Efficacy and safety of TNF antagonists in sarcoidosis: data from the Spanish registry of biologics BIOBADASER and a systematic review

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CRD summary
This review concluded that there was insufficient evidence on the efficacy of TNF antagonists in sarcoidosis; this conclusion appears to be appropriate given the small volume of poor quality evidence available. A secondary conclusion that infliximab may be effective in selected manifestations of the disease may not be reliable.

Authors' objectives
To evaluate the safety, efficacy and effectiveness of TNF antagonists in patients with sarcoidosis.

Searching
MEDLINE, EMBASE and Cochrane Library databases were searched from 1998 to July 2011 for relevant articles published in English, Spanish, French, Italian or Portuguese. Search terms were not reported. Conference abstracts and reference lists were searched for relevant studies.

Study selection
Randomised controlled trials (RCTs), case series and case studies that measured safety or efficacy of any TNF antagonist in any patients with histologically diagnosed sarcoidosis were eligible for inclusion in the review.

Two reviewers independently selected studies; disagreements were resolved by a third reviewer.

Nine out of 10 of the included patients received infliximab and one in 10 received etanercept. Mean patient age was 42 (range 35 to 56), average disease duration was seven years (range four to 12) and 55% of patients were women.

Pathogenesis and degree of involvement in different organs varied widely between patients and included lung, eye, skin, heart, bone, liver, muscle, brain and systemic involvement.

The systematic review was supplemented with a summary of cases taken from the Spanish BIOBADASER registry of biological therapies.

Assessment of study quality
Individual study risk of bias was not assessed. The included studies were rated using a modification of the Oxford Levels of Evidence criteria. It was not clear how many authors performed this assessment.

Data extraction
Participant and study characteristics were extracted from the included studies; it was not clear how many authors performed the extraction.

Methods of synthesis
Studies were combined in a narrative synthesis.

Results of the review
Sixty-eight studies were included in the review: three RCTs, 12 case series and 53 individual case reports; a total of 258 patients were included in the RCTs and case series. Mean length of follow-up was 15 months (range two to 36). Level of evidence ratings suggested that the included RCTs were of low quality.

Two RCTs of infliximab reported a positive effect on vital capacity in patients with lung involvement. One RCT that included nine patients with eye involvement found no benefit of etanercept treatment. Results of case series and individual case studies were diverse.

Base on data from RCTs and case series, mean weighted rates of adverse events, infections, serious infections and malignancy were 39.9, 22.1, 5.9 and 1.0 per 100 patient-years.
Eight patients in the BIOBADASER registry who received infliximab for sarcoidosis were described briefly.

**Authors' conclusions**
There was insufficient evidence on the efficacy of TNF antagonists in sarcoidosis. Infliximab may be effective in selected manifestations of the disease.

**CRD commentary**
This review found very little evidence on the efficacy of TNF antagonists for sarcoidosis and most appeared to be of poor methodological quality. Much of the evidence was uncontrolled. A large proportion of patients received concomitant steroids and/or DMARDs. The methods and results of the systematic review were not reported clearly and this creating further uncertainty about the reliability of its findings. The available research evidence appeared to report inconsistent results for a very diverse group of sarcoidosis patients. Therefore, the authors’ conclusion that there was insufficient evidence on efficacy is appropriate. However, the secondary conclusion that infliximab may be effective in selected manifestations of the disease may not be reliable as it was based on a small volume of poor quality evidence.

**Implications of the review for practice and research**
The authors did not make any recommendations for practice and research.

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