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REVIEW

Cardiovascular Risk and Psoriasis: the Role of Biologic Therapy☆

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KEYWORDS
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Anti-p40;
Interleukin 17;
Interleukin 12;
Interleukin 23

Abstract One of the most clinically important aspects of recent advances in our understanding of psoriasis has been the detection of an association between this disease and an increased prevalence of cardiovascular risk factors. This increase in prevalence is, in turn, linked to a greater risk of morbidity and mortality related to acute myocardial infarction, cerebrovascular accident, and peripheral arterial disease. The chronic systemic inflammation present in psoriasis could explain why moderate to severe psoriasis is an independent risk factor for cardiovascular disease. The introduction of biologic therapies has greatly improved the expectations of treatment as well as the long-term control of psoriasis, and there is epidemiological evidence that these therapies may lower cardiovascular risk in psoriasis as they do in rheumatoid arthritis. Caution should, however, be exercised when prescribing biologic drugs in this setting, because adverse effects have been reported in association with the use of tumor necrosis factor inhibitors in patients with advanced congestive heart failure. Furthermore, a numerical imbalance (without statistical significance) between the groups receiving the biologic drug and the placebo groups was recently observed in the incidence of major cardiovascular events (nonfatal myocardial infarction and cerebrovascular accident and cardiovascular death) during the controlled periods of clinical trials of briakinumab and ustekinumab, 2 monoclonal antibodies that target the p40 subunit shared by IL-12 and IL-23. We review the current scientific evidence on this topic.

PALABRAS CLAVE
Psoriasis;
Comorbilidades;
Riesgo cardiovascular;
Infarto de miocardio;
Acontecimientos adversos cardiovasculares mayores;

Riesgo cardiovascular y psoriasis: papel de la terapia biológica

Resumen Uno de los aspectos clínicamente más relevantes de los recientes avances en el conocimiento de la psoriasis es su asociación con un aumento en la prevalencia de factores de riesgo cardiovascular, que determina un mayor riesgo de morbimortalidad relacionada con infarto agudo de miocardio, accidente cerebrovascular y arteriopatía periférica. La inflamación sistémica crónica asociada podría explicar en gran medida que la psoriasis moderada-grave sea un factor de riesgo independiente de enfermedad cardiovascular. La introducción de la terapia biológica ha mejorado en gran medida nuestras expectativas terapéuticas y el control a largo plazo de la enfermedad, y existen evidencias epidemiológicas de que puede mejorar también el riesgo cardiovascular, como ocurre en los pacientes con artritis reumatoide. Sin embargo, se

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Biológicos;
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Anti-p40;
Interleucina 17;
Interleucina 12;
Interleucina 23

han descrito algunos efectos adversos del tratamiento con agentes bloqueadores del factor de necrosis tumoral alfa en pacientes con insuficiencia cardíaca congestiva avanzada que obligan a tener especial precaución con su empleo en estos pacientes. Por otra parte, recientemente se ha observado un desequilibrio (aunque no estadísticamente significativo) en el número de acontecimientos adversos cardiovasculares mayores, que incluyen infarto de miocardio no letal, accidente cerebrovascular no letal y muertes de causa cardiovascular, en la fase controlada con placebo de los ensayos clínicos con briakinumab y ustekinumab, 2 anticuerpos monoclonales dirigidos contra p40, la subunidad común a IL-12 e IL-23. En el presente artículo se revisa la evidencia científica disponible en este campo.

Introduction

The present article reviews the association between psoriasis and both cardiovascular risk factors and cardiovascular disease, paying special attention to the implications of this association for treatment, particularly with biologic therapies.

Certain conventional systemic treatments have effects that are counterproductive when viewed from the standpoint of the comorbidities associated with psoriasis. It is well known that ciclosporin can potentially cause or exacerbate hypertension, diabetes mellitus, and dyslipidemia, and that dyslipidemia is a common side effect of acitretin. The fact that biologic drugs lack these contraindications would tend to justify their use in patients with these and other comorbidities. However, there is also evidence to suggest that the treatment of psoriasis with biologic agents may, in some cases, be counterproductive from the point of view of cardiovascular risk.

The possibility that tumor necrosis factor (TNF) inhibitors may exacerbate congestive heart failure (CHF) obliges us to exercise particular caution when prescribing them in these patients, as stated in the Summaries of Product Characteristics for these drugs. Furthermore, the possibility has recently been raised that certain biologic agents may increase cardiovascular morbidity and mortality: an analysis of the clinical trials of monoclonal anti-p40 antibodies has shown a statistically nonsignificant numerical imbalance compared to the placebo group in the occurrence of major adverse cardiac events (MACE), especially at the start of treatment.[1] MACE are defined as nonlethal myocardial infarction, nonlethal stroke, and death from cardiovascular causes.

Psoriasis and Cardiovascular Risk

There is abundant scientific evidence supporting the association of moderate to severe psoriasis with an increased prevalence of cardiovascular risk factors and we will not discuss this topic in depth because it has already been the subject of excellent review articles.

A number of multivariate models for calculating cardiovascular risk in asymptomatic and apparently healthy individuals have been developed in recent years. The Framingham charts were designed to estimate the 10-year risk of myocardial infarction or death from cardiovascular disease. The risk factors initially used included age, sex, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, blood pressure, diabetes, and smoking.[2] The Framingham score identifies 3 categories of risk: low ($\leq$ 10% risk of myocardial infarction), intermediate (10% to 20% risk), and high (> 20% risk). The Framingham criteria were developed from the study of a cohort of residents in Framingham, Massachusetts and are not strictly applicable to other populations, and the risk estimate does not include stroke and other manifestations of cardiovascular disease. Despite extensive usage elsewhere, the Framingham risk score and other similar scales (REGICOR, Reynolds, SCORE) have been little used in the routine assessment of cardiovascular risk in patients with moderate to severe psoriasis.

The authors of a case-control study found that the 10-year cardiovascular risk in patients with psoriasis calculated using the Framingham score was intermediate (mean 11.2), but nonetheless significantly higher than in a control cohort matched for age and sex.[3] In a clinical trial enrolling patients with moderate to severe psoriasis and a Psoriasis Area and Severity Index (PASI) greater than 10, while the average Framingham Risk score at 10 years was 5.63, 41% of the patients had metabolic syndrome[4]; the presence of elevated levels of C-reactive protein (CRP) was indicative of increased risk of cardiovascular disease in this population.[5]

A recently published cohort study based on the UK General Practice Research Database (GPRD) indicates that severe psoriasis (defined by the use of systemic therapy) confers an increased risk of MACE (hazard ratio [HR] 1.53; 95% CI, 1.26-1.85) after adjustment for age, sex, presence of diabetes, hypertension, smoking, and hyperlipidemia[6]; the estimated absolute increase in risk of MACE at 10 years is 6.2%.

The UK GPRD has provided extensive data, but questions have been raised concerning how psoriasis was diagnosed in these patients, the definition of severe disease as disease requiring systemic treatment, and the applicability of the findings to other geographical areas. In 2006, Gelfand et al.[7] published a prospective, population-based cohort study based on data from the UK GPRD in patients with psoriasis aged 20 to 90 years. They compared the incidence of myocardial infarction in patients with and without a diagnosis of psoriasis. Psoriasis was classified as severe if the patient had ever received systemic therapy. The data had been collected by general practitioners between 1987 and 2002 and mean follow-up was 5.4 years. Adjustments were made for hypertension, diabetes, history of myocardial infarction, hyperlipidemia, age, sex, smoking, and body mass index. Up to 5 controls without psoriasis were selected