

Editorial Focus

"To drink or not to drink" – is this really the question?

Benjamin Brenner, Giris Jacob

Thrombosis and Hemostasis Unit and Recanati Autonomic Dysfunction Center, Rambam Health Care Center and Rappaport Faculty of Medicine, Technion-IIT, Haifa, Israel

Travel-related thrombosis is a major public health issue which attracts growing attention worldwide. The risk for thrombosis in air travelers depends on flight duration, passenger-related factors and cabin conditions. Long-haul flight duration is directly related with increased thrombotic risk (1). Passenger-related risk factors include age above 40 years, thrombophilia, hormonal therapy and comorbid disease states such as congestive heart failure, chronic lung disease, cancer and recent surgery (2). The question, whether too much sitting or too much clotting occurs during long-haul flight, has recently been resolved in part. In fact, while prolonged immobilization is of concern, increased coagulation activation also occurs in a fraction of healthy young adults, especially those with thrombophilia and in women receiving hormonal therapy (3). Whether these results can be directly extrapolated to older travelers with comorbidity is questionable.

Cabin-related risk factors include aircraft inner altitude, which correlates with a decrease in oxygen saturation. The low humidity conditions in the cabin lead to the advice commonly given by the airlines, as well as by physicians, to drink ample amounts of water. Concerns of dehydration have resulted in the advice to avoid alcoholic beverages during long-haul flight. This is based on the assumption that dehydration may increase the risk of thrombosis, which indeed is supported by reports in other clinical conditions involving dehydration (4–6).

In this issue of *Thrombosis and Haemostasis* Schreijer et al. (7) report on a crossover study in healthy young volunteers exposed to eight hours of flight, immobilization in a cinema and a daily-life control situation. Fluid loss markers (haematocrit [Hct], serum albumin and osmolality) and fluid intake were assessed in correlation with coagulation activation. This is a sub-study of a previously reported trial on coagulation activation during air travel (3).

The main finding of the current study is that the hydration status of subjects during flight was not associated with coagulation activation. Sequential Hct and serum albumin concentrations were assessed in order to demonstrate changes in plasma volume during flight and other conditions. However, this methodological approach may present some limitations. Hct is con-

sidered a delicate sensor of acute changes in plasma volume, at least in healthy individuals (8–10). The corrected Hct is more accurate than the measured one (11). It is corrected for trapped plasma (0.96) and whole body Hct (0.91), ($0.96 \times 0.91 = 0.87$), therefore the corrected Hct is about 87% of the measured one. Sequential assessment of corrected Hct gives an estimation of the changes in plasma volume. For example, upright posture causes a passage of fluids (water and micromolecules) from the intravascular compartment to the surrounding one. This plasma shift, as calculated from Hct changes, is estimated to be about 13% in healthy subjects. Similar results are obtained from sequential measurements of total plasma protein (10, 11), and are supported by direct plasma volume measurement (11). Of note, a recent observation demonstrates that prolonged standing results in an increase in procoagulant activity and impaired anticoagulant activity (12).

The reported Hct in the present study is calculated (from red blood cell concentration and mean corpuscular volume), rather than directly measured, which may be less accurate. Furthermore, since Hct values depend on posture, standing and prolonged sitting affect Hct values in particular (9, 12). Assessment of Hct during supine posture (at least 15 minutes), being seated before take-off and at the end of the flight may give a more accurate approach for the estimation of intravascular volume changes reflecting the hydration status of participants.

Total protein concentration linearly correlates with plasma volume changes obtained from corrected Hct. Albumin, however, does not offer similar accuracy. It is estimated that 5% of serum albumin crosses to the extravascular compartment during standing and possibly less when sitting, therefore it could not be considered a delicate sensor of plasma volume changes (13, 14).

Nevertheless, even if coagulation activation is not related to hydration status, there are other potential mechanisms through which dehydration may increase thrombotic risk involving leukocytes, platelets and endothelial activation (15, 16).

While the present investigation offers a valuable approach, future studies, taking into account the aforementioned considerations, are needed in order to give a final answer whether hydration status contributes to the “economy-class syndrome”.

Correspondence to:
Benjamin Brenner, MD
Director Thrombosis & Hemostasis Unit
Rambam Health Care Center
Haifa 31096, Israel
Tel.: +972 4 854 3560, Fax: +972 4 854 2343
E-mail: b_brenner@rambam.health.gov.il

Received April 11, 2008
Accepted May 2, 2008

Prepublished online May 7, 2008
doi:10.1160/TH08-04-0229

References

1. Cannegieter SC, Doggen CJ, van Houwelingen HC, et al. Travel-related venous thrombosis: results from a large population-based case control study (MEGA study). *PLoS Med* 2006; 3: e307.
2. Gallus AS. Travel, venous thromboembolism, and thrombophilia. *Semin Thromb Hemost* 2005; 31: 90–96.
3. Schreijer AJ, Cannegieter SC, Meijers JC, et al. Activation of coagulation system during air travel: a cross-over study. *Lancet* 2006; 367: 832–838.
4. Nowak-Göttl U, Kosch A, Schlegel N. Neonatal thromboembolism. *Semin Thromb Hemost* 2003; 29: 227–234.
5. Pearson TC. The risk of thrombosis in essential thrombocythemia and polycythemia vera. *Semin Oncol* 2002; 29 (Suppl 10): 16–21.
6. Prandoni P. Cancer and venous thromboembolism. Clinical implications of strong association. *Pathophysiol Haemost Thromb* 2006; 35: 111–115.
7. Schreijer AJ, Cannegieter SC, Caramella M, et al. Fluid loss does not explain coagulation activation during air travel. *Thromb Haemost* 2008; 99: 1053–1059.
8. Dill DB, Costill DL. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol* 1974; 37: 247–248.
9. Hagan RD, Diaz FJ, Horvath SM. Plasma volume changes with movement to supine and standing positions. *J Appl Physiol* 1978; 45: 414–417.
10. Jacob G, Raj SR, Ketch T, et al. Postural pseudoanemia: posture-dependent change in hematocrit. *Mayo Clin Proc* 2005; 80: 611–614.
11. Jacob G, Ertl AC, Shannon JR, et al. Effect of standing on neurohumoral responses and plasma volume in healthy subjects. *J Appl Physiol* 1998; 84: 914–921.
12. Masoud M, Sarig G, Brenner B, et al. Orthostatic Hypercoagulability: A novel physiologic mechanism to activate the coagulation system. *Hypertension* 2008; in press.
13. Bjerkhoel P, Lindgren P, Lundvall J. Protein loss and capillary protein permeability in dependent regions upon quiet standing. *Acta Physiol Scand* 1995; 154: 311–320.
14. Lundvall J, Lindgren P. F-cell shift and protein loss strongly affect validity of PV reductions indicated by Hb/Hct and plasma proteins. *J Appl Physiol* 1998; 84: 822–829.
15. Bradford A. The role of hypoxia and platelets in air travel-related venous thromboembolism. *Curr Pharm Des* 2007; 13: 2668–2672.
16. Kratz A, Wood MJ, Siegel AJ, et al. Effects of marathon running on platelet activation markers: direct evidence for in vivo platelet activation. *Am J Clin Pathol* 2006; 125: 296–300.