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Title A Systematic Review of Effectiveness and Economic Evaluation of New Drug Treatments for Juvenile Idiopathic Arthritis: Etanercept

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Aim

To review the background on juvenile idiopathic arthritis (JIA), including epidemiology, current and emerging therapy options, and impact of disease on individuals and health services.

To systematically review the clinical benefits and hazards of the anti-TNF agent etanercept in JIA compared with currently available treatments and to review economic evidence on the cost effectiveness of this agent compared with other treatment options.

Conclusions and results

One high quality RCT of etanercept in patients with methotrexate-resistant JIA was identified. Compared to placebo, etanercept reduces relapse rates in children and young people. In an open phase, 51 of 69 children (74%) improved on etanercept (30% response based on 6 outcome variables). In the randomized phase, 28% of the etanercept arm experienced disease flare compared to 81% of the placebo arm. At the end of the study, 20 (80%) of the etanercept double-blind phase group compared to 9 (35%) of the placebo group still met the definition of improvement ($p < 0.01$). 18 (72%) compared to 6 (23%) met the definition of improvement set at 50% improvement, and 11 (44%) compared to 5 (19%) met the definition of improvement set at 70%. The trial continued with an open-label extension phase. At 20 months, 83% of all patients had achieved a 30% response, 78% a 50% response, and 63% a 70% response. Adverse events occurred infrequently and were comparable to placebo. The manufacturer's submission included a cost-utility analysis. No other economic analyses were found. Sensitivity analyses ranged between £3900 (cost offsets assumption changed to exclude nursing home and home help costs, but to include indirect costs) and £34,000, though changes in most variables did not make a great difference. The validity and accuracy of this estimate must be questioned due to insufficient knowledge about the outcomes of JIA, particularly the quality of life and long-term outcomes; the model was constructed for rheumatoid arthritis in adults; the strong assumptions used were not based on evidence; and technical problems were identified with the model.

Recommendations

Given the novel biological action of etanercept, long-term followup is desirable and required by regulatory agencies to detect unexpected adverse events. No evidence compares etanercept with other treatments in this patient group. Safety concerns and relative lack of efficacy would place ethical constraints on trials of relative effectiveness. The effectiveness of etanercept in treating other forms of JIA, including psoriatic and enthesitis arthritis, is unknown.

Methods

A systematic review of effectiveness was undertaken. Databases (MEDLINE, EMBASE, Science Citation Index, Cochrane Library) were searched from 1966 through 2000. RCTs comparing etanercept with any agent in JIA and other rheumatic childhood diseases were considered. Manufacturer and sponsor submissions to the National Institute for Clinical Excellence (NICE) were reviewed. For the health economic and cost studies, the databases MEDLINE, DARE, and UK health economic websites were searched from 1997 through February 2001, and manufacturer and sponsor submissions to NICE were reviewed.

Further research/reviews required

The effectiveness of etanercept in the treatment of other forms of JIA including psoriatic and enthesitis arthritis is unknown. International trials would be required due to the rarity of these conditions. Using etanercept earlier in the disease process and in less severe disease might yield greater health gains. Trials are required to test these hypotheses.

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