Comparative efficacy of pharmacological and somatic interventions in adult patients with treatment-resistant depression: a network meta-analysis

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INTRODUCTION

- Major depressive disorder (MDD) affects around 10-15% of the population in a lifetime, and is associated with significant morbidity and mortality. It is one of the leading causes of disability in younger adults.
- Treatment options for MDD include both pharmacological and somatic interventional options. Selective serotonin reuptake inhibitors (SSRIs) are the first choice of antidepressant drugs, followed by serotonin and noradrenaline reuptake inhibitors (SNRIs). Other classes of antidepressants include monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs). Somatic strategies encompass psychotherapy (often in conjunction with pharmacotherapy), electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), among others.
- MDD that fails to respond to ≥ 2 antidepressant treatment regimens, prescribed at adequate dose and duration, is a commonly used and accepted definition for treatment-resistant depression (TRD). The currently approved treatment options for TRD is very limited. Treatment strategies for TRD include augmentation, switching or combination of antidepressant and non-antidepressant drugs.
- New treatments for TRD aiming at rapid onset of action (hours to days) and robust effect size are currently under development to improve outcomes of TRD patients.

OBJECTIVE

The objective of this network meta-analysis was to compare the efficacy of pharmacological and somatic interventions in patients with treatment-resistant depression (TRD). Comparative treatment regimens prescribed as adequate dose and duration, with at least one failure in the current episode.

METHODS

- Systematic Literature review
  - A systematic literature review (SLR) covering the period from 2003 to 2014 was performed (Cochrane Library, Embase, PsycINFO) databases and the Cochrane library were searched using a predefined search strategy.
  - The screening process was based on predefined criteria for the study design, patients and outcomes.
  - Study design: RCTs with ≥ 20 patients overall.
  - Interventions: SSRIs, SNRIs, TCAs, MAOIs, atypical antidepressants, antipsychotics, SPECT (single photon emission computed tomography), antidepressants, electroconvulsive therapy (ECT), and repetitive transcranial magnetic stimulation (rTMS).
  - Outcomes: disease severity change from baseline measured on the Montgomery-Asberg Depression Rating Scale (MADRS), remission and response rate at time points of interest provided that the mean change in MADRS from baseline score at that timepoint was reported. A measure of uncertainty was included.
  - Efficacy data were not available for all treatment strategies in all time points.

RESULTS

- The SLR identified 55 publications (reporting 55 unique RCTs) eligible for inclusion in the NMA. (Figure 1)
  - Overall, 11 of the 55 RCTs formed a connected network (Figure 2): 19 RCTs investigating 13 pharmacological interventions and 12 RCTs investigating ECT and TMS.

CONCLUSIONS

- Based on the evidence synthesis of available RCTs investigating the efficacy of treatment-resistant depression, quetiapine had the most robust effect size and demonstrated superior efficacy compared to placebo/sham and to competing pharmacological and somatic interventions.
- Efficacy analysis at 6 weeks showed that quetiapine augmentation of 800 mg and TMS (80-120%) treatment were the most efficacious treatments.
- No data were available for ketamine at time points beyond 2 weeks. There was no clear distinction in terms of efficacy for the remaining competing somatic interventions.
- This analysis revealed scarcity of long-term data (i.e. data on sustained remission) that would allow a comparative long-term efficacy assessment.

REFERENCES

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