Air Flights and Venous Thromboembolism – A Preventable Condition

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The association between air flights and venous thromboembolism was first brought to public attention by the well-known surgeon Homans in 1954 [1]. With the onset of regular long-distance flights in the 1960s, an increasing number of case reports and series of cases connecting air travel and VTE were published [2–4]. Cruickshank and colleagues [5] termed this association "Economy Class Syndrome" to emphasize the importance of prolonged sitting in a cramped position in the pathogenesis of deep vein thrombosis [5]. The phenomenon is well known today, although VTE may also occur in patients who travel in business class since its occurrence depends on cabin and patient-related factors [3,5,6].

In this issue of *IMAJ*, Galili and Bass [7] review the historical perspective of air travel-associated VTE, the pathogenesis of the condition, and means of preventing it. According to the authors, very little was known about the incidence of this condition until recently, for several reasons. The clinical picture of VTE ranges from symptomless DVT, which is usually undetected, to life-threatening pulmonary embolism [8,9]. The time of presentation varies among passengers: the symptoms and the signs can appear during the flight, after the embarkation, or up to 4 weeks after the flight [3,4,6]. Many patients with mild signs do not seek the help of a physician, while most published cases describe more disabled hospitalized patients [3,4]. Media attention is attracted to cases of tragic death caused by fatal pulmonary embolism in young and apparently healthy passengers [10]. VTE is probably rare in this group of patients [11]. In fact, we could not find any case of VTE in aircraft crew members, who spend long periods in the air. On the other hand, the incidence of VTE can be surprisingly high in elderly and high risk passengers. In a prospective trial cited by Galili and Bass, the incidence of DVT was assessed after prolonged air flight by duplex ultrasonography in a group of passengers over 50 years old without known risk factors for VTE [12]. In 10% of these 116 passengers, who comprised the control group of this trial, asymptomatic DVT of calf was detected. In similar recently published and well-conducted LONFLIT2 and LONFLIT3 studies, ultrasonography was performed before and after long-haul flights in large groups of patients with high risk for VTE [11,13], revealing DVT in 4.5–4.8% of these patients.

Lapostolle et al. [14] reviewed cases of severe PE diagnosed in patients who required medical assistance on their arrival at Charles de Gaulle airport over a 7 year period [14]. Of the more than 135 million passengers only 56 cases of PE were diagnosed. The researchers found a direct correlation between the length of the flight and the incidence of severe PE. The incidence of PE increased 150 times in passengers who traveled more than 5,000 kilometers as compared to patients who traveled less, and reached 4.77 cases per million passengers for distances longer than 10,000 km. It should be noted that the true incidence of flight-associated PE is probably much higher because most cases of mild PE are diagnosed after the patient leaves the airport [3,4,8].

The aforementioned studies represent part of the growing body of evidence that ties air travel to VTE. Since DVT can only be detected by sensitive ultrasonographic methods, more than 60% of DVT cases among air passengers are symptomless [12,13]. This explains the inability of previous studies, which did not use these techniques, to discover this connection [15].

DVT can lead to PE and disabling chronic venous insufficiency [16]. What can be done to prevent this condition in air travelers? Galili and Bass suggest that passengers take simple physical measures, such as leg stretching, exercising calf muscles, frequent walking, and changing the position of the legs. Although these measures were not prospectively studied, about 85% of VTE cases occur in passengers sitting in non-aisle seats, who tend to walk about less than those in aisle seats [13]. Furthermore, alcohol should not be imbibed because it leads to apathy and dehydration, and gas-containing beverages should also be avoided since they cause gastric dilatation and thus impede venous return from the legs.

We were among the first researchers to suggest the use of elastic compression stockings in air travelers who have risk factors for VTE [4]. This hypothesis was confirmed by two recently published studies. In the LONFLIT2 study, the incidence of DVT in 411 high risk passengers who were wearing below-knee stockings was 0.24–18.75% times lower than in the control passengers [11]. In another randomized trial, no cases of DVT were found in 115 passengers who wore compression stockings [12]; 4 passengers in this group (3%) developed superficial vein thrombosis as compared with no cases of SVT in the control group.

As Galili and Bass propose, medical treatment should be considered in high risk passengers. A very recently published LONFLIT3 study compared the use of aspirin and low molecular weight heparin for the prevention of DVT in high risk passengers

VTE = venous thromboembolism
DVT = deep vein thrombosis
PE = pulmonary embolism

SVT = superficial vein thrombosis

who intended to travel by plane for more than 10 hours [13]. In the aspirin treatment group 100 patients received three doses of 400 mg oral soluble aspirin, one dose daily, starting 12 hours before the flight. DVT was diagnosed by ultrasonography in 3.6% of passengers in this group, and SVT in three passengers. In the LMWH group one weight-adjusted dose of enoxaparine was injected to 100 patients 2–4 hours before the flight. No cases of DVT were observed, but one case of SVT was diagnosed in this group.

It is not yet clear whether moderate or high risk passengers should receive prophylactic LMWH treatment, or whether it is sufficient to advise them to wear compression stockings. Comparative studies on this issue are awaited. It is also not known whether aspirin should be used in air travelers with risk factors for VTE. It is possible that providing aspirin to passengers for a longer period than in the regimen of the LONFLIT3 study may be more efficacious in the prevention of VTE. However, gastrointestinal side effects of aspirin should be carefully considered. Until new studies appear, we do not propose the routine use of aspirin in high risk passengers.

It is important to remember that air travel-associated VTE is a preventable condition. Much can and should be done to inform the wide public through newspaper articles, leaflets, and videotaped movies that should be screened in the aircraft together with the security information. Travelers who buy air tickets for far destinations should be encouraged by their travel agents to consult their physician about their risk of VTE and the measures for prevention.

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LMWH = low molecular weight heparin

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The cook was a good cook as cooks go; but as cooks go, she went

Anonymous

Capsule

Is more p53 better?

The p53 tumor suppressor protein has been dubbed the guardian of the genome because it prevents the proliferation of cells containing damaged DNA – cells that have the potential to become cancerous. Indeed, defects in p53 itself or in the pathways that activate it occur in the vast majority of human cancers. To explore whether an extra copy of p53 might boost an organism's ability to defend against cancer, Garc et al. generated transgenic mice carrying a third copy of wild-type p53, the expression properties of which closely resembled those of the endogenous p53 alleles. These "super p53" mice not only showed enhanced activation of the p53-dependent response to DNA damage, but they developed significantly fewer tumors after exposure to chemical carcinogens. Interestingly, the "super p53" mice had a normal life-span, a finding that contrasts with results of an earlier study that had linked elevated p53 activity in mice to premature aging. Therapeutic up-regulation of p53 expression may help prevent cancer development.

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