



The Disturbances Of Protein C Among Cardiac Valve Replacement Patients Undergoing Cardiopulmonary Bypass

KEYWORDS

Protein C , Cardiac Valve Replacement , Cardiopulmonary Bypass

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ABSTRACT *Background: Protein C deficiency, either congenital or acquired, may lead to serious thrombotic events such as thrombophlebitis, deep vein thrombosis, or pulmonary embolism. This study was conducted to investigate the disturbances of protein C among cardiac valve replacement patients undergoing cardiopulmonary bypass.*

Objectives: To determine the disturbances of protein C in Sudanese patients among Mechanical valve replacement undergoing cardiopulmonary bypass.

Design: Descriptive Cross sectional study

Methodology: A prosthetic valve was implanted in 150 patients between August 2013 to March 2014. The age of patients ranged between 20 to 80 years with mean of 41years. Protein C was measured by ELISA method.

One hundred and fifty patients underwent valve replacement: 60 patients (40%) had isolated mitral valve replacement (MVR), 46 patients (30.7%) had isolated aortic valve replacement (AVR), 26(17.3%) had duple valve replacement (DVR) and 18(12%) had coronary artery bypass graft (CABG), and 50 healthy individuals were recruited as control group.

Results: Protein C was decreased significantly after cardiopulmonary bypass. Protein C was decreased in about 78.7% of the cases(118patients) and the mean was ($59.8 \pm 21.1\%$) versus the control the mean($111.3 \pm 26.1\%$) and there was significant variation ($p.value < 0.05$) between the patients and controls. About 43 cases(28.7%) had decreased protein C level under 50% postoperative. These results suggest a disturbance of protein C system by extracorporeal circulation. Protein C was decreased significantly after cardiopulmonary bypass and this finding is considered to reflect the activation and consumption of the protein C system in response to generated thrombin.

Conclusions: These results suggest a disturbance of the protein C system by extra corporeal circulation. Protein C was decreased significantly after cardiopulmonary bypass and this finding is considered to reflect the activation and consumption of the protein C system in response to generated thrombin.

Introduction:

Protein C is a vitamin K-dependent protein synthesized primarily by hepatocytes in the liver and plays an important physiologic role in the Protein C Anticoagulant System^(1,2). Protein C, thrombin from blood clots, and endothelial cells, through complex interactions with other factors of the coagulation cascade, contribute to the maintenance of normal hemostatic mechanisms by down-regulating clot formation and by promoting fibrinolysis. The Protein C Anticoagulant System is activated by the binding of thrombin to thrombomodulin, a transmembrane protein receptor on endothelial cells.⁽³⁾ The thrombin-thrombomodulin binding on endothelial cell membranes activates circulating Protein C. Activated Protein C binds to Protein S on the membrane of endothelial cells or platelets. In this Protein C-Protein S complex, activated Protein C is now capable of inactivating coagulation factors Va and VIIIa, down-regulating clot formation. Activated Protein C also enhances the function of tissue plasminogen activator (TPA) by dissociating this molecule from its inhibitor, plasminogen activator inhibitor-1 (PAI-1), thereby facilitating clot dissolution or fibrinolysis.^(1,3)

Protein C deficiency, either congenital or acquired, may lead to serious thrombotic events such as thrombophlebitis, deep vein thrombosis, or pulmonary embolism.⁽⁴⁾ Patients with a congenital heterozygous deficiency may present with venous thrombosis in young adulthood, while patients with the rare homozygous deficiency present with massive thrombosis (purpura fulminans) during the neonatal period.⁽⁵⁾

The prevalence of Protein C deficiency in the general population has been estimated at 1 in 300. In younger patients (<40-45 years) with recurrent venous thrombosis, the frequency of Protein C deficiencies may be as high as 10 to 15%.⁶⁻⁷ Acquired Protein C deficiency may be seen in liver disease, extensive thrombotic episodes, surgery, oral anti-coagulant therapy, antiphospholipid syndrome, etc. A decreased Protein C activity in plasma may be the result of low concentrations and function (type I) or only low function (type II).⁽⁶⁾

Patients with prosthetic valves are at risk of thromboembolic complications, including systemic embolization, most commonly cerebral, and prosthetic thrombosis causing valve obstruction and/or regurgitation. The risk of thromboembolic events is higher with mechanical than with bioprosthetic valves, higher with mitral than with aortic prosthetic valves, and higher in the early (<3 months) versus late postoperative phase.^(7,8,9)

The risk also is increased in the presence of concomitant risk factors for thromboembolism, including atrial fibrillation, left ventricular (LV) dysfunction, left atrial dilation, previous thromboembolism, and hypercoagulable condition.⁽¹⁰⁾

Patients with mechanical prostheses require lifelong anticoagulation with warfarin. The choice of optimum international normalized ratio (INR) target for oral anticoagulation should also take into account the thrombogenicity of the individual

prosthesis.⁽¹¹⁾

The protein C pathways are the specific chemical reactions that control the level of expression of activated protein C (APC) and its activity in the body. Protein C is pleiotropic, with two main classes of functions: anticoagulation and cytoprotection (its direct effect on cells).⁽¹²⁾

A genetic protein C deficiency, in its mild form associated with simple heterozygosity, causes a significantly increased risk of venous thrombosis in adults. If a fetus is homozygous or compound heterozygous for the deficiency, there may be a presentation of purpura fulminans, severe disseminated intravascular coagulation and simultaneous venous thromboembolism in the womb.⁽¹³⁾ This is very severe and usually fatal.⁽¹⁴⁾

Materials and Methods:

This is a descriptive Cross sectional study done during the period of August 2013 to March 2014 in Alshaab teaching hospital and Ahmed Qasem teaching hospital in Khartoum state to measure protein C disturbances in Sudanese patients among Mechanical valve replacement undergoing cardiopulmonary bypass. 150 patients with mechanical valve replacement undergoing cardiopulmonary bypass and 50 healthy individuals control groups.

Preparation of platelet poor plasma(PPP): The blood samples were collected from patients and controls in tri-sodium citrate(3.2%) anticoagulant (ratio 1:9). Platelet poor plasma sample were prepared by centrifugation at 2000g for 15 min. The samples were being kept at room temperature for protein C measurement using the Elisa technique.

Data analysis: All data are presented as mean \pm SD using Statistical Package for the Social Sciences, unless otherwise noted. Statistical comparisons were performed using unpaired student's t-test with $p<0.05$ considered as significant.

Results:

One hundred and fifty patients of either sex underwent valve replacement: 60 patients(40%) had isolated mitral valve replacement (MVR), 46 patients(30.7%) had isolated aortic valve replacement (AVR), 26(17.3%) had duple valve replacement (DVR) and 18(12%) had coronary artery bypass graft (CABG) (Table 1).

The controls were normal individuals of either sex. 52% of the patients were male and 48% of them were female. The age of patients ranged between 20 to 80 years with mean of 41 years and the controls have the same age range. The results showed that 54.7% of patients were in age group of 20-40 years, 31.3% of the patients were between 41-60 years and 14% were between 61-80 years.

Protein C was decreased significantly after cardiopulmonary bypass. Protein C was decreased in about 78.7% of the cases(118 patients) and the mean was ($59.8\pm21.1\%$) versus the control the mean($111.3\pm26.1\%$). About 43 cases(28.7%) had decreased protein C level under 50% postoperative (Table 2).

These results suggest a disturbance of protein C system by extracorporeal circulation. Protein C was decreased significantly after cardiopulmonary bypass and this finding is considered to reflect the activation and consumption of the protein C system in response to generated thrombin.

Conclusions:

These results suggest a disturbance of the protein C system by extra corporeal circulation. Protein C was decreased significantly after cardiopulmonary bypass and this finding is considered to reflect the activation and consumption of the protein C system in response to generated thrombin.

Table (1): The frequency of patients under valve replacement:

Case	Frequency	Percent
MVR	60	40%
AVR	46	30.7%
DVR	26	17.3%
CABG	18	12%

Table (2): The mean of the protein C in patients and controls:

	Count	Mean	STD Deviation
Patients	150	59.8%	21.1
Control	50	111.3%	26.1%

Figure (1): The frequency of patients underwent valve replacement according to the type of valve:

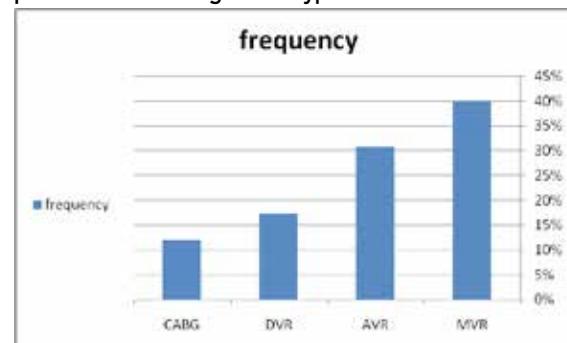
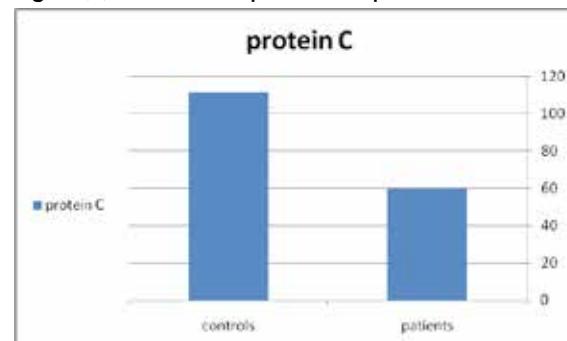


Figure (2): The mean of protein C in patients and controls:



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