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IZBOR PARAMETARA HEMOSTAZE ZA PRAĆENJE NORMALNE I KOMPLIKOVANE TRUDNOĆE

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Koncentracije proteina plazme uključenih u proces koagulacije se menjaju tokom normalne trudnoće što remeti ravnotežu koja postoji između prokoagulantnog i antikoagulantnog sistema. Ove promene obuhvataju povećanje aktivnosti faktora koagulacije, povećano stvaranje fibrina i supresiju fibrinolize. Na ovaj način se fiziološkim mehanizmima smanjuje rizik od gubitka krvi u trudnoći, ali se povećava rizik od pojave tromboze. Usled tromboze placentarnih krvnih sudova može se javiti placentarna insuficijencija koja dovodi do pojave ponavljajućih abortusa, zastoja u rastu fetusa, eklampsije, intrauterine smrti ploda i prevremenog porođaja. Uzroci ovih pojava su promene koje se dešavaju unutar protein C koagulantnog sistema. Mutacija na genu za faktor V (tzv. Factor V Leiden mutacija) gde je arginin 506 zamenjen glutaminom, stvara mutirani faktor V koji ispoljava normalnu prokoagulantnu aktivnost, ali je manje osetljiv na APC. Stanje koje karakteriše slab antikoagulantni odgovor na APC naziva se APC rezistencija. Cilj ovog rada je bio da se ispita stanje koagulantnog, antikoagulantnog i fibrinolitičkog sistema u normalnoj i komplikovanoj trudnoći kao i funkcionalnost protein C antikoagulantnog sistema u trudnoći različitih gestacijskih starosti i APC rezistencija. Za procenu stanja hemostaznog sistema određivani su sledeći parametri: protrombinsko vreme, parc. protrombinsko vreme, fibrinogen, fibrin monomer, D-dimer, antitrombin III, TAT kompleks, plazminogen, PAI, faktor XIII, protein C, protein S, Protein C Global i aktivirani protein C. Ispitivane su trudnice sa normalnom i komplikovanom trudnoćom različite gestacijske starosti. Posebnu grupu činile su trudnice koje su imale dva ili više uzastopnih pobačaja. Za određivanje parametara hemostaze korišćeni su komercijalni testovi firme »Behring« zasnovani na spektrofotometrijskom i koagulometrijskom merenju i ELISA metodi. Pokazano je da su fibrinogen, fibrin

CHOICE OF HAEMOSTASIS PARAMETERS FOR MONITORING OF NORMAL AND COMPLICATED PREGNANCY

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The concentrations of plasma proteins involved in the process of coagulation are changed during the normal pregnancy, disturbing the balance between procoagulant and anticoagulant system. These changes include the increased activity of coagulation factors, the increased fibrin production and suppression of fibrinolysis. In this way, the risk of loosing blood during pregnancy is reduced by physiological mechanisms, but the hazard of developing thrombosis is increased. Placental insufficiency may occur due to thrombosis of placental blood vessels, leading to repeated miscarriages, retardation of foetal growth, eclampsia, intrauterine foetal death and preterm birth. The causes of these incidents are the changes occurring within protein C coagulation system. The mutation in gene for factor V (so-called Factor V Leiden mutation), where the arginine 506 is replaced by glutamine, produces the mutated factor V having normal procoagulant activity but it is less responsive to APC. The condition characterized by poor anticoagulant response to APC is called the APC resistance. The aim of this study was to test the condition of coagulant, anticoagulant and fibrinolytic system in normal and complicated pregnancy as well as the function of protein C anticoagulant system in pregnancy of various gestation periods and APC resistance. The following parameters were measured for the evaluation of haemostasis system: prothrombin time, partial prothrombin time, fibrinogen, fibrin monomer, D-dimer, antithrombin III, TAT complex, plasminogen, PAI, factor XIII, protein C, protein S, Protein C Global and activated protein C. The testing was performed in pregnant women with normal and complicated pregnancy of various gestation periods. A special group consisted of pregnant women having two or more consecutive miscarriages. Commercial »Behring« tests based on spectrophotometric and coagulometric measure-

monomer, TAT kompleks i PAI kao parametri hemostaze dobri markeri veličine hiperkoagulabilnog stanja kod trudnica. U ovom radu statistički značajno niže vrednosti PC-NR i APC-NR dobijene su u sva tri vremenska perioda kod trudnica sa hipertenzijom i ponavljajućim pobačajima u odnosu na zdrave trudnice čime je pokazano da je antikoagulantna aktivnost aktiviranog proteina C značajno smanjena u trudnoći, naročito u trudnoći praćenoj komplikacijama. Dijagnostička vrednost parametara hemostaze kao markera trombotičkih promena kod trudnica ispitana je analizom. Prema dobijenim podacima PC-NR i APC--NR su pokazali zadovoljavajuću dijagnostičku tačnost kao markeri trombotičkih promena u trudnoći tačnije kao dobri pokazatelji razvoja rezistencije na aktivirani protein C u trudnoći.

Ključne reči: tromboza placente, Protein C rezistencija, faktor V Leiden, trudnoća.

ments and ELISA method were used to determine the parameters of haemostasis. It was shown that fibrinogen, fibrin monomer, TAT complex and PAI, as parameters of haemostasis, were good markers for the extent of hypercoagulable condition in pregnant women. In this study, significantly lower values of PC-NR and APC-NR were obtained in all three time periods in pregnant women with hypertension and repeated miscarriages in comparison to healthy controls, what verified that anticoagulant activity of activated protein C was significantly reduced during pregnancy, and especially in pregnancy associated with complications. The diagnostic value of haemostasis parameters as markers of thrombotic changes in pregnant women was tested by ROC analysis. According to the obtained results, PC-NR and APC-NR showed satisfactory diagnostic accuracy as markers of thrombotic changes in pregnant women, more precisely, they were found to be good indicators of resistance to activated protein C in pregnancy.

Key words: placental thrombosis, protein C resistance, Factor V Leiden, pregnancy.