High dose pregabalin is effective for the treatment of generalised anxiety disorder


What is the efficacy and safety of pregabalin in people with generalised anxiety disorder?

METHODS

- Design: Randomised controlled trial.
- Allocation: Unclear.
- Blinding: Double blind (clinicians, participants).
- Follow up period: Five weeks.
- Setting: Four centres in USA; time period not stated.
- Patients: 271 people with a primary diagnosis of generalised anxiety disorder (GAD) according to DSM-IV criteria. At initial screening and after a one week washout period, eligible participants had a Covi Anxiety Scale total score > 9, a Raskin Depression Scale total score < 7, and a Hamilton Anxiety Rating Scale (HAM-A) score = 20. Exclusions: comorbid axis I disorder (not including dysthymia, simple phobia, social phobia, somatisation disorder, history of major depressive disorder); severe personality disorder; history of substance abuse in the previous 6 months, and suicide risk. Psychotropic medication was stopped for 2 weeks before enrolment (5 weeks for fluoxetine), and was not allowed during the study period (except for zolpidem 5 mg, less than twice weekly).
- Intervention: Four weeks of: pregabalin 150 mg/day (50 mg tid; n = 70); pregabalin 600 mg/day (200 mg tid; n = 66); lorazepam 6 mg/day (2 mg tid; n = 68); or placebo (n = 67). Dosage was titrated to target dose over 6 days. After 4 weeks, medication was tapered off over 1 week.
- Outcomes: Anxiety symptoms measured with the HAM-A total score; discontinuation due to adverse events.
- Patient follow up: 68%.

MAIN RESULTS

High dose pregabalin (600 mg/day), but not low dose pregabalin (150 mg/day), significantly improved symptoms compared with placebo at 4 weeks (mean decrease in HAM-A score: 13.2 with high dose pregabalin v 9.3 with placebo; p = 0.001). Early discontinuation due to adverse effects was significantly more common for high dose pregabalin than for placebo (AR: 21% with high dose pregabalin v 6% with placebo; p = 0.01). Early discontinuation due to adverse effects was higher for lorazepam than for high dose pregabalin but did not reach statistical significance (AR: 21% with high dose pregabalin v 35% with lorazepam; p = 0.07).

CONCLUSIONS

Pregabalin is effective and safe for the short term treatment of GAD.

Commentary

The introduction of an anticonvulsant, which has efficacy against anxiety, represents a novel treatment strategy for generalised anxiety disorder. Previous studies have reported effectiveness for pregabalin in people with seizure disorders and neuropathic pain.1 2 Pregabalin is similar structurally to gabapentin, but is three to ten times more potent as a GABA analogue than gabapentin.3 A reduced side effect burden is implied by this research. Current treatments for anxiety disorders have significant disadvantages. If buspirone or selective serotonin reuptake inhibitors (SSRIs) are used, people with anxiety disorders must expect a two week to two month delay in the onset of therapeutic benefit. High rates of sexual dysfunction are common with SSRIs. The authors have reported a much lower rate of sexual dysfunction and a more rapid onset of action with pregabalin.

The clinician may simplify his practice. Anxiety disorders usually require long term treatment. People taking benzodiazepines as prescribed may be reluctant to agree to discontinuation trials. Many cannot do this without re-emergence of anxiety. Pregabalin was found to have a lesser risk for withdrawal symptoms than lorazepam. Tapering pregabalin should be more acceptable to patients. Re-evaluation of the patient’s continued need for treatment is thus facilitated.

Treatment with pregabalin should generalise to people with multiple illnesses. Anxious individuals with comorbid pulmonary disease or dementia are ordinarily poor candidates for benzodiazepines. Non-benzodiazepine, non-antidepressant anxiolytics are needed in people with bipolar disorder with substance abuse and high potential for destabilisation with antidepressants. Pregabalin has the advantages of no known medication interactions3 and low potential for withdrawal symptoms.4 Is pregabalin an effective anxiolytic? The low effect size, the brief study period, and the high placebo response rate mandate further investigations. This research provides optimism, however, for improved treatment of the many people that suffer from anxiety.

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