine malformation, previous cesarean section and history of placental abruption remained significant by multivariate analysis. During the index pregnancy maternal alcohol consumption and smoking and smoking by the partner turned out to be the major independent risk factors for placental abruption. Smoking by both partners multiplied the risk. The liberal use of ultrasound examination contributed little to the management of women with placental abruption.

Although second-trimester MSAFP levels were higher in women with subsequent placental abruption, clinical usefulness of this test is limited due to low sensitivity and high false positive rate. Similarly, angiogenic factors in early second trimester, or CRP levels, or chlamydial antibodies in the first trimester failed to predict placental abruption.

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