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Flight-related DVT

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ABSTRACT Vascular thrombosis associated with long-haul air travel has attracted considerable public attention. Most research has used case control studies where selection bias can reduce reliability, but RCTs would be impracticle. Symptomatic DVT probably occurs up to 0·28% of passengers, and asymptomatic DVT in up to 10·3%. Pulmonary embolous is the feared complication. Immobility is probably a main factor in flight DVT, but other unknown factors may also be important. Passengers with risk-factors for DVT should consider prophylaxix; LMWH for those at high risk, and compression stockings in all risk groups.

KEYWORDS Air travel, immobility, prophylaxis, risk factors, thrombosis.

LIST OF ABBREVIATIONS Deep vein thrombosis (DVT), Low molecular weight heparins (LMWH), post-thrombotic syndrome (PTS), pulmonary embolism (PE), randomised controlled trials (RCTs), thrombin-antithrombin complex (TAT)

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Earlier this year, a BBC news item[1] brought to our attention, once again, the issue of DVT and its association with travel, in particular long-haul air travel. It has yet to be fully established that air travel is a risk factor for DVT, though an association between the two is generally accepted and conceivable despite the limited evidence available to us. Most research in this field has been carried out using case controlled studies where selection bias reduces reliability of results. Randomised controlled trials are not a useful means of assessing the incidence of DVT from air travel due to the impracticalities of randomising, the large number of passengers that would be required to provide accurately powered results,[2] and also because occurrences of flight-related DVT are low and often asymptomatic. In spite of the limited evidence available, a systematic review[3] investigating DVT in relation to air travel found the incidence of symptomatic DVT ranged from 0% to 0·28%; and the incidence of asymptomatic DVT ranged from 0% to 10·34%. The condition and its potential to evolve into PE, has led to a great deal of media attention, with phrases such as 'economy class syndrome' and 'travellers' thrombosis' being coined. Consequently, it is a cause for widespread concern. In addition, researchers are still trying to ascertain why flight-acquired DVT occurs. While prolonged immobilisation has been assumed to be the reason for the condition, research indicates that it may not be the only mechanism involved. What is also unclear is exactly who is at risk and what (if any) advice and preventative measures should be recommended by clinicians.

AIR TRAVEL VS IMMOBILITY

It is inevitable during the course of a long-haul flight for passengers to experience periods of prolonged immobilisation. Immobility is certainly a recognised risk factor associated with DVT as lack of muscle motion leads to blood stasis which in turn can lead to thrombus formation. Other situations where mobility is decreased, such as surgery, hospitalisation or limb paralysis, are also acknowledged for their potential to precipitate a diagnosis of DVT. As a result, it is generally accepted that immobilisation during long-haul air travel is the foundation of flight-related DVT. It is unclear whether the same risk applies to other modes of prolonged travel or sitting, for example, long-distance coach journeys. This question complicates the whole flight-related DVT issue and has led to theories that there are additional underlying risk factors specific to air travel that increase the risk of DVT. A recent study in the *Lancet*[4] attempts to provide further insight into this particular uncertainty. The aim of the study was to discover whether flying leads to a hypercoagulable state. The researchers measured activated coagulation markers, TAT, prothrombin fragment 1 and 2 (F1 and F2) and D-dimer, in a sample of 71 healthy volunteers aged between 18 and 40 years; some of this number had the factor V Leiden mutation and/or took the oral contraceptive pill, both of which are recognised risk factors for venous thrombosis. Blood samples were taken before, during and after an eight-hour flight; the volunteers then had the same tests performed for two additional control scenarios, eight hours of movie-watching, and daily life, with a 2–3 week gap between each

session. This research demonstrated more coagulation abnormalities after a flight than after movie-watching or normal daily activity. Those found to have the highest rise in activated coagulation markers had both the factor V Leiden mutation and took the oral contraceptive pill. No participants developed an actual venous thrombosis during the course of the study. The researchers conclude their results demonstrate that flight induces a mechanism for thrombus formation in addition to immobilisation alone, in some individuals. One possible mechanism for thrombus formation associated with flight is a condition known as 'hypobaric hypoxia'. This condition can occur due to decreased pressure in the aircraft cabin resulting in a diminished supply of airborne oxygen and might induce coagulation.[5] However, a recent study failed to substantiate this possibility.[6]

WHO IS AT RISK?

Formation of a DVT often involves the cumulative effects of multiple risks. It is therefore advisable for those who already have high or moderate risk factors associated with the condition to avoid additional risk factors. Thus, for example, an individual with a previous DVT, who is obese and over 50 years of age, who requests hormone replacement therapy, may be advised against taking it. Where additional risk factors cannot be avoided, prophylactic measures during times of increased risk, as with hospitalisation, surgery and pregnancy should be considered in an attempt to avoid acute thrombus formation. Low molecular weight heparins might be considered for these individuals. Those with predisposing risk factors for DVT ought to regard long-haul flight as an additional risk factor, and should consider a preventative intervention to avoid flight-related thrombosis; available evidence suggests that though these events are rare, they are more likely to occur in those at increased high risk. Not all predisposing risk factors threaten the same degree of risk and a physician should be consulted regarding an individual's relative risk prior to a long-haul air journey.

HOW TO PREVENT DVT

Primary care physicians are often challenged by worried expectant travellers regarding measures to help avoid flight-related DVT. They may be hesitant to prescribe pharmacological interventions because of the potential side effects, yet be sceptical regarding the benefits of mechanical aids, namely elastic compression stockings. Both LMWH[7] and elastic compression stockings[8] have been shown to reduce the risk of travel-related DVT and its symptoms. Cesarone *et al.*[7] compared LMWH, high-dose aspirin and no prophylaxis by randomising 300 high-risk participants (249 completed the study). The results showed thrombotic events (including 'superficial events' – thromboses in the superficial veins of the leg which should not be classified as DVTs) occurred in 4·8% of the no prophylaxis group, 3·6% of the aspirin group, and in 0·6% of the LMWH group. Elastic compression stockings are known to be effective in preventing DVT in hospitalised patients,[9] and in individuals with a previous DVT, they reduce the risk of thrombus recurrence and damage caused by PTS.[10] The value of these stockings in relation to protection for long-haul flight passengers has been evaluated in a systematic review, including the results of ten trials that randomised between compression stockings and no stockings.[8] A pooled sample of 2,856 participants, with varying degrees of risk, whose flights were of at least seven hours were included. There were no deaths, PEs or DVTs reported during the research; during follow-up, 50 participants developed asymptomatic DVT, five from those randomised to wear stockings and 45 from those without stockings ($P<0{\cdot}00001$). The researchers also noted that wearing stockings had a significant impact on reducing oedema in the legs. In those at low or moderate risk, 1·45% (21 out of 1,446) developed asymptomatic DVT compared with 2·43% (29 out of 1,191) of those at high-risk. Differentiating between low- and moderate-risk individuals would have been of interest here, but in practical terms, 90% of all events occurred in those without stockings, regardless of risk.

POST-FLIGHT TROUBLE: WHAT TO DO

There have been several media reports of travellers going on to develop overt DVTs and/or PEs. The clinical diagnosis of PE is notoriously difficult, and investigation is always required where individuals present with suggestive symptoms. Travellers who develop leg stiffness, pain or swelling, or chest tightness, pain or breathlessness, in the weeks after long-haul air travel should consult a doctor, and doctors consulted by such travellers need to consider DVT and PE very seriously.

KEYPOINTS

- Unknown factors additional to immobility may lead to flight-related DVT, possibly by activation of blood coagulation.
- Those who have predisposing risk factors are at greatest risk of flight-related DVT and should consider preventative measures.
- Low molecular weight heparins may be considered for high-risk individuals embarking on a long-haul flight.
- Elastic compression stockings reduce asymptomatic DVT and leg oedema associated with air travel in all risk groups.

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