Anticoagulant Proteins in a Population of Mexican Mestizo Donors

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Background: To determine the activity of antithrombin (AT), protein C (PC), and protein S (PS), as well as the frequency of deficiencies of these proteins in a population of healthy Mexican mestizo blood donors.
Methods: AT, PC, and PS were determined from 1,502 plasma samples of healthy blood donors by using commercial kits in a coagulometer 4 STA (Diagnostica Stago, Asnières, France).
Results: A total of 741 women and 761 men were under study. They were divided into age range groups (18–24, 25–34, 35–44, 45–54, and 55–64 years). Activity of AT, PC, and PS was determined. For AT, activity values were specific for each age group according to gender when it had to do with PS, as well as when PC was determined. Frequencies of AT, PC, PS, and activated PC resistance activity deficiencies were obtained from reference levels (RLs) and average levels of this study. Differences were found between both frequencies for AT, PC, and PS, and the average levels obtained were used in this study. The frequencies of the activity deficiencies obtained through the values gotten in this population were: AT, 0.6%; PC, 1.06% (which is higher than the one obtained using the RLs described by commercial kits 0.33% and 0.66%, respectively); and PS, 1% (which is less than 4.5%).
Conclusions: It is necessary to know the characteristics and biological behavior of the coagulation proteins in the Mexican population because the RLs used have been established for populations that are genetically different.

INTRODUCTION

Hypercoagulable states are disorders related to hemostatic imbalance and predispose individuals to develop thromboembolic events.[1] In hereditary thrombophilia, the most common disorders are deficiencies of antithrombin (AT), protein C (PC), and protein S (PS), as well as mutations of prothrombin gene (*PT20210*), which leads to elevated factor II plasma levels, dysfibrinogenemia, and activated protein C resistance (APCR)

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secondary to the factor V Leiden mutation (FVL), among others.[2]

The coagulation factors activity is regulated by natural plasmatic inhibitors such as AT, PC, and PS.[3] It has been reported that the inherited deficiency of these proteins occurs in ~15% of patients aged younger than 45 years with venous thrombosis.[4,5]

Plasmatic concentration of AT varies with race, age, gender, and the methodology used.[6,7] In women aged between 19 and 60 years, slightly lower values have been reported compared with those who are older than 60 years. In men, AT concentration decreases along with age particularly after the age of 60.[8]

Deficiency of PC is inherited in an autosomal dominant way. The 2 main types of heterozygous PC (types I and II) deficiency have been determined by immunoassay for antigenic levels or by functional assay.[9]

PS is a protein that serves as a cofactor of activated PC, the deficiency of this protein is characterized by its low levels and reducing its activity. Several factors, including age, gender, hormonal state, pregnancy, liver disease, and inflammation, may influence plasma PS levels.[10]

APCR has been described as an important cause of venous thrombosis and familial thrombophilia. There are different acquired or inherited causes for APCR including elevated factor VIII levels, oral contraceptives, anti−β2-glycoprotein I antibodies that interfere with the PC/PS system, and FVL, that induces resistance to inactivation of factor V by PC.[11,12] The prevalence of FVL in general population varies. High prevalence has been reported in southeast Europe (9−15%) and the Middle East (13%). It is low in Afro-Americans and Asian population[11,13,14] and very low or absent in Native Americans.[11,15,16] It has been reported that APCR+ is present in healthy Mexican mestizo population (MMP), but FVL has been found with a prevalence of 0.85%,[17] therefore, it is not clear that the APCR+ phenotype is present in this population.

The aim of this study was to determine the activity of the anticoagulant proteins AT, PS, and PC and the frequency of deficiencies of these proteins in a population of healthy Mexican mestizo blood donors (HBD).

MATERIAL AND METHODS

In all, 1,502 HBD of the Centro Médico Nacional siglo XXI (CMN sXXI) were included (Fig. 1). The study was conducted in the Special Coagulation Laboratory, Specialty Hospital CMN sXXI and in the Hematopathology Laboratory of the Morphology Department at the Escuela Nacional de Ciencias Biológicas of the Instituto Politécnico Nacional.

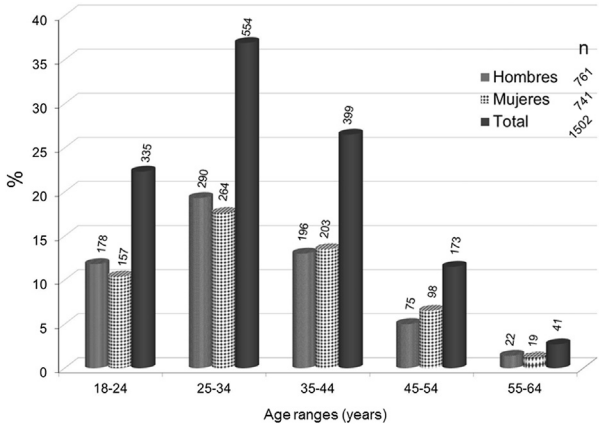

Fig. 1. Distribution percentage of the study population per age.

Procedure

A blood sample from each participant was taken, citrated plasma was obtained at 3.8%. The samples were analyzed using commercial kits in a coagulometer 4 STA (Diagnostica Stago, Asnières, France). Samples with evidence of hemolysis or clot formation were not included.

The functional assay for AT was performed by using an STA-Stachrom® AT Kit (Roche Diagnostics, Mannheim, Germany). This test is considered deficient if the activity is <80%. The normal range proposed in the kit is between 80% and 120%.

The tests for PC and PS were performed by using the STA-Staclot® Protein C and S kits (Roche Diagnostics). The tests are considered deficient if the activity is <70%. (normal range proposed in kit: 70−140%) for PC; and for PS it is considered deficient if PS activity is <65% (normal range proposed in kit 65−140%).

Function of APCR in plasma was determined by using the Coatest APC-R kit (modified APCR method; Chromogenix, Stockholm, Sweden). The results were expressed in a normal range ≥2.1, according to the kit.

In all positive tests (low activity of AT, PC, PS, and APCR), a new sample was obtained, at least 3 months after the first one, to confirm the results. Acquired APCR was determined according to the criteria previously published such as the presence of APCR in the absence of FVL.[18] In all the cases with APCR phenotype, the polymerase chain reaction analysis for the FV R506Q mutation was performed according to the Zöller method.[19]

Statistical Analysis

The Kolmogorov−Smirnov test was used to check whether data distribution was consistent with a