A systematic review of the literature on the treatment of pityriasis rubra pilaris type 1 with TNF-antagonists

Petrof G, Almaani N, Archer CB, Griffiths WA, Smith CH

CRD summary
This review found insufficient evidence to determine the efficacy of tumour necrosis factor (TNF)-antagonists (immunosuppressants) in the treatment of pityriasis rubra pilaris type 1 (a chronic skin disorder) in adults. The authors reliably concluded that no firm recommendations could be made about the management of pityriasis rubra pilaris with TNF-antagonists on the basis of the existing evidence.

Authors' objectives
To assess evidence of efficacy of tumour necrosis factor (TNF)-antagonists in the treatment of pityriasis rubra pilaris type 1 in adults.

Searching
The Cochrane Library, PubMed, MEDLINE and EMBASE were searched (January 1999 until October 2011) with no language restriction, using specified search terms. The review authors' own case studies were also included.

Study selection
Studies were eligible for inclusion if they included adults with a definite or likely diagnosis of pityriasis rubra pilaris type 1 who were being treated with TNF-antagonists. Pityriasis rubra pilaris was defined as meeting two or more diagnostic criteria: a compatible clinical history; typical clinical features and/or diagnostic histopathology findings; clinical photographs consistent with pityriasis rubra pilaris.

Among the included studies, one third of participants were women (median age of 59 years; 30 to 65 years) and two-thirds were men (median age 56 years; 24 to 79 years). A definite diagnosis of pityriasis rubra pilaris (meeting all three of the diagnostic criteria) was found in 53% of patients. The mean disease duration was nine months. Infliximab, etanercept and adalimumab (TNF-antagonists) were used individually or in combination with oral immunosuppressants such as methotrexate and acitretin. A combination of one TNF-anatagonist agent with an oral immunosuppressant (acitretin and methotrexate were most common) appeared to be the treatment of choice in most cases. Infliximab was administered following the psoriasis protocol at week zero, two, six and every eight weeks thereafter using the standard dose of 5mg/kg.

The number of reviewers selecting studies was not stated, but disagreements were resolved by consensus.

Assessment of study quality
Study quality was not formally appraised.

Data extraction
Patient characteristic data were abstracted with details of type of intervention and clinical response. The authors considered to what extent the clinical response could be clearly assigned to the TNF-antagonists based on concomitant systemic therapy. Clinical response was defined as complete, partial or poor. Complete response was defined as 'dramatic or spectacular improvement', 'near clearance', 'almost clear' or 'complete regression', supported by photographic evidence showing adequate body surface area. Partial response was based on the physician's global evaluation of 'partial clearing' or 'partial response' and/or photographic evidence showing 50% of skin disease improvement. 'Poor response' or 'no response' was defined by the use of these terms in the article.

The number of reviewers extracting data was not stated.

Methods of synthesis
Narrative review and vote counting procedures were used to summarise the evidence.
Results of the review
Fifteen case studies were included in the review.

Twelve out of the 15 cases showed complete response, two cases showed partial response and one case showed no response. Only eight of the 15 cases had a definite diagnosis of pityriasis rubra pilaris. The mean time to initial response was five weeks; mean time to best response was five months.

Authors' conclusions
TNF-antagonists may be of value in treating adult type 1 pityriasis rubra pilaris refractory to other systemic agents, but selective reporting bias, together with the lack of standard diagnostic criteria and established spontaneous resolution in pityriasis rubra pilaris, prevent any firm recommendations on their place in management.

CRD commentary
This review used appropriate methods to minimise bias in the searching and acquisition of evidence. The embryonic nature of the evidence-base precluded any formal meta-analysis, so the authors resorted to vote-counting to summarise results.

The authors reported problems relating to uncertain diagnosis, use of concomitant therapies, spontaneous resolution of the condition and potential for selective reporting, along with small sample sizes, lack of comparators and diversity of treatment modalities; this made any conclusions on the efficacy of TNF-antagonists for pityriasis rubra pilaris type 1 premature. The authors suggestion for further research appeared to be well founded. The extent to which generalisations could be made across related conditions may also warrant further consideration in the context of pragmatic decision-making.

The authors' conclusion that the evidence-base was insufficient to provide recommendations is both reliable and judicious.

Implications of the review for practice and research
Practice: The authors stated that no firm recommendations can be made on the place of TNF-antagonists in the management of pityriasis rubra pilaris.

Research: The authors stated that prospective clinical data from well-designed clinical studies of adult type pityriasis rubra pilaris were needed to establish accurately the efficacy of TNF-antagonists.

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