

Review: Riluzole increases 12-month survival in amyotrophic lateral sclerosis

Miller RG, Mitchell JD, Moore DH. Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND). Cochrane Review, latest version 26 Oct 1999. In: The Cochrane Library. Oxford: Update Software.

QUESTION

Is riluzole efficacious for increasing survival in patients with amyotrophic lateral sclerosis (ALS)?

DATA SOURCES

Studies were identified by searching the Cochrane Neuromuscular Diseases Group register with the terms amyotrophic lateral sclerosis, motor neuron disease, and motoneurone disease. Authors and the manufacturer of riluzole were contacted; 6 journals were hand searched; and reviews were obtained from the U.S. Food and Drug Administration, U.K. Trent Institute, and European Agency for the Evaluation of Medicinal Products.

STUDY SELECTION

Randomized controlled trials were selected if adults had a clinical diagnosis of ALS and treatment was oral riluzole or placebo. The primary outcome was mortality at 12 months for patients who received riluzole, 100 mg/d. Secondary outcomes were mortality at other time points for riluzole, 100 mg/d and all doses combined; muscle strength; function; quality of life; and adverse effects.

DATA EXTRACTION

Data were extracted on methodologic quality, patient and study characteristics, dose of riluzole, outcomes, and adverse effects.

MAIN RESULTS

2 trials (794 patients who received riluzole and 320 who received placebo) met the inclusion criteria. Doses were 100 mg/d in 1 trial and 50, 100, and 200 mg/d in the other trial. Analysis of the data for riluzole, 100 mg/d, showed reductions in mortality at 6, 9, 12 (Table), and 15 months but not at 3 or 18 months. When the analysis combined data from different doses, a reduction in mortality was shown at 6, 9, 12 (Table), and 15 months but not at 3 or 18 months. Subgroup analyses, however, showed benefit only at 12 months. Riluzole showed a positive effect on limb function but not on muscle strength or bulbar function. Patients in the riluzole groups remained in a moder-

ately affected health state longer (weighted mean difference [WMD] 36 d, 95% CI 6 to 65 d) and in combined mild and moderate health states longer (WMD 35 d, CI 5 to 66 d) than did patients in the placebo groups. Nausea, asthenia, circumoral paresthesias, and elevated serum alanine transferase levels were more frequent in the riluzole group; the groups did not differ for vomiting, diarrhea, anorexia, and dizziness or for low hemoglobin levels.

CONCLUSION

Riluzole, 100 mg/d, was associated with increased survival in patients with amyotrophic lateral sclerosis.

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For correspondence: Dr. R.G. Miller, Department of Neurology, California Pacific Medical Center, 2324 Sacramento Street, San Francisco, CA 94115, USA. FAX 415-923-6567. ■

Mortality at 12 months with riluzole vs placebo (12 trials) in amyotrophic lateral sclerosis*

Riluzole dose	Weighted event rates		RRR (95% CI)	NNT (CI)
	Riluzole	Placebo		
100 mg/d	26%	39%	32% (14 to 46)	9 (6 to 20)
All doses	28%	39%	28% (13 to 40)	10 (6 to 23)

*Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The Cochrane review by Miller and colleagues of the efficacy of riluzole in the treatment of ALS is accurate, but as can occur with such critical statistical reviews, it lacks a clinical perspective. The first included trial by Bensimon and colleagues (1) was criticized for the unexpectedly high death rate in placebo-treated patients with bulbar onset. If the data from this trial were considered to be aberrant, then the combination of data from the 2 trials may not be reasonable. Regardless, none of the secondary end points in the second trial by Lacomblez and colleagues were improved by the use of riluzole (2). Hence, conservative interpretation of the data suggests that any improvement in survival is gained only when meaningful stabilization of other important clinical measures is absent. The post-hoc analysis of disease "stages" is also of concern because these "stages" have not been prospectively validated (3). It is difficult to reconcile improved survival at 12 months, regardless of how marginal, with no significant difference at 18 months. Therefore, although the review is accurate, the clinical utility of riluzole remains controversial.

The outcome of magnetic resonance spectroscopic studies assessing the ability of riluzole to retard the rate of neuronal loss in patients

with ALS may be of considerable interest in clarifying the biological effects of riluzole in the treatment of ALS (4).

*Michael J. Strong, MD
University of Western Ontario
London, Ontario, Canada*

References

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