Conitec

Recomendation report

DRUGS

Nº 503
January/2020

Diagnostic tests for thrombophilia in pregnancy

Brasília – DF
2020

Technologies: Testing for prothrombin gene mutation (G202110A), protein C functional assay, protein S functional assay, anti-beta2-glycoprotein I - IgG, lupus anticoagulant

Indication: Diagnosis of thrombophilia in pregnancy

Applicant: Secretariat of Science, Technology and Strategic Inputs (Ministry of Health of Brazil)

Background: The G202110A mutation of the prothrombin gene causes an increase in plasma levels of this protein in approximately 30%, resulting in increased thrombin generation and exacerbation of coagulation, associated with a 3-fold higher risk for venous thrombosis compared to the general population. Protein C is a natural anticoagulant, vitamin K-dependent, synthesized in the liver, and its deficiency can be inherited or acquired. Inherited protein C deficiency leads to a hypercoagulable state, observed in 2%-4% of patients with a first episode of venous thrombosis. Protein S is a vitamin K-dependent plasma glycoprotein synthesized in the liver, which acts as a cofactor for activated protein C in the proteolytic degradation of activated factors V and VIII. Due to better reproducibility and clinical specificity compared with anticardiolipin antibodies (aCL), antibodies against β_2GPI (anti-β_2GPI) of IgG and IgM classes have been included as laboratory criteria for antiphospholipid antibody syndrome (APS). Several studies have shown an association between the presence of aβ_2GPI and thrombosis. The lupus anticoagulant is an antibody that prolongs phospholipid-dependent coagulation by binding to a part of an antigenic determinant on the phospholipid portion of prothrombinase. It prolongs all phospholipid-dependent coagulation tests, including the activated partial thromboplastin time and prothrombin time (1.5–7).

Scientific evidence: Currently, the recommendation to perform thrombophilia testing includes all the tests mentioned above, but only in the following situations: (a) Pregnant women with a personal history of venous thromboembolism (VTE), with or without recurrent risk factor, and without previous thrombophilia testing; and (b) Pregnant women with a first-degree relative with a history of high-risk inherited thrombophilia. Hereditary factors: factor V Leiden; prothrombin gene mutation; deficiencies of protein C, protein S and antithrombin III; APS: aCL IgG and IgM, anti-β2GPI IgG and IgM; lupus anticoagulant.

Budget impact analysis: The total budget impact of incorporating diagnostic tests for thrombophilia in pregnancy into the Brazilian Public Health System (SUS), in a scenario with market share, was estimated to range from approximately BRL 5.4 to BRL 12.2 million after five years.

Considerations: Considering that tests for accurate diagnosis of thrombophilia in pregnancy are not yet available in SUS – which have been indicated in the Recommendation Report No. 502/2019 - Clinical Protocol and Therapeutic Guidelines for the Prevention of Venous Thromboembolism in Pregnant Women with Thrombophilia (6), approved by the Deliberation Record No. 493/2019 –, the Conitec's members decided to recommend the incorporation of diagnostic tests for thrombophilia in pregnancy.

Final Recommendation: The Conitec's members present at the 84th Ordinary Meeting, on December 4th, 2019, unanimously decided to recommend the incorporation of the following diagnostic tests for thrombophilia in pregnancy, in the scope of SUS, according to the Clinical Protocol and Therapeutic Guidelines: a) Prothrombin gene mutation; b) Protein C functional assay; c) Free protein S assay; d) Anti-beta2-glycoprotein - IgG; e) Anti-beta2-glycoprotein - IgM; and f) Lupus anticoagulant. The Deliberation Record No. 494/2019 was signed.

Decision: To incorporate the following diagnostic tests for thrombophilia in pregnancy, in the scope of SUS, according to the Clinical Protocol and Therapeutic Guidelines: a) Prothrombin gene mutation; b) Protein C functional assay; c) Free protein S assay; d) Anti-beta2-glycoprotein - IgG; e) Anti-beta2-glycoprotein - IgM; and f) Lupus anticoagulant, according to Ordinance No. 1, published in the Official Gazette of the Federal Executive No. 8, Section 1, page 65, on January 13th, 2020.