Review: there is limited evidence about the effectiveness of interventions for treatment-refractory depression

Stimpson N, Agrawal N, Lewis G. ***Randomised controlled trials investigating pharmacological and psychological interventions for treatment-refractory depression.*** *Brit J Psy 2002 Oct;* ***181****:284–94.*

QUESTION: How effective are different pharmacological and psychological interventions for treatment-refractory depression?

Design

Systematic review with narrative synthesis.

Data sources

Studies were identified using the Cochrane Controlled Trials Register, Embase, Medline, PsychLit, PsychInfo and LILACS (to January 2001).

Study selection

Eligible studies were randomised controlled trials of pharmacological or psychological interventions for people aged 18 to 75 years with treatment-refractory unipolar depression (no response to a 4-week course of antidepressant treatment at the recommended dose). The authors identified 17 trials with 645 participants: 4 compared an antidepressant with placebo or other treatment; 4 compared 2 active drug treatments; 7 compared an antidepressant plus augmentor with antidepressant plus placebo, and 3 were augmentation trials without a placebo group. The authors did not find any trial assessing the efficacy of psychotherapy.

Data extraction

Data were extracted on intervention, participant characteristics, sample size, definitions used, duration of intervention and recovery rate. The main outcome was recovery (50% or greater reduction in the Hamilton Rating Scale for Depression score).

Main results

There was little high quality evidence to guide clinical practice in treatment-refractory depression. There was weak evidence that lithium augmentation improved recovery. Quantitative synthesis was limited given the diversity of interventions and outcomes.

Conclusions

There is little evidence about the effectiveness of pharmacological and psychological interventions for treatment-refractory depression.

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COMMENTARY

There is little consensus about either the definition of treatment-resistant depression or how best to manage the condition in clinical practice. At the very least, the patient should have undergone an adequate antidepressant trial. There are a number of viewpoints about what constitutes an "adequate" treatment regimen, however, which differ according to medication dose, duration of treatment and sequencing of interventions. This diversity of opinion results in lack of consensus about criteria for treatment response[1–2] and makes it difficult to compare studies.

Stimpson *et al* provide a timely synthesis of randomised controlled trials of pharmacological and psychological interventions for treatment-refractory depression. The review is conducted in accordance with Cochrane Collaboration guidelines and avoids some of the shortfalls of previous reviews in this field. Unfortunately, the trials identified in the review tended to be of poor quality (none of the trials would have met all of the CONSORT guidelines on reporting the results of randomised trials). The authors conclude that few evidence-based recommendations can be made on the basis of the studies included. A similar conclusion was drawn in a recent review of studies combining antidepressants in people with treatment-resistant depression.[3] Current guidelines also tend be vague, recommending that treatment decisions be individualised based on clinicians' judgments and patient preferences.

Although this review does not provide much clinical guidance, it does highlight the limitations of current evidence and suggest areas of future research. For example, there have been no robust trials of psychotherapy for treatment-resistant depression. There is preliminary evidence that combining antidepressant medications with psychotherapy may increase remission rates over monotherapy alone in chronic depression.[4] Comparable studies are called for in treatment-resistant populations.

Stimpson *et al* focused upon response rates (usually defined as a 50% reduction in Hamilton Rating Scale for Depression or HAM-D scores) rather than remission rates (usually defined as a score on the HAM-D within the normal range). People with residual depressive symptoms may relapse up to five times faster than people with asymptomatic recovery.[5] This suggests that the goal of acute treatment for depression should be complete remission of symptoms. Future research in this field should include analyses of remission rates. Finally, few studies of treatment-resistant depression have used quality of life measures to assess outcome. The ultimate clinical goal is not just to achieve symptomatic response, but also full remission of symptoms and optimal quality of life.

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