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Review

International travelers receiving pharmacological immunosuppression: Challenges and opportunities☆

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ABSTRACT

There is an increasing number of international travellers receiving immunosuppressive therapy due to the better life expectation and quality offered by this kind of treatment.

The complexity of pre-travel counselling in these patients lies in their greater susceptibility to certain travel-related infections and the potential severity of these, as well as in the contraindications and interactions that may occur between certain vaccines and/or prophylaxis and their base therapy.

Counselling the traveller represents a challenge for clinicians who have to tailor vaccinations and other recommended preventive measures to the immunosuppressed patients. Thus, pre-travel assessment of patients receiving immunosuppressive therapy should be performed in a specialized Traveler's Medical Unit, working closely with the specialist doctor in charge of treating the patient's underlying medical condition.

The purpose of this article is to review available evidence on the health recommendations indicated in the pre-travel administration of vaccines, antimalarial chemoprophylaxis and other measures to prevent communicable diseases in travellers receiving immunosuppressive therapy.

El viajero internacional con inmunodepresión farmacológica: retos y oportunidades

Palabras clave:
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RESUMEN

El número de viajeros internacionales bajo inmunodepresión farmacológica (IDF) ha aumentado debido a la mejor expectativa y calidad de vida que proporcionan estas terapias.

La complejidad de la asesoría previaje en estos pacientes radica en su mayor susceptibilidad y gravedad ante determinadas infecciones relacionadas con el viaje, así como en las contraindicaciones e interacciones de determinadas vacunas y/o profilaxis con sus terapias de base.

El consejo al viajero representa un reto para el clínico, que tiene que adaptar las vacunas y otras medidas preventivas a los pacientes inmunodeprimidos. Por ello, la valoración previa al viaje en pacientes con IDF debe realizarse en una unidad de medicina del viajero, de forma coordinada con el médico especialista que maneja su enfermedad de base.

El objetivo de este artículo es revisar la evidencia disponible sobre las recomendaciones sanitarias indicadas en viajeros bajo tratamiento inmunosupresor en relación con la aplicación de vacunas, quimioprofilaxis antimalárica y otras medidas de prevención de enfermedades transmisibles.

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Introduction

Travellers with pharmacological immunosuppression (PI) constitute a growing group within the total group of travellers.[1] In recent years, new biologic drugs have been developed and their use has increased due to the growing number of autoimmune and chronic inflammatory diseases over which they have proved beneficial.[2,3] The use of suppressive therapies has contributed to improve the health of patients with chronic diseases such as rheumatoid arthritis (RA) or inflammatory bowel disease (IBD).[4] All this has favoured a significant increase in the number of travellers with PI travelling to exotic destinations.[5]

The percentage of exotic-destination travellers with immunosuppression of any type (pharmacological, transplanted, HIV/AIDS, haematological neoplasms, thymectomised, or splenectomised) range between 1.6% and 4.2% according to various studies.[1,6] Regarding the drugs that determine PI, the most used in this group of travellers are glucocorticoids (GCC) at high doses, drugs that inhibit tumour necrosis factor and methotrexate.[6]

Within the broad spectrum of immunosuppressive drugs, Table 1 lists the most commonly used drugs by travellers with PI.[7,8]

Regarding travel-related diseases, evidence shows that this group of patients imports infectious disease more often,[9,10] that these have a longer course and that they are associated with greater morbidity and mortality than travellers without PI.[11–13] Despite this, the most common medical problem during a trip abroad in this type of travellers usually derives from the exacerbation/complication of their underlying disease, rather than from a disease strictly related to travel.[1,14] Compared to healthy travellers, PI travellers have more demand for medical care and a greater number of episodes of hospitalization during the trip or in the month after the trip, and are repatriated for health reasons more often than non-PI travellers.[15]

Characteristically, this group of travellers requests health information prior to travelling in a percentage higher than that of the healthy population, but the information is requested primarily from the specialist treating their underlying disease (rheumatologist, gastroenterologist, etc.) and less than 20% asks for advice from a specific traveller's medicine unit.[16,17] This identifies a point of potential intervention in the protection of the traveller with PI, since medical specialists are an important source of detection of travellers at risk.

However, the management of interactions between immunosuppressive therapy and drugs used as prophylaxis in travel (antimalarials or antibiotics, among others) or the relevance of the administration of vaccines that may be contraindicated or produce a suboptimal immune response in travellers with PI[16] can be complex. Therefore, the prior-to-travel assessment in patients with PI must be done in a traveller's medicine unit, in a coordinated manner with the specialist doctor who manages his/her underlying disease.[3,18]

Among health professionals there is little knowledge of preventive health interventions in relation to travel in this type of patients. Therefore, this review article includes current knowledge on health recommendations indicated in travellers with PI, including those in treatment with biological drugs, immunomodulators and GCC at high doses. We also review the available evidence regarding interactions and contraindications of the most frequently recommended vaccines in international travel. Finally, we summarize the behaviour of the main diseases imported by the patient with PI, as well as the specific pre-travel recommendations that should be made in this particular group of travellers.

Table 1
Immunosuppressive therapies most frequently used by travellers with pharmacological immunosuppression.

Immunosuppressive therapy	Mechanism	Observations
Glucocorticoids	Interferes at different levels in the immune and inflammatory response	Risk if: Prednisone > 2 mg/kg/day Prednisone ≥ 20 mg/day (or equivalent dose of another glucocorticoid) for more than 14 days
Antimetabolite agents (methotrexate, azathioprine, 6-mercaptopurine)	Inhibit the proliferation of B/T cells	Risk if: Methotrexate > 4 mg/kg/week Azathioprine > 3 mg/kg/day 6-Mercaptopurine > 1.5 mg/kg/day
Biological: tumour necrosis factor (anti-TNF) inhibitors, monoclonal ab, receptor inhibitors	Blocks the development of the inflammatory cascade	Increased risk especially with alemtuzumab and rituximab

General recommendations for the traveller with pharmacological immunosuppression

Despite their medical condition, the traveller with PI faces the same risks as healthy travellers during the trip (intake of food without sanitary control, unprotected sexual intercourse, having tattoos/*piercings*, etc.).[16,17] Therefore, the general recommendations should not differ from those given to any other traveller in terms of measures to prevent insect bites, traveller's diarrhoea or sexually transmitted diseases.[19]

Vaccines recommended for travellers with pharmacological immunosuppression

The administration of the vaccines indicated for the specific destination of the traveller with PI should be carefully evaluated, since some of them may be contraindicated or require modifications in the vaccination schedule due to the PI condition. The administration of any vaccine prior to the start of immunosuppressive therapy is recommended (at least 4 weeks before for live vaccines and 2 weeks for attenuated vaccines).[20,21]

The vaccines most frequently indicated in international travel, as well as the specific recommendations in travellers with PI are shown in Table 2.

Vaccines of killed or inactivated microorganisms

They can be administered without any safety concerns and at any time or phase of the disease that determines the immunosuppressive treatment.[12,22] However, it is advisable to administer them before the start of immunosuppression to guarantee a better immune response[23–26] (at least 2 weeks before). It is generally recommended to postpone vaccination if there is intense activity (flare-up) of an autoimmune disease at that time.[27]

In case of vaccination during the immunosuppression period, it is recommended to monitor the serological response after one month from the last dose in cases where it is feasible (for example, anti-HB_s Ab after vaccination against hepatitis B) or assess revaccination after 3 months from the end of the immunosuppressive treatment.[27,28]

Hepatitis A

Hepatitis A (HAV) is a viral disease of faecal-oral transmission widely distributed in the world that can be devastating in travellers with PI.[29] The vaccine against HAV is one of the most frequently prescribed to the traveller.[4,30] The standard administration regimen