Review: Antidepressants are effective for clinical improvement in unexplained physical symptoms and syndromes

O'Malley PG, Jackson JL, Santoro J, et al. **Antidepressant therapy for unexplained symptoms and symptom syndromes.** J Fam Pract. 1999 Dec;48:980-90.

QUESTION

In adults who have medically unexplained physical symptoms (MUPS), do antidepressants improve outcomes?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to 1998), PsycLIT (1974 to 1998), EMBASE/Excerpta Medica (1974 to 1998), the Cochrane Library, the Federal Research in Progress database, and bibliographies of relevant articles.

STUDY SELECTION

2 reviewers independently selected studies that were randomized controlled trials (RCTs) (including crossover trials), involved adults with MUPS, compared antidepressants with placebo or a nonantidepressant intervention, reported measurable outcomes, and were published in English.

DATA EXTRACTION

Data extracted included symptoms, setting, treatment (regimens and follow-up), patient characteristics, assessment of comorbid psychiatric disease, adverse effects, outcomes, statistical analysis of reported results, and quality of study methods (Jadad scale).

MAIN RESULTS

94 RCTs on 6 symptom syndromes met the selection criteria. 6595 patients (76% women) were studied for a median of 9 weeks. The dropout rate was > 20% in 40% of the RCTs. A meta-analysis combined results for improvement: global assessment (patient or physician), summary symptom index scores, or pain-severity scale scores (Table). 4 patients (95% CI 3 to 7) would need to be treated to improve 1 additional patient's condition. A meta-analysis of the results for continuous outcomes reported a pooled standardized mean difference of 0.87 (CI 0.59 to 1.14).

CONCLUSION

In patients with medically unexplained physical symptoms or syndromes, antidepressants are effective for improving outcomes, including symptoms and disability.

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Antidepressants vs placebo for unexplained symptoms or syndromes*

Symptom groups	Number of RCTs for each antidepressant type				Mean quality score	Pooled OR (95% CI)†
	TCA	SSRI	Anti-S	Other		
Chronic headache	21	8	23	—	4.6	3.4 (2.7 to 4.4)
Fibromyalgia	12	4	—	3	5.8	5.1 (3.1 to 8.5)
Functional GI disorders	11	—	2	1	4.1	4.4 (2.5 to 7.7)
Idiopathic pain	8	2	2	—	4.2	2.0 (1.4 to 2.8)
Tinnitus	2	—	—	—	4.0	—
Chronic fatigue	—	2	—	—	4.0	—
All	56	17	28	3	4.8	3.4 (2.6 to 4.3)

*Anti-S = antiserotonin; GI = gastrointestinal; OR = odds ratio; RCTs = randomized controlled trials; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant. Median follow-up was 9 weeks.

†Odds ratios show a benefit for the antidepressant group.

COMMENTARY

Patients with MUPS are common in primary and secondary care. Increasing evidence exists that such psychological therapies as cognitive behavior therapy (CBT) are effective in the treatment of these symptoms (1, 2). Unfortunately, suitably trained therapists are scarce, and psychological therapy is unacceptable to some patients. Thus, effective pharmacologic therapies have a potentially substantial role in the treatment of patients with MUPS.

The review by O'Malley and colleagues supports the use of antidepressants for treating MUPS. The number needed to treat of 4 for short-term improvement is clinically significant and is similar to that obtained with CBT (1, 2). Persons with a wide range of MUPS seem to benefit from antidepressants, even though not all are depressed. An important caveat is that most evidence applies to patients in secondary care who have chronic symptoms.

Clinicians therefore have 2 evidence-based types of therapy for MUPS: psychological (CBT) and pharmacologic (antidepressants). If CBT is available, the choice between it and antidepressants is difficult. Patient choice should therefore be encouraged because compliance with and enthusiasm for the chosen therapy may profoundly influence outcome. Persons with MUPS who reject psychological therapy, however, may also reject the use of antidepressants for "physical" problems. The term "antidepressants" is unhelpful in this situation and is increasingly inappropriate as evidence for other indications accumulates.

Several other decisions face clinicians. First, which antidepressant should be used? No convincing evidence exists for 1 group. Second, what dose should be given? Little evidence is available, although, as therapeutic action seems independent of antidepressive action, low doses may be effective. Finally, how long should the patient receive the medication? Antidepressants are effective for persons with MUPS over periods of weeks. It is unclear, however, whether treatment can be withdrawn and what the optimal duration of treatment is. Several key knowledge gaps must therefore be addressed by more primary research. Until then, clinicians should consider prescribing antidepressants that are safe and well tolerated, with dose and duration determined empirically.

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