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REVIEW

Travel risk assessment, advice and vaccinations in immunocompromised travellers (HIV, solid organ transplant and haematopoeitic stem cell transplant recipients): A review

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Summary International travellers with immunocompromising conditions such as human immunodeficiency virus (HIV) infection, solid organ transplantation (SOT) and haematopoietic stem cell transplantation (HSCT) are at a significant risk of travel-related illnesses from both communicable and non-communicable diseases, depending on the intensity of underlying immune dysfunction, travel destinations and activities. In addition, the choice of travel vaccinations, timing and protective antibody responses are also highly dependent on the underlying conditions and thus pose significant challenges to the health-care providers who are involved in pre-travel risk assessment. This review article provides a framework of understanding and approach to aforementioned groups of immunocompromised travellers regarding pre-travel risk assessment and management; in particular travel vaccinations, infectious and non-infectious disease risks and provision of condition-specific advice; to reduce travel-related mortality and morbidity.

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1. Introduction

International travel has become exceedingly common among immunocompromised hosts (ICH), particularly among those with human immunodeficiency virus (HIV) infection, or in solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) recipients, due to recent advancements in treatment leading to better survival and improved quality of life [1,2]. On the other hand, in those with end-stage immunosuppressive diseases, a strong desire to take the last chance to travel may prevail [1]. Such travellers are at a significant risk of contracting opportunistic infections and severe travel-related illnesses whilst abroad, and their responses to pre-travel vaccines may also be sub-optimal [3]. Travel-related infection risks are also dependent on the degree of immune suppression, travel destinations, duration and personalised itinerary. Therefore, it is paramount for the travel medicine, infectious diseases and transplant physicians to become aware of potential travel-related infections in immunocompromised travellers to aid pre-travel risk assessment and vaccinations. Ideally, this high risk group of travellers should be assessed in specialised travel medicine clinics prior to travel, preferably with concerted input from primary care, infectious diseases and transplant physicians to ensure best possible risk minimisation.

This review focuses on the pre-travel risk management, in particular infection risks and vaccinations, of HIV-infected and SOT and HSCT recipients who are traveling overseas on a short-term basis. Management of longer-term travellers, paediatrics and pregnant travellers, those with solid organ or non-transplanted haematological malignancies, chronic autoimmune conditions, or transplant tourism will not be covered in this review.

2. Epidemiology

A large observational cohort study of 15,440 travellers documented that a significant proportion (17.9%) were medically high risk travellers, of whom 23.3% were immunocompromised (HIV and transplant recipients) [4]. Conversely, 20—45% of HIV-infected individuals and up to 36% of SOT recipients engaged regularly in international travel [5—7]. However, almost a third of them failed to seek pre-travel health advice and vaccinations [7,8] and this rate may be as high as 60—90% in some cohorts [5,9,10]. When travel advice was sought, only 12.8% attended specialist travel clinics and transplant physicians were the first port-of-call in >50% of cases [8,10]. Yet, greater than 85% of these high-risk travellers visited countries with medium to high risks of malaria and typhoid and a further 22.8% visited yellow fever endemic countries [4]. Close to 60% of HIV infected travellers were born in countries endemic for tropical diseases; these people were likely to have longer duration of travel and more likely to be visiting friends and relatives (VFRs) in high risk areas than their counterparts [11]. In addition, risk taking behaviours were common with 23.3% of HIV-infected travellers engaging in casual sexual activity with new partners whilst overseas and of those only 58.1% used condoms [5]. Overall, compliance to malaria chemoprophylaxis and preventative measures against insect bites and food hygiene were also very poor [5,7]. Therefore, early engagement and risk assessment is essential to provide tailored advice, promote preventative and risk-modifying behaviours, and administer appropriate vaccines to prevent travel-related morbidity and mortality.

3. Intensity of immunosuppression and concept of immune maturity

The range of immunosuppression is dependent on medical condition and affected immune pathways.

3.1. HIV

In HIV infection, depletion of memory T-cells affects mainly the cellular and adaptive immune responses, and to a lesser degree innate immune responses in advanced disease. HIV immune deficiency is proportional to functioning peripheral CD4 T-cells, nadir CD4 T-cell levels, presence or absence of anti-retroviral therapy (ART) and whether HIV viral load suppression and immunological recovery has occurred.

3.2. SOT

In SOT recipients, anti-rejection medications such as calcineurin inhibitors (CNIs: cyclosporine or tacrolimus) and mTOR-inhibitors (sirolimus or everolimus) mainly impair interleukin-2 dependent T-cell proliferation whilst mycophenolate and azathioprine inhibit antigen dependent T and B-cell interactions and proliferation [12,13]. In addition, SOT recipients may be on varying amount of glucocorticoids (e.g. prednisolone) at varying time-points. Glucocorticoids functionally impair all components of the immune system including granulocytes. Therefore, the degree of immunosuppression in SOT recipients is dependent on the time after transplant, immunosuppression dosing including glucocorticoids, and the presence of acute or chronic rejection episodes that necessitates higher doses of immunosuppressants. The degree of immune suppression is considered greatest in the first 3 months following SOT and reduces to not insignificant levels at 12 months when medication doses have been reduced [14].

3.3. HSCT

Immune suppression in HSCT recipients is dependent on the chemotherapeutics employed prior to transplant, whether autologous (auto-HSCT) or allogeneic (allo-HSCT) transplant, and the degree of graft vs. host disease (GVHD) necessitating further immunosuppressive therapy. In addition to impaired humoral and cellular immunity, both allo- and auto-HSCT recipients have deficiencies in innate immunity in first few weeks to months after transplant until successful engraftment has occurred. Allo-HSCT recipients are also considered functionally asplenic in the first 2 years of transplant [15]. In addition, the immunomodulatory effect of biologics, such as anti-CD20 antibody rituximab and anti-CD52 antibody alemtuzumab used commonly in allo-HSCT, may take 6—12 months to recover [16,17]. Certain