

Routine Chemoprophylaxis for Travel-Associated Thrombosis? No

Aharon Lubetsky MD

National Hemophilia Center and Institute of Thrombosis and Hemostasis, Sheba Medical Center, Tel Hashomer, Israel
 Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Key words: air travel, thrombosis, prophylaxis, elastic compression stockings, low molecular weight heparin

IMAJ 2006;8:862–863

In 1954, Homans suggested an association between travel and venous thromboembolism. During the 50 years since then we have learned a great deal more about this association and the risks caused by travel, and today, in 2006, we are able to state that:

- **Travel and thrombosis are associated.** Four case-control studies [1-4] and five cohort and randomized controlled studies [5-9] have clearly established that thrombosis is associated with travel. In the four case-control studies, 11.8% of patients with venous thromboembolism had a history of recent travel, by air or other means of transportation, compared to 6.3% of controls with an odds ratio of 1.98 (1.52–2.57). In the cohort studies (as well as in control arms of randomized studies) about 2.1% of patients suffered a thrombotic event following air travel. Although two case-control studies [3,10] failed to detect a direct association between travel and thrombosis and despite the fact that two other studies [7,8] recruited volunteers responding to media ads, all the studies lumped together prove an association.

- **The predisposition for VTE is patient and travel related.** It is evident from the majority of studies published to date that most VTE episodes occur in patients with baseline risks for thrombosis. Patient-related risk factors include a previous deep vein thrombosis episode, severe obesity or limitation of mobility, neoplastic disease in the preceding 2 years, or large varicose veins [5,6], while in other studies surgery, pregnancy, hormone use, and family history of thrombosis were also considered risk factors. In flyers without risk factors the rate of DVT was 0% (among 355 such low risk patients), whereas the rate was 2.7% in high risk patients [5]. A documented thrombophilic disorder was also recognized in recent studies to be a significant risk factor; it increased the risk as high as 17-fold in air travelers in one such study [4] and to a less extent in others [11]. Prolonged sitting in a cramped position is a significant travel-related risk factor. Both stasis of blood in leg veins and a possible effect of pressure exerted by the seat edge on calf muscles promote clot formation. This was already

suggested by Homans in 1954 and is further stressed by the fact that many patients suffering a VTE episode never leave their seats during a flight – 95% of patients with major pulmonary embolism in the report by Lapostolle et al. [12], or occupy a window or middle seat – 76% of patients in the LONFLIT studies [6]. Furthermore, in two case-control studies [1,3], only 27% of passengers suffered a thrombosis following air travel, while all the rest developed thrombosis after car or train travel.

Unique to the situation of air travel are cabin-related risk factors. Hypoxemia, low cabin humidity, and dehydration leading to changes in plasma viscosity, reduced fibrinolytic activity and activation of coagulation, have all been proposed as underlying mechanisms [11,13], but their contribution to the thrombotic risk beyond the above-mentioned risk factors is uncertain. Interestingly, two recent studies have clearly shown that a long-distance (10 hours) bus trip can significantly activate coagulation [14] and lead to thrombosis in 4.9% of bus passengers [15]. Moreover, thrombosis in completely healthy young people following prolonged sitting in front of computers was also recently reported (from several places) [16].

- **Prophylactic means are available and are effective.** Recent studies suggest that VTE secondary to prolonged air travel is preventable. In two randomized controlled studies [5,9], patients allocated to wear elastic compression stockings during air travel had a significantly reduced risk for thrombosis (0–0.24% compared to 4.5–10.0% in controls). In another study [6], administration of a single dose of low molecular weight heparin prevented completely (0% incidence) the occurrence of VTE, whereas administration of aspirin did not.

Taking into consideration the above points one could easily be tempted to recommend VTE prophylaxis for all travelers. However, routine prophylaxis for all travelers is not necessary and occasionally may be harmful. Although many patients sustaining a new travel-related VTE episode will eventually be identified as having at least one co-morbid condition, using female hormones or suffering from some form of thrombophilia [11], this is not true for all travelers. From the prospective studies it is evident that about 6–10% of patients have some form of thrombophilia,

DVT = deep vein thrombosis

up to 30% use female hormones, and around 40% have some co-morbid condition [8]; therefore, in a significant proportion of travelers no risk factor can be identified and these travelers can be considered at low risk for thrombosis. On the other hand, routine use of elastic compression stockings (used in 17% of travelers in one study) was not enough to prevent thrombosis and in one prospective study 44% of patients suffering a new episode of VTE did so despite the use of elastic stockings [8].

Therefore, the use of prophylactic measures should be based on an individual risk assessment. Patients at the lower risk should receive no specific prophylactic measure but they should be encouraged (like all other travelers) to stand up occasionally, stretch, exercise, drink water, avoid alcoholic beverages and avoid tight clothing during travel. In contrast, patients perceived to be in the highest risk group (patients with various mobilization problems and carrying an additional significant risk factor for thrombosis, e.g., a previous VTE episode, varicose veins, cancer or thrombophilia) should be considered as candidates for low molecular weight heparin prophylaxis, in addition to elastic stockings and the above-mentioned instructions. Patients perceived to be at intermediate risk for thrombosis (mainly obese patients or patients with limitation of mobility due to bone or joint problems) should be encouraged to wear elastic compression stockings. There is no evidence to support the administration of antiplatelet agents (aspirin) in any of these risk groups, and in fact in one study the use of aspirin had no effect on the risk of thrombosis [6].

To summarize, travel-associated thrombosis occurs mainly in travelers with risk factors for thrombosis. Prophylactic treatment, however, should not be administered routinely since travelers present with a wide range of VTE risks and therefore treatment should be tailored specifically for each traveler after consideration of risks, benefit and the traveler's preferences.

References

1. Ferrari E, Chevalier T, Chapelier A, Baudouy M. Travel as a risk factor for venous thromboembolic disease: a case control study. *Chest* 1999;115:440-4.
2. Samama MM for the Sirius study group. An epidemiological study of risk factors for deep vein thrombosis in medical outpatients. *Arch Intern Med* 2000;160:3415-20.
3. Kraaijenhagen RA, Haverkamp D, Koopman MMW, Prandoni P, Piovella F, Büller HR. Travel and risk of venous thrombosis. *Lancet* 2000;356:1492-3.

4. Martinelli I, Taioli E, Battaglioli T, et al. Risk of venous thromboembolism after air travel: interaction with thrombophilia and oral contraceptives. *Arch Intern Med* 2003;163:2771-4.
5. Belcaro G, Gerulakos G, Nicolaidis AN, Myers KA, Winford M. Venous thromboembolism from air travel: the LONFLIT study. *Angiology* 2001;52:369-74.
6. Cesarone MR, Belcaro G, Nicolaidis AN, et al. Venous thrombosis from air travel: the LONFLIT3 study. Prevention with aspirin vs. low molecular weight heparin (LMWH) in high-risk subjects: a randomized trial. *Angiology* 2002;53:1-6.
7. Schwarz T, Siebert G, Oettler W, et al. Venous thrombosis after long haul flights. *Arch Intern Med* 2003;163:2759-64.
8. Hughes RJ, Hopkins RJ, Weatherall M, et al. Frequency of venous thromboembolism in low to moderate risk long distance air travelers: the New Zealand Air Traveler's Thrombosis (NZATT) study. *Lancet* 2003;362:2039-44.
9. Scurr JH, Machin SJ, Bailey-King S, Mackie IJ, McDonald S, Smith PD. Frequency and prevention of symptomless deep vein thrombosis in long haul flights: a randomized trial. *Lancet* 2001;357:1485-9.
10. Arya R, Barnes J, Hossain U, Patel RK, Cohen AT. Long-haul flights and deep vein thrombosis: a significant risk only when additional factors are also present. *Br J Haematol* 2002;116:653-4.
11. Scriver AJM, Cannegieter SC, Meijers JCM, Middeldorp S, Buller HR, Rosendaal F. Activation of coagulation during air travel. *Lancet* 2006;367:832-8.
12. Lapostolle F, Surget V, Borron SW, et al. Severe pulmonary embolism associated with air travel. *N Engl J Med* 2001;345:779-83.
13. Bendz B, Rostrup M, Sevre K, Andersen TO, Sandset PM. Association between acute hypobaric hypoxia and activation of coagulation in human beings. *Lancet* 2000;356:1657-8.
14. Schobersberger W, Mittermayr M, Innerhofer P, et al. Coagulation changes and edema formation during long-distance bus travel. *Blood Coagul Fibrinolysis* 2004;15:419-25.
15. Cesarone MR, Di Renzo A, Ippolito E, et al. The Pilgrim Syndrome. Epidemiology and investigations of long-travel pilgrimage-related thrombosis. VF-E Web Journal, 2004; www.venousforum-europe.org/index.php
16. Beasley R, Heuser P, Raymond N. SIT (seated immobility thromboembolism) syndrome – a 21st century lifestyle hazard. *N Z Med J* 2005;118:U1379.

Correspondence: Dr. A. Lubetsky, National Hemophilia Center and Institute of Thrombosis and Hemostasis, Sheba Medical Center, Tel Hashomer 52621, Israel.

Phone: (972-3) 530-2120

Fax: (972-3) 535-1806

email: aharon.lubetsky@sheba.health.gov.il

A single rose can be my garden... a single friend, my world

Leo Buscaglia (1924-1998), author, orator and professor of education who believed that social bonds are essential for transcending the stresses of everyday life and enriching it above the limitations of poverty as well as crossing communication gaps between generations. Buscaglia worked actively to overcome social and mental barriers that inhibited the expression of love between people, from family to acquaintances to the disabled, institutionalized, and elderly, to complete strangers, often making his own forwardness on the subject a topic of self-deprecating humor. The profundity of his subject, however, almost invariably struck a responsive chord regarding an area many regarded as deficient in their lives, and by 1998 eighteen million copies of his books were printed in seventeen languages.