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PRACTICAL DERMATOLOGY

Practical Management of Immunosuppressants in Dermatology☆

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Abstract The treatment of inflammatory and autoimmune diseases is challenging because of their frequency and complexity. Treatment of these diseases is based on the suppression of the patient's immune system using corticosteroids, corticosteroid-sparing immunosuppressive agents, and biologic drugs, making an understanding of the management of immunosuppressive therapy essential. Before an immunosuppressive agent is prescribed, a study must be carried out to identify contraindications, detect latent infections, and determine the most appropriate dose. During treatment, regular monitoring is required to detect adverse effects. The clinician must be familiar with the time lag between start of treatment and onset of the immunosuppressive effect as well as the maximum recommended duration of treatment and cumulative dose for each drug. As dermatologists we are accustomed to using these immunosuppressive agents, but we should have a good knowledge of the guidelines for their use and the monitoring required in each case if we are to reduce variability and avoid potentially serious adverse effects.

PALABRAS CLAVE
Metotrexato;
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Ciclofosfamida;
Azatioprina;
Micofenolato;
Inmunosupresión

Manejo práctico de inmunosupresores en dermatología

Resumen Las enfermedades inflamatorias y autoinmunes constituyen un desafío terapéutico por frecuencia y complejidad. Su tratamiento se basa en la inmunosupresión del paciente con glucocorticoides, inmunosupresores ahorradores de corticoides y fármacos biológicos, siendo imprescindible por tanto conocer su manejo. Cuando se va a pautar un inmunosupresor es necesario realizar un estudio previo para detectar contraindicaciones, infecciones latentes o determinar la dosis más adecuada del fármaco. Durante el tratamiento se deben realizar

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controles periódicos para detectar efectos secundarios. Cada fármaco tiene un tiempo de inicio de acción que es preciso conocer, así como una duración o dosis acumulada máxima recomendada. Los dermatólogos estamos habituados al uso estos fármacos inmunosupresores, pero es necesario tener claras las pautas y los controles necesarios con cada uno, para disminuir la variabilidad y evitar efectos adversos potencialmente graves.

Introduction

Dermatologic autoimmune or inflammatory diseases are usually managed with immunosuppressants. Care must be taken to find a point of balance that attenuates the abnormal inflammatory response while causing the least possible immunosuppression.

The prescriber must be aware of each immunosuppressant's unique time to onset of action, level of acute toxicity, and dosage regimens. An intense, rapid response is sometimes warranted, but a goal in other circumstances might be a treatment that can be followed over the long term.

This review deals with classic immunosuppressants. Neither glucocorticoids nor biologics will be discussed.

Pretreatment Tests and Vaccinations

Before suppressing a patient's immune response, information is required for ruling out contraindications, tailoring the dosage, and planning measures to reduce inherent risk.

Certain laboratory tests are needed for prescribing any of these drugs, but particular immunosuppressants also have specific requirements[1] (Table 1).

Because vaccination coverage should be on record for all patients, serology is included in the test battery.[2–5] If the patient's clinical condition permits, required vaccinations or booster doses should be scheduled at least 2 weeks before immunosuppressant therapy starts. If vaccination is not feasible beforehand, it should not be undertaken until at least 3 months after treatment stops given that live virus vaccines carry the risk of infection, and immunization may not be achieved if inactivated viruses are used.

Vaccination against varicella should be tailored to the individual. If a pediatric vaccination schedule must be followed, immunosuppressants should be interrupted 2 weeks before vaccination and not restarted until 2 weeks afterwards.[6]

Two types of pneumococcal vaccines are available: the 23-valent polysaccharide (PPSV23) and 13-valent conjugate (PCV13) versions. Spanish health authorities stipulate a sequential vaccination schedule for patients on

Table 1 Complementary Tests to Order Before Starting Immunosuppressant Therapy.

Methotrexate	Ciclosporin	Azathioprine	Mycophenolate Mofetil and Mycophenolate Sodium	Cyclophosphamide
Complete blood count, including differential white blood cell counts Biochemistry, including glucose, ion concentrations, kidney function, liver function (transaminase, alkaline phosphatase, bilirubin, albumin), lipids, uric acid Serology for HBV, HBC, and HIV Full vaccination coverage Tuberculosis screening (Mantoux test or quantitative interferon gamma release assay) Pregnancy test in women of childbearing age				
Contraindicated if total bilirubin concentration is > 5 mg/dL Urinalysis Chest x-ray P3NP level	Estimated GFR to dermine renal function and adjust dosage. Blood pressure	TPMT level		Chest x-ray (consider) Urinalysis. Rule out adrenal insufficiency (baseline cortisol and ACTH levels, stimulation test to measure cortisol before and after injection of 250 μg of ACTH). Spermogram and sperm banking prior to treatment.

Abbreviations: ACTH, adrenocorticotropic hormone; GFR, glomerular filtration rate; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; P3NP, procollagen type III N-terminal peptide; TPMT, thiopurine methyltransferase.