High altitude thrombosis—Evidence for underlying mechanisms from a large prospective longitudinal study

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Despite constant progress in prevention and therapy, thrombotic events (arterial or venous), remain a major health concern world-wide due to morbidity and mortality.[1] Hypoxia and subsequent sojourn at high altitude have long been suggested as risk factors for thrombosis. A few small studies and case reports supporting this view have been earlier reviewed by Gupta & Ashraf.[2]

Besides increased blood viscosity, a reduced fibrinolytic capacity, a procoagulatory state and an inflammatory activation of the endothelium have been proposed as possible reasons for high altitude induced thrombosis.[3–6] Recently the long noncoding RNAs *LINC00659* and *UXT-AS1* have been identified as possible molecular modulators of high altitude induced thrombotic events.[7]

In this issue of *The Lancet Regional Health – Southeast Asia*, Velu Nair and colleagues[8] report the results of a challenging, large prospective longitudinal study that investigated thrombotic events in a cohort of 960 acclimatized lowlanders at high altitude.[8] Of these 960 male soldiers, 750 ascended to altitudes above 15.000ft (4472 m). Clinical screening and determination of markers of coagulation and fibrinolysis were performed in blood samples obtained from these individuals once at sea level and twice at high altitude (at 12–15,000ft and at >15,0000ft, respectively).

The authors reported 15 thrombotic events in their cohort, of which twelve were venous and three were arterial. The affected individuals showed significantly higher levels of procoagulant Factor VIIa and Xa, and lower levels of the anticoagulant modulators thrombomodulin and tissue factor pathway inhibitor (TFPI) compared to healthy controls. Also, the fibrinolytic capacity in these individuals was affected by a moderate, albeit not significant, reduction in tissue-type plasminogen activator (tPA), a profibrinolytic serine protease. In addition, Velu Nair and colleagues[8] provide strong evidence that not only coagulation and fibrinolysis are affected by staying at high altitude but that such environment might also impact on activation of the endothelium as indicated by the increased levels of adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM), and CD40 ligand in the individuals who experienced a thrombotic event. Such activation of the endothelium most likely can be linked to a generalized inflammatory state as evidenced by increased C-reactive protein (CRP) and myeloperoxidase (MPO) levels.

Intriguingly, already at sea level, plasma levels of MPO, the inflammatory mediator monocyte chemoattractant protein-1 (MCP-1) and plasmin-alpha-2-antiplasmin (PAP) complexes were significantly higher in those individuals who suffered a thrombotic event at high altitude as compared to the respective plasma levels in individuals of the control group. Thus, one could speculate that a particular marker profile would allow the identification of individuals at risk to develop thrombosis at high altitude. Therefore, adequately powered prospective studies to conclusively identify such biomarkers which might also include other biomolecules such as PA inhibitor-1 (PAI-1) or long noncoding RNAs that have been shown to be involved in high altitude induced thrombosis, seem warranted.[5–7] In conclusion, this challenging study improves our understanding on the mechanisms that might underly high altitude induced thrombosis.[8]

Contributors

JW conceptualised and wrote the paper.

Declaration of interests

None.

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