Use of oral antidepressants in patients with chronic pruritus: A systematic review

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Background: Chronic pruritus is a common skin symptom with marked impact on quality of life. Adequate treatment can be challenging for clinicians, demanding the exploration of new treatment options such as oral antidepressants.

Objective: To evaluate the use of oral antidepressants in chronic pruritus by a systematic overview of the available relevant literature.

Methods: The PubMed, EMBASE, Cochrane, and Web of Science databases were searched. Studies providing original data on the efficacy of oral antidepressants in patients with chronic pruritus were included. We assessed the risk for bias by using the Cochrane Risk of Bias tool for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies.

Results: A total of 35 studies evaluating the oral use of fluoxetine, fluvoxamine, paroxetine, sertraline, amitriptyline, nortriptyline, doxepin, and mirtazapine were included. The majority of included articles showed a marked improvement of pruritus during treatment with oral antidepressants.

Limitations: Recommendations are mainly based on open-label trials, case series, and case reports.

Conclusion: Oral antidepressants should be considered in patients with chronic pruritus that is unresponsive to topical treatment and oral antihistamines, particularly in patients with uremic pruritus, cholestatic pruritus, or paraneoplastic pruritus. More evidence based on randomized-controlled trials is required. (J Am Acad Dermatol 2017;77:1068-73.)

Key words: amitriptyline; antidepressant; doxepin; itch; paroxetine; pruritus; systemic treatment.

Itch is a common skin sensation, and it can be as debilitating as pain.[1] Chronic pruritus (itch present for 6 weeks or more) can cause mood disturbances and disarranged sleep patterns and is often associated with a decreased quality of life.[2,3] Besides cutaneous disorders, pruritus can have various other causes, for example, systemic, neuropathic, or psychogenic conditions.[4] Adequate treatment for patients with chronic pruritus can be challenging, demanding development and evaluation of new therapeutic options, such as the use of oral antidepressants.

Abbreviations used:

RCT: randomized controlled trial
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant
VAS: Visual Analogue Scale

Oral antidepressants are thought to have an antipruritic effect on account of their influence on serotonin and histamine levels, and they were recommended in the European Guideline for Chronic Pruritus for forms of chronic pruritus not

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responding to other therapies.[4,5] A systematic overview of the available literature describing the efficacy of oral antidepressants in chronic pruritus was performed to provide evidence-based recommendations for daily practice.

METHODS

We conducted a systematic literature search on the efficacy of antidepressants in patients with chronic pruritus. Four electronic databases (PubMed, EMBASE, Cochrane, and Web of Science) were systematically searched for articles published from January 1980 to December 2016. The search terms were *itch*, *pruritus*, and *antidepressants*, with all possible synonyms and generic names included. An extensive overview of the search terms is available upon request from the corresponding author. Methods for the selection process and data extraction were determined a priori and documented in a written protocol. We included studies conducted in adults and children and providing original data on chronic pruritus (defined as pruritus present for a minimum of 6 weeks) and oral use of antidepressants. Description of an outcome measure was mandatory. Articles in languages other than English were excluded.

A total of 1464 articles were identified (Supplemental Fig 1; available at http://www.jaad.org). Titles and abstracts were screened for eligibility by 2 independent reviewers; any differences regarding inclusion between reviewers were resolved by discussion. The references of all included articles were checked for additional relevant studies.

The following data were extracted from the included articles: study characteristics, number of included subjects, etiology of pruritus, use of antidepressants, reduction of pruritus, adverse events, and follow-up. The Cochrane Risk of Bias tool was used for assessment of risk of bias in randomized controlled trials (RCTs), with studies graded as having low risk, high risk, or unclear risk of bias.[6] For observational studies, the Newcastle-Ottawa Scale was used.[7] Level of evidence was determined by using the Oxford 2011 Levels of Evidence guidelines (Supplemental Table I; available at http://www.jaad.org).[8]

CAPSULE SUMMARY

- Oral antidepressants are thought to have an antipruritic effect because of their influence on serotonin and histamine levels.
- There is evidence-based support for the use of antidepressants to treat chronic pruritus.
- Clinicians should consider antidepressant therapy for those with pruritus due to chronic kidney disease, cholestasis, or malignancy, or with pruritus refractory to conventional treatment.

RESULTS

A total of 35 studies evaluating the use of selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and/or atypical antidepressants (Supplemental Table II; available at http://www.jaad.org) fulfilled the criteria of this study.[9-40] One article evaluated the use of oral antidepressants in general, analyzing treatment outcomes in 385 patients with chronic pruritus.[41] In this cohort, the use of oral antidepressants was limited (16 of the total of 385 patients [0.04%]) but highly effective (relief of pruritus in 12 of those 16 patients [75%]).

SSRIs

Fluoxetine. The use of fluoxetine was described in 1 case report in 1989; it described the almost immediate disappearance of aquagenic pruritus, defined as exacerbation of itch after water exposure, after initiation of fluoxetine treatment.[9] The dosage used was not reported.

Fluvoxamine. A total of 72 patients with chronic pruritus of different etiologies and refractory to at least 1 therapeutic attempt were included in an open-label trial comparing fluvoxamine treatment with paroxetine.[10] In all, 33 patients were treated with fluvoxamine, starting at a dose of 25 mg/d, which was increased to a maximum of 150 mg/d according to the clinical efficacy, for an average duration of 21.5 weeks. The mean Visual Analogue Scale (VAS) score reduction was 3.2 plus or minus 2.7, showing no significant difference compared with paroxetine treatment. The overall response to treatment was 68%, with the best response observed in pruritus due to atopic dermatitis, systemic lymphoma, and solid tumors.

Paroxetine. Eight publications describing use of the SSRI paroxetine were identified.[10-17] In an RCT with crossover design, paroxetine, 20 mg/d, was compared with placebo for a duration of 7 days per treatment.[11] Patients were recruited from palliative care centers, most of them with pruritus associated with malignant disease. Irrespective of order of treatment, patients receiving paroxetine 20 mg/d had lower VAS scores for pruritus.

As described earlier, paroxetine was compared with fluvoxamine treatment in an open-label trial.[10]