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[Intervention Review]

Anti-TNF agents for paediatric psoriasis

Gloria Sanclemente[1], Ruth Murphy[2,3], Javier Contreras[4], Hermenegildo García[5], Xavier Bonfill Cosp[6]

[1]Grupo de Investigación Dermatológica (GRID), Universidad de Antioquia, Medellín, Colombia. [2]Department of Dermatology, Sheffield Children's Hospital, Sheffield Children's NHS Foundation Trust, Sheffield, UK. [3]Department of Dermatology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK. [4]Department of Pediatrics, School of Medicine, Universidad de Antioquia, Medellin, Colombia. [5]c/o Cochrane Skin Group, The University of Nottingham, Nottingham, UK. [6]Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB Sant Pau), CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain

Contact: Gloria Sanclemente, Grupo de Investigación Dermatológica (GRID), Universidad de Antioquia, Carrera 25 A #1 A Sur 45, Of 2026, Torre Medica El Tesoro, Medellín, Colombia. sanclementegloria@gmail.com, gsanclementem@gmail.com.

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ABSTRACT

Background

Psoriasis is a chronic skin disease that may develop at any age. Estimates for the United States and Europe suggest that psoriasis accounts for 4% of skin diseases in children. In most cases, the condition is mild and can be treated with creams. However, a small percentage of children have moderate to severe disease that requires drugs, such as ciclosporin or methotrexate, and some will require injections with newer biological agents, such as anti-TNF (tumour necrosis factor) drugs. Anti-TNF drugs (among them etanercept, infliximab, and adalimumab) are designed to reduce inflammation in the body caused by tumour necrosis factor. Evidence for the safety and efficacy of these biological agents in paediatric psoriasis is lacking.

Objectives

To assess the efficacy and safety of anti-TNF agents for the treatment of paediatric psoriasis.

Search methods

We searched the following databases up to July 2015: the Cochrane Skin Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 6), MEDLINE (from 1946), Embase (from 1974), and LILACS (from 1982). We also searched 13 trials registers and checked the reference lists of included studies and key review articles for further references to relevant randomised controlled trials (RCTs). We handsearched conference proceedings and attempted to contact trial authors and relevant pharmaceutical manufacturers. We searched the US Food and Drug Administration's and European Medicines Agency's adverse effects databases.

Selection criteria

All relevant RCTs that evaluated the efficacy and safety of anti-TNF agents for the treatment of chronic plaque psoriasis in individuals less than 18 years of age.

Data collection and analysis

Two review authors independently checked titles and abstracts and performed data extraction and 'Risk of bias' assessment of the included studies. One review author entered data into Review Manager (RevMan), and a second review author checked the data. We also attempted to obtain unclear data from the trial authors where possible.

Our primary outcomes were investigator-assessed number of participants achieving a 75% improvement in Psoriasis Area and Severity Index-75 (PASI 75) compared to baseline, improvement in quality of life using an instrument such as Children's Dermatology Life Quality

Index (CDLQI), and adverse effects. Our secondary outcomes included the proportion of participants achieving PASI 50 and the Physician's Global Assessment (PGA).

Main results

We included one study with 211 participants (median age 13 years), in which etanercept (dosage ranged from 0.8 to 50 mg per kilogram of body weight) was compared to placebo. Follow-up was over a 48-week period.

At week 12, 57% versus 11% who received etanercept or placebo, respectively, achieved the PASI 75 (risk ratio 4.95, 95% confidence interval (CI) 2.83 to 8.65; high-quality evidence). Absolute risk reduction and the number needed to treat to obtain a benefit with etanercept was 45% (95% CI 33.95 to 56.40) and 2 (95% CI 1.77 to 2.95), respectively.

The percentage improvement from baseline of the CDLQI scores at week 12 was better in the etanercept group than the placebo group (52.3% versus 17.5%, respectively (P = 0.0001)). Analysis between the groups showed an effect size that was clinically important (mean difference 2.30, 95% CI 0.85 to 3.75; high-quality evidence). However, means, medians, and minimal important difference results and results of the Pediatric Quality of Life Inventory, Stein Impact on Family Scale, and Harter Self-Perception Profile for Children scores must be interpreted with caution, as they were not prespecified outcomes.

Three serious adverse events were reported, but they were resolved without sequelae. Deaths or other events such as malignant tumours, opportunistic infections, tuberculosis, or demyelination were not reported in the included study.

Also, 13% of participants in the placebo group and 53% in the etanercept group had a PGA of clear or almost clear (risk ratio 3.96, 95% CI 2.36 to 6.66; high-quality evidence) at week 12.

Authors' conclusions

This review found only one RCT evaluating the use of this type of biological therapy. Although the risk of publication bias was high, as we included only one industry-sponsored RCT, the risk of allocation, selection, performance, attrition, and selective reporting biases for all outcomes (except for CDLQI) was low, and no short-term serious adverse events were found.

We can conclude, based on this single included study, that etanercept seems to be efficacious and safe (at least in the short term) for the treatment of paediatric psoriasis. However, as the GRADE approach refers not to individual studies but to a body of evidence, we shall wait for the results of the ongoing studies in a future update of this review. In addition, future studies should evaluate quality-of-life endpoints established a priori and standardise primary outcome measures such as PASI 75, and should include the PGA as a secondary endpoint. Also, collating and reporting adverse events uniformly is required to better evaluate safety.

PLAIN LANGUAGE SUMMARY

Anti-TNF agents for paediatric psoriasis

Background

Psoriasis is a long-term skin disease that may develop at any age. Estimates for the United States and Europe suggest that psoriasis accounts for 4% of skin diseases in children. In most cases, the condition is mild and can be treated with creams. However, a small percentage of children have moderate to severe disease that requires drugs, such as ciclosporin or methotrexate, and some will require injections with newer biological agents, such as anti-TNF (tumour necrosis factor) drugs. Anti-TNF drugs (among them etanercept, infliximab, and adalimumab) are designed to reduce inflammation in the body caused by tumour necrosis factor.

Review question

Are anti-TNF drugs such as etanercept, infliximab, and adalimumab safe and effective for treating moderate to severe psoriasis in children under 18 years of age?

Study characteristics

We searched for all randomised controlled trials (RCTs) that assessed the efficacy and safety of anti-TNF agents for the treatment of long-term plaque psoriasis in individuals younger than 18 years of age. We searched databases up to July 2015. Only one study (with three phases: a 12-week randomised, double-blind, placebo-controlled phase; a 24-week open-label phase, and a 12-week phase of a randomised, double-blind, withdrawal–retreatment design) investigating one anti-TNF agent (etanercept) in 211 participants met the inclusion criteria.

Key results

Evidence from this single included study suggests that by week 12 etanercept reduced the extent of the psoriasis in children when compared with placebo. Although a few adverse events were reported, they were resolved without subsequent problems. We did not find any evidence on long-term side effects of this drug from this included study.

Quality of the evidence

Although this one RCT provided high-quality evidence for the Physician's Global Assessment and all Psoriasis Area and Severity Index scores (75, 90, and 50) and moderate-quality evidence for quality-of-life outcomes, we found no further randomised studies either evaluating etanercept or comparing other anti-TNF agents, highlighting the need for further well-designed randomised studies involving the use of biological therapies in children and young people with psoriasis. Several studies are ongoing that have not yet been completed or published. We plan to include the results of these in future updates of this review.