Therapy with glatiramer acetate for multiple sclerosis (Cochrane Review)

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ABSTRACT

A substantive amendment to this systematic review was last made on 08 June 2003. Cochrane reviews are regularly checked and updated if necessary.

Background: Some clinical data have shown that glatiramer acetate (Copaxone ®), a synthetic amino acid polymer empirically found to suppress experimental allergic encephalomyelitis (EAE), might help improve the outcome of patients with multiple sclerosis (MS).

Objectives: We performed a Cochrane review of all randomised, placebo-controlled trials of GA in MS, whatever the disease course.

Search strategy: We searched the Cochrane MS Group Trials Register (December 2004), the Cochrane Central Register of Controlled Trials (CENTRAL) "The Cochrane Library, Issue 4, 2004", MEDLINE (PubMed) (January 1966 to December 2004), EMBASE (January 1988 to December 2004) and hand searching of symposia reports (1990-2004) from the neurological Associations and MS Societies in both Europe and USA.

Selection criteria: All randomised controlled trials (RCTs) comparing glatiramer acetate and placebo in patients with definite MS, whatever the administration schedule and disease course, were eligible for this review.

Data collection and analysis: Both patients with relapsing-remitting (RR) and chronic progressive (CP) MS were analysed. Study protocols were comparable across trials. No major flaws were found in methodological quality. However, efficacy of blinding should be balanced against well-known side effects, including injection-site reactions in glatiramer acetate-treated patients.

Main results: A total of 646 patients contributed to this review. Glatiramer acetate did not show any significant effect on disease progression, measured as a sustained worsening in the Expanded Disability Status Scale (EDSS). On the other hand, a slight decrease in the mean EDSS score, driven by a major study, should be considered in the light of the limited validity of this endpoint. No benefit was

shown in CP MS patients (progression at two years: RR=0.69, 95% CI [0.33 to 1.46]). The frequency of reported adverse events does not support any major toxicity associated with glatiramer acetate administration. The most common systemic adverse event was a transient and self-limiting patterned reaction of flushing, chest tightness, sweating, palpitations, anxiety (relative risk = 3.40 (95% CI [2.22 to 5.21], p <0.00001]). Local injection-site reactions were observed in up to a half of patients treated with glatiramer acetate, thus making a blind assessment of outcomes questionable.

Authors' conclusions: Glatiramer acetate did not show any beneficial effect on the main outcome measures in MS, i.e. disease progression, and it does not substantially affect the risk of clinical relapses. Therefore its routine use in clinical practice is not currently supported. More investigations are needed. Further research should also develop more reliable measures of patient disability over time and include quality of life among primary outcomes.

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