Review: Low dose tricyclic antidepressants may be effective for adults with acute depressive disorder


QUESTION: What are the beneficial and adverse effects of low dose tricyclic antidepressants for adults with acute phase depression?

Design
Systematic review with meta-analysis.

Data sources
Studies were identified using the Cochrane Collaboration depression, anxiety and neurosis controlled trials register (to November 2000) which incorporates searches of Medline, Embase, CINAHL, PsycInfo, PSYNDEX and LILACS. Major psychiatric and medical journals and bibliographies were hand searched and experts were contacted for additional studies.

Study selection
Eligible studies were randomised trials lasting at least 4 weeks that compared low dose tricyclics with placebo or standard dose tricyclics in adults with acute phase depression. “Low dose” was defined as less than or equal to 100 mg per day, most commonly between 75 and 100 mg/day. Nortriptyline was excluded because the standard dose is debatable. 35 studies with 2013 participants compared low dose tricyclics with placebo. 6 studies with 551 participants compared low dose tricyclics with standard dose tricyclics.

Data extraction
Data were extracted on sample size, study design, participant characteristics, interventions and outcomes. The main outcome measures were response to treatment, overall dropouts and dropouts due to adverse effects (relative risk using a random effects model). Response was defined according to classifications in the original papers, but usually involved a 50% or greater reduction in severity of depression.

Main results
People receiving low dose tricyclics were 1.65 times more likely to respond to treatment at 6–8 weeks as compared to placebo (95% CI 1.12 to 1.94). 1.47 times more likely to respond to treatment at 6–8 weeks (95% CI 1.12 to 1.94). People receiving standard dose tricyclics were not clearly more likely to respond to treatment than those receiving low dose tricyclics (relative risk at 4 weeks 0.89, 95% CI 0.74 to 1.07; relative risk at 6–8 weeks 1.11, 95% CI 0.76 to 1.61). Standard dose tricyclics had a higher dropout rate due to adverse effects compared to low dose tricyclics.

Conclusions
Low dose tricyclics may be effective for some adults with depressive disorder. It is uncertain if standard dose therapy is more effective; but low dose therapy results in fewer dropouts due to adverse effects. Minimum effective dose ranges have yet to be established.