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<td><strong>Author(s)</strong></td>
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Lack of Activated Protein C Resistance in Healthy Hong Kong Chinese Blood Donors – Correlation with Absence of Arg506-Gln Mutation of Factor V Gene

Dear Sir,

Recent advances in the understanding of the anticoagulant pathways have revealed deficiencies of antithrombin, Protein C, Protein S and activated protein C (APC) resistance as major risk factors for thromboembolism in the Caucasian population (1, 2). Of these factors, APC resistance due to a mutation Arg 506-Gln of the Factor V gene is now recognised as the most common abnormality found in thrombotic patients and may itself account for more than one fifth of all cases of thrombophilia (3). In the general population, the reported prevalence rate of APC resistance is 5-7% (3, 4). Given the relatively low incidence of thromboembolism in the Chinese compared to the West (5, 6) which may reflect genetic or environmental factors e.g. diet or exercise, we were interested in the APC resistance prevalence rate in

References


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the local blood donor population. The results were compared with the
blood donor population of Caucasians in the UK.
Two hundred and ninety-three healthy Hong Kong Chinese blood
donors were tested for APC resistance. There were 177 males and 116
females, age 16-58 years (mean 26.5 years). The APC resistance test
was performed using the Coatest APC resistance kit (Chromogenix
Sverige) on the ACL 3000R (Instrumentation Laboratory, Milan,
Italy) or, in some cases, the Cobas Fibrin. There was good correlation
between the two instruments (correlation coefficient = 0.94). The APC
resistance ratio was calculated by dividing the activated partial throm-
oblastin time (APTT) obtained with APC in the calcium chloride
solution by that obtained using calcium chloride alone.
All Hong Kong Chinese blood donors had APC ratios above 2.
The range was 2.5-5.1 (mean 3.2, SD 0.51). The lower limit of normal
was in a study of 301 healthy controls by Koster et al. (3) has been re-
ported to be 2.17 (mean minus 1.96 SD).
In addition to the functional coagulation assay for APC resistance,
analysis for the Arg 506-Gln mutation was performed on DNA extract-
ed from peripheral blood buffy coat samples. A sequence of 267 bp of
factor V gene at Arg506 was amplified using primers as previously de-
scribed (7). Following amplification, the DNA was restricted with 2
MluI (Stratagene) and subjected to agarose gel electrophoresis.
The presence of the G to A mutation (nucleotide 1691) in the codon G
Arg506 would result in loss of this restriction site. Samples were anal-
ysed in pools of 10, each sample supplying 50 ng genomic DNA to the
pool. A duplicate pool which included 50 ng of a known heterozygote
for the Arg 506-Gln mutation of factor V was run in parallel as a posi-
tive control. Mutation analysis was also performed on DNA extracted
from 150 healthy Caucasian blood donors (age range 18-65 years).
The results from the PCR studies revealed, no patients in the Chinese
group had the Arg 506-Gln mutation in Factor V. Six out of fifteen
pools were positive for the Arg 506-Gln mutation in the Caucasian
blood donor group. Previous studies in the UK population have
revealed a prevalence of 3.5-5.6% (8, 9).
Our finding of a lack of APC resistance in Hong Kong Chinese
blood donors may be the single most important factor to account for the
low incidence of thromboembolism in the Chinese population. The
test observation that APC resistance is rare in the Japanese population
(10) is of interest. Whether the gene defect is absent or rare in the
oriental population per se can be answered by similar studies in
different geographical settings.

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notype (Gln 506) of coagulation factor V are rare in Japanese population.

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Warfarin Induced Skin Necrosis Associated with Activated
Protein C Resistance

Dear Sir,

Warfarin induced skin necrosis (WISN) is a rare condition that has
been described following warfarin treatment especially of patients with
familial thrombophilia, such as deficiencies of protein C (1) and protein
S (2). For most cases reported however no such association has been
found (3). We describe a case of WISN in a patient with activated
protein C resistance (APCR), the commonest cause of familial throm-
bophilia (4).

The 21 year old patient presented at the 12th week of pregnancy with a
painful right leg and a clinical diagnosis of a DVT was made. No
venogram was performed and she was treated with subcutaneous

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