Activated Protein C (APC) Resistance in Young Stroke Patients

Dear Sir,

The role of APC resistance (APC-R) in arterial thromboembolism is controversial, with reports claiming its prevalence between 4 and 17% (1, 2). In the present communication, we report its prevalence in patients with non-embolic cerebral arterial infarction. Thirty-seven patients (M:F = 19:18; age range = 4-42 years; mean age = 20.16 years) with sudden onset of stroke, presenting to the Neurology Department at the All India Institute of Medical Sciences, New Delhi, were the subjects. No patient had history of diabetes mellitus, hypertension, smoking, oral contraceptive, prolonged bed rest or lupus anticoagulant. CT and MRI examination revealed thrombus in the middle cerebral and vertebral arteries in 21 and 3 patients respectively, infarcts in parietal, occipital and frontal lobes in 5, 3 and 5 patients. All patients had cardiac evaluation including echocardiogram to exclude cardiac source of embolism thereby suggesting these infarcts to be secondary to thrombosis. Fifty normal subjects served as controls. Blood samples were withdrawn 3 months after the episode of stroke, after withdrawing heparin and warfarin for 7 days and 10 days respectively. APC-R was measured using Asoleetin (New York Associates), Kaolin (Sigma, USA) and APC (Diagnostica Stago, France) (3) by the classical Dahlbäck’s and the modified method (4) using FV deficient plasma in all cases and expressed as normalised APC sensitivity ratio (n-APC-SR) (3). Its normal range was 0.76-1.12 and 0.79-1.02 by Dahlbäck’s and modified APC test respectively. Eight (21.62%) patients with arterial cerebrovascular disease showed APC-R by the modified APC test. Four of them also showed APC-R by classical APC test, whereas the other 4 had borderline nAPC-SR (0.76-0.80) by classical APC test. One (2%) normal subject showed APC-R by both methods of testing. The difference in prevalence of APC-R in stroke patients and normal subjects was significant (p = 0.004).
Our results are comparable to those of Halbmayer et al. (2) where APC-R was observed in 17% of patients with juvenile strokes. However, it is significantly higher than the 7% observed by Cushman et al. (1) in patients with idiopathic arterial thrombosis. This difference may be due to inclusion of the lower age group (<40 years) and only non embolic cerebral arterial infarct cases in our study in contrast to higher age (<55 years) and a large variety of arterial diseases in his study. Subsequent studies by Halbmayer et al., using the modified APC test, didn’t confirm the high APC-R by classical method in their previous study. This was attributed to large number of pre-analytical factors. On the contrary, in our study all cases which had APC-R by Dahlbäck’s method were observed to be positive by the modified test as well. This may be because of strict exclusion of patients with lupus anticoagulant, or oral anticoagulant therapy in our study, thereby reducing its false positivity. Moreover, the modified test, which is considered as specific as genotyping of FV Leiden detected APC resistance in patients with borderline results of classical APC test. This might suggest an added diagnostic advantage of the modified over the classical APC test especially when the preanalytic factors affecting it are minimised.

It is thus concluded that APC resistance may have a prethrombotic potential in arterial thrombosis and must be identified to enable administration of adjunct prophylactic oral anticoagulant therapy in these patients. However further studies on genetic identification of factor V Leiden mutation in them are required.

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References


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