

Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND)

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Date edited: 21/08/2006

Contribution of reviewers

This review was jointly written by all four reviewers. The lead author (RGM) coordinated the review, abstracted data from the papers, requested additional data from authors, entered the data into Revman and wrote the review. The co-reviewers (JDM, DHM) checked the data, appraised the quality of the studies (especially for allocation concealment) and offered revisions of the review. One co-reviewer is a statistician (DHM). He offered help and advice to the lead author at all stages, and performed the additional statistical analysis of survival at multiple timepoints not provided by Revman. One co-reviewer (ML) is a nurse and patient advocate and offered revisions of the review.

Internal and external sources of support: None

What's new

A search of the Cochrane Neuromuscular Disease Group Register in December 2004, MEDLINE (January 1966 to December 16 2004) and EMBASE (January 1980 to December 16 2004) identified one potentially relevant new trial for which we are attempting to obtain additional data. Two randomized trials looking at add-on therapy to riluzole have been added to the 'Discussion' section.

Plain language summary

Riluzole for Amyotrophic Lateral Sclerosis (ALS)/ Motor Neuron Disease (MND)

ALS/MND is a fatal neurological disease which produces paralysis of the limb, swallowing and breathing muscles. There is no available treatment to stop or reverse its progressive course.

In this review, the evidence from 4 randomized clinical trials involving 1477 patients with ALS is examined. The results indicate that riluzole 100 mg probably prolongs median survival in patients with amyotrophic lateral sclerosis by two to three months and the safety of the drug is not a major concern.

The evidence from randomized controlled trials indicates that patients taking riluzole probably survive longer than patients taking placebo. The beneficial effects are very modest and the drug is expensive. Adverse effects from riluzole are relatively minor and for the most part reversible after stopping the drug.

Abstract

Background

Riluzole has been approved for treatment of patients with ALS/MND in most countries. Questions persist about its clinical utility because of high cost and modest efficacy.

Objectives

To examine the efficacy of riluzole in prolonging survival, and in delaying the use of surrogates (tracheostomy and mechanical ventilation) to sustain survival.

Search strategy

We searched the Cochrane Neuromuscular Disease Group Register for randomized trials in December 2004 and made enquiries of authors of trials, Aventis (manufacturer of riluzole) and other experts in the field. We searched MEDLINE and EMBASE (January 1980 to August 25, 2006).

Selection criteria

Types of studies: randomized trials

Types of participants: adults with a diagnosis of amyotrophic lateral sclerosis

Types of interventions: treatment with riluzole or placebo

Types of outcome measures:

Primary: pooled hazard ratio of tracheostomy-free survival over all time points with riluzole 100 mg.

Secondary: per cent mortality with riluzole 50, 100 and 200 mg riluzole; neurologic function, muscle strength and adverse events.

Data collection & analysis

We identified four eligible randomized trials.

Main results

The four trials examining tracheostomy-free survival included a total of 974 riluzole treated patients and 503 placebo treated patients. The methodological quality was acceptable and three trials were easily comparable, although one trial included older patients in more advanced stages of amyotrophic lateral sclerosis and one had multiple primary endpoints.

Riluzole 100 mg per day provided a benefit for the homogeneous group of patients in the first two trials (**P value** = 0.042, hazard ratio 0.80, 95% confidence interval 0.64 to 0.99) and there was no evidence of heterogeneity (**P value** = 0.33). When the third trial (which included older and more seriously affected patients) is added, there is evidence of heterogeneity (**P value** < 0.0001) and the random effects model, which takes this into account results in the overall treatment effect estimate falling just short of significance (**P value** = 0.056, hazard ratio 0.84, 95% confidence interval 0.70 to

1.01). This represents a 9% gain in the probability of surviving one year (57% in the placebo and 66% in the riluzole group). There was a small beneficial effect on both bulbar and limb function, but not on muscle strength. A threefold increase in serum alanine transferase was more frequent in riluzole treated patients than controls (weighted mean difference 2.62, 95% confidence interval 1.59 to 4.31).

Reviewers' conclusions

Riluzole 100 mg daily is reasonably safe and probably prolongs median survival by about two to three months in patients with amyotrophic lateral sclerosis.