P-358 Characteristics of patients with inherited thrombophilia and anticoagulant treatment in repeated implantation failure (RIF) and recurrent pregnancy loss (RPL)

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Study question: Do patients with inherited thrombophilia associated to RIF and RPL benefit from anticoagulant therapy?

Summary answer: Low molecular weight heparin (LMWH) in patients with medium and high risk of hereditary thrombophilia, associated with RIF could improve the reproductive prognosis.

What is known already: Thrombophilia is a condition that can be acquired and/or inherited genetically, that is characterized by the predisposition of patients to form venous and arterial thromboembolic events. Inherited thrombophilia has been associated with different complications during pregnancy, such as RPL. Genetic variants linked to hereditary thrombophilia can be classified by the thromboembolic risk: low (F12, F13A1, FGB), medium (MTHFR, PROCR, PROS1, SERPINC1, SERPINC1 PAI-1) and high (F2, F5, GP1BA), according to Martinez - Zamora. RPL rate may reduce with anticoagulant therapy. However, there is no conclusive evidence that prophylactic treatment improves the pregnancy rate in infertile women during IVF.

Study design, size, duration: We performed a prospective observational study which included patients referred to Ceras Clinic between March 2018 and March 2020, due to RPL (n=38) and RIF (n=40). All patients underwent genetic analysis for hereditary thrombophilia(F13, F2, F5, FGB, GP1BA, MTHFR C677T, MTHFR A1298C, PAI1,, PROCR, SERPIN1 CM910058, SERPIN 1 CM920113 ,F12, PROS1) by Sanger sequencing. The characteristics of anticoagulant therapy with clinical pregnancy rate and LBR were analyzed, using chi-squared test with STATA version 16.

Participants/materials, setting, methods: Patients have been included in the study according to their past medical history (stroke or myocardial infarction, personal or familiar history of deep vein thrombosis or pulmonary embolism, smoking, hormone replacement therapy), and reproductive history. Two groups were formed, the first group (n=40) corresponds to RIF, and the second (n=38), RPL. Genetic study of hereditary thrombophilia (11 genes) was performed to examine the genetic risk and assess the administration of anticoagulant therapy.

Main results and the role of chance: The prevalence of pathological antecedents in patients with RIF and RPL was not statistically significant (p>0,05), indicating that the factors that contribute to poor reproductive outcomes in these two groups of patients could be similar. Patients with RIF had a medium risk of thrombophilia in 65%, followed by low risk in 32.5% and high risk in 2.5%. RPL group presented 78.95%, 15.79% and 5.26%, respectively. All patients with medium and high risk for thrombophilia received anticoagulation. Clinical pregnancy rate (69.7%) and live birth rate (63.64%) were not statistically significant (p> 0.05) in RPL with anticoagulant therapy, compared to RPL group who did not received treatment (clinical pregnancy rate and live birth rate in 60%). Therefore, it is proposed that there may be other factors associated with abortions that require investigation. However, clinical pregnancy rate (77.14%) and live birth rate (74.29%) were statistically significant (p < 0.05) in RIF with anticoagulant therapy, compared to RIF group that did not received treatment (clinical pregnancy rate and live birth rate in 20%). This suggests that there could be a beneficial factor due to anticoagulation. Further studies are needed to assess that anticoagulant treatment could improve obstetric outcomes in patients with RIF and RPL.

Limitations, reasons for caution: The small number of patients assessed is the main limitation of this work. Larger studies must be designed to accurately determine participation of each mutation associated with recurrent implantation failure and recurrent pregnancy loss. The role of anticoagulant therapy should be evaluated in randomized clinical trials.

Wider implications of the findings: Establishing a stronger evidence base implies that future studies should include large population groups. It is primordial to assess whether it is cost-effective to determine the risk of inherited thrombophilia in RIL and RPL, to increase the live birth rate by anticoagulant therapy. The information is controversial to this day.

Trial registration number: 'not applicable'