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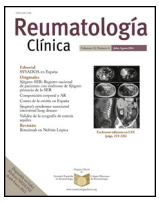

Original Article

Is Obesity in Psoriatic Arthritis Associated With a Poorer Therapeutic Response and More Adverse Effects of Treatment With an Anchor Drug?☆

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ABSTRACT

Objectives: To assess the association between obesity, control of inflammatory activity and increased adverse effects in psoriatic arthritis (PsA) with disease-modifying anti-inflammatory drugs (DMARD).
Methods: A systematic literature review was performed using MEDLINE and EMBASE databases following the guidelines of the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) consensus statement. Studies were selected if they included patients with PsA, obesity was studied as a predictive factor, and the outcome was adverse effects, including efficacy failure. Quality was assessed using an ad hoc risk of bias tool. A qualitative analysis was carried out by type of study and study population, quality and specific results.
Results: We found 1043 articles, discarding most of them on the basis of title and abstract. Ten articles were studied in detail and finally excluded three. The majority concluded, with statistically significant results, that in patients with PsA and treated with TNFα inhibitors (TNFαi), obesity is associated with poorer chances of achieving and maintaining a minimal disease activity, higher treatment discontinuation rates, and lower skin response. Regarding conventional synthetic DMARD, a trend toward a moderate increase in transaminases with methotrexate (MTX) was observed in obese patients with PsA.
Conclusions: Obesity is a negative predictor of clinical response in patients with PsA being treated with TNFαi. Except MTX hepatotoxicity, no other adverse effects, either with TNFαi or other drugs, were found in relation to obesity in PsA.

¿Se asocia la obesidad en la artritis psoriásica a una menor respuesta terapéutica y más efectos adversos con el tratamiento de fondo?

Palabras clave:
Obesidad
Artritis psoriásica
Efectos adversos
Biológicos
Fármacos modificadores de la enfermedad

RESUMEN

Objetivos: Estudiar si en la artritis psoriásica (APs) hay asociación entre la obesidad, el control de la actividad inflamatoria y el aumento de efectos adversos con los fármacos modificadores de la enfermedad (FAME).
Métodos: Revisión sistemática de la literatura utilizando las bases de datos Medline y Embase según las guías del consenso MOOSE. Se incluyeron estudios en pacientes con APs, en los que la obesidad fuera factor predictor de efectos adversos y el desenlace fuera toxicidad, incluido fallo de eficacia. La calidad se evaluó mediante una escala de riesgo de sesgos ad hoc. Se realizó un análisis cualitativo por tipo de estudio y población estudiada, calidad y resultados específicos.

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Resultados: Se encontraron 1.043 artículos, la mayoría se descartaron por título y abstract. Se estudiaron en detalle 10, excluyéndose finalmente 3. La mayoría concluye con resultados estadísticamente significativos que la obesidad en pacientes con APs e inhibidores del TNF-α (iTNF-α) se asocia a una probabilidad menor de alcanzar y mantener la mínima actividad inflamatoria, con mayor tasa de interrupción del tratamiento y menor tasa de respuesta cutánea. En relación con los FAME sintéticos convencionales, se observó en obesos una tendencia a un aumento moderado de las transaminasas con metotrexato (MTX).
Conclusiones: La obesidad es un factor predictivo negativo de la respuesta clínica en pacientes con APs e iTNF-α. Exceptuando la hepatotoxicidad por el MTX, no se encontraron otros efectos adversos ni por otros fármacos en relación con la obesidad.

Introduction

Obesity and its complications are common in patients with psoriatic disease.[1–5] A number of epidemiological studies have identified a higher risk of developing certain metabolic alterations in patients with psoriasis and psoriatic arthritis (PsA), which also includes obesity. This is also because obesity and psoriasis seem to be linked by a common pathophysiological mechanism, which is explained by a chronic low-grade inflammation,[2] with an increase in local and systemic inflammatory markers. In obesity, adipocytes show an imbalance resulting in an excessive secretion of the cytokines most detrimental from the cardiovascular point of view, such as interleukin (IL)-6, IL-18, tumor necrosis factor-alpha (TNFα) and leptin, as well as, a decreased release of protective cytokines, like adiponectin.[2,6]

It is known that obesity is associated with a higher incidence and severity of psoriasis, and that its presence affects the therapeutic response.[7–9] This relationship is less widely studied in PsA. On the other hand, treatment with TNFα inhibitors (TNFαi) has been associated with an increase in weight both in psoriasis and in PsA,[10] a fact that should be taken into account in the follow-up of these patients. It is for this reason that we propose studying whether obesity is associated with a higher incidence of adverse effects than treatments using an anchor drug in PsA, including the lack of response as an adverse effect.

Methods

The study involved a systematic review of the literature, in a search for observational studies, using the guidelines of the MOOSE consensus.[11]

Search Strategy

We performed a search using Medline (via PubMed) and EMBASE databases (until 28 May 2015). The major PICO terms used for this analysis were "obesity" and "psoriatic arthritis". Table 1 shows the terms utilized for the search. We introduced no limits concerning language, dates or ages, and only considered studies in humans.

Table 1
Search strategies.

Medline	EMBASE
"Obesity" [Mesh]	"Obesity"/exp
Obesity [tw]	"Overweight"/exp
Obesity [ti]	————————
Obesity [ab]	Weight gain/exp
"Overweight" [Mesh]	—————————
"Overweight" [tw]	Adipose tissue hyperplasia
"Overweight" [ti]	Adipositas
"Overweight" [ab]	Adiposity
"Body Mass Index" [Mesh]	Alimentary obesity
"Body Mass Index" [tw]	Body weight, excess
"Body Mass Index" [ti]	Fat overload syndrome
"Body Mass Index" [ab]	Nutritional obesity
"Body Weight/adverse effects" [Mesh]	Obesitas
"Body Weight/drug effects" [Mesh]	Overweight
"Abdominal Obesities" OR "Abdominal Obesity" OR "Obesities, Abdominal" OR "Central Obesity" OR "Central Obesities" OR "Obesities, Central" OR "Obesity, Central" OR "Obesity, Visceral" OR "Obesities, Visceral" OR "Visceral Obesities" OR "Visceral Obesity" OR "Morbid Obesities" OR "Obesities, Morbid" OR "Obesity, Severe" OR "Obesities, Severe" OR "Severe Obesities" OR "Severe Obesity" OR "Morbid Obesity"	IMC (body mass index) Body ban mass Body mass index Quetelet index Weight increase ——————— "Psoriasis" AND "arthritic" "Psoriatic" AND "arthritis" "Psoriasis" AND "arthritis" "Psoriatic arthritis"/exp OR "Psoriatic arthritis"
("Arthritis, Psoriatic" [Mesh] OR "psoriatic arthritis" OR (psoriasis AND arthritic) OR (arthritic AND psoriasis) OR "Psoriasis Arthropathica" OR (arthritis AND psoriasis))	

Study Selection

The following selection criteria were established: (1) all the patients should have PsA or there should be an analysis differentiating patients with PsA; (2) the effect of the obesity factor or body mass index (BMI) should have been studied as a primary or secondary outcome measure; (3) the study had to be a clinical trial, a prospective or retrospective longitudinal or a case-control design, but series of case reports were not accepted; and (4) the outcome (primary measure) could be toxicity, whether specific or in general: hepatotoxicity (increase in enzymes, fibrosis, cirrhosis, hepatocarcinoma), insulin resistance, dyslipidemia, hypertension, hyperuricemia, a shorter survival than that attributed to the treatment or better therapeutic efficacy.

Two reviewers screened the articles according to title and abstract, and maintained for in-depth review any that offered doubts as to whether or not they complied with the selection criteria. We include the articles selected using this system, and record those that were not. The reason for exclusion is offered in the detailed review.

Variables and Data Collection

From the articles reviewed in detail, we gathered all the data from the sample description and the study objective, the design and duration of patient follow-up, the drugs employed, the definition of obesity, the variables utilized and their units of measure, with and without adjustment, as well as the variables included in the adjustment.

The quality was measured using an ad hoc risk of bias tool, that included: (1) design (low bias in prospective longitudinal and high bias in retrospective or case-control studies); (2) drug exposure time (high bias if the time is short, less than 3 months); (3) clarity