

An open-label study of Escitalopram (Lexapro[®]) for the treatment of ‘Depression of Alzheimer’s disease’ (dAD)

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SUMMARY

Background Depression is a frequent neuropsychiatric complication of Alzheimer’s Disease.

Methods This study investigated the safety and effectiveness of escitalopram (LEXAPRO) for depression in AD (dAD) as defined by the NIMH consensus criteria in an 8-week, open-label treatment study.

Conclusion Escitalopram was efficacious and safe for the treatment of dAD in this study. Larger, controlled studies are warranted to further assess the efficacy for mood and behavioral disturbances in this medically fragile population. Copyright © 2006 John Wiley & Sons, Ltd.

KEY WORDS — Escitalopram; depression in Alzheimer’s disease

INTRODUCTION

Depression in Alzheimer’s disease (AD) is common. A group of experts assembled by the National Institute of Mental Health (NIMH) proposed diagnostic criteria for ‘Depression of AD’ (dAD) (Olin *et al.*, 2002). The main differences between the DSM-IV criteria for major depression and the dAD criteria are the presence of three additional symptoms and the requirement of only 3/11 to diagnose dAD. The goal was to enhance uniformity in diagnosis and to explore pathology and management of dAD.

A review by Lyketsos and Olin (2002) cited eight placebo controlled studies on the treatment of major depression in AD: four reported superiority of antidepressants while four reported no difference. However, there are no treatment studies using the dAD criteria.

We conducted a pilot study to assess the clinical effects, safety, and tolerability of escitalopram

(Lexapro[®]) for the treatment of dAD. We chose escitalopram for two reasons: (1) it has been reported as efficacious, safe and tolerable in the treatment of major depression (Masilamani and Ruppelt, 2003) and (2) SSRIs have been recommended as appropriate first line antidepressants in AD (Lyketsos and Olin, 2002).

METHODS

This study was approved by the Johns Hopkins Institutional Review Board. Participants were recruited from Johns Hopkins outpatient clinics. All patients were evaluated at baseline and weeks 4 and 8 on a series of outcome measures: Cornell Scale for Depression in Dementia (CSDD), General Medical Health Rating Scales (GMHR), Mini Mental State Exam (MMSE), Clinician’s Global Impression Scale (CGI), NeuroPsychiatry Inventory (NPI), Activities of Daily Living Inventory (ADCS), and Alzheimer’s Disease Related Quality of Life (ADRQL).

Inclusion criteria included: diagnosis of probable Alzheimer’s disease (NINDS/ADRDA criteria), MMSE > 11, NIMH diagnostic criteria of dAD, CSDD > 7, age 50–90 years, stable medical health (no acute medical problems), ability to provide con-

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Table 1.

Variable	Baseline	Follow-up 4 Weeks	Follow-up 8 Weeks	<i>F</i> (df), <i>p</i>
CSDD	16.47 (4.44)	10.27 (7.41)	6.67 (6.67)	<i>F</i> (2) = 19.67 , <i>p</i> < 0.001
GMHR	2.87 (0.834)	3.00 (1.07)	3.00 (0.926)	<i>F</i> (2) = 0.48, <i>p</i> = 0.62
MMSE	19.33 (4.19)	19.80 (5.51)	18.73 (5.30)	<i>F</i> (2) = 0.85, <i>p</i> = 0.44
NPI F*S Total	28.87 (12.53)	18.67 (14.65)	18.93 (20.25)	<i>F</i> (2) = 4.32 , <i>p</i> = 0.02
ADCS	56.60 (17.65)	56.93 (18.94)	53.73 (20.09)	<i>F</i> (2) = 1.26, <i>p</i> = 0.30
ADRQL (Total %)	79.52 (12.92)	82.99 (13.94)	83.81 (14.96%)	<i>F</i> (2) = 2.21, <i>p</i> = 0.13
CGI (Very Much or Much Improved)	NA	4 (33.3%)	9 (75%)	NA

Outcome variables (*n* = 15), Baseline, 4-Week Follow-up & 8-Week Follow-Up, Repeated Measures ANOVA (Within-Subjects) Test of Effect; **Bold** indicates *p* < 0.05.

sent either by the participant or legal guardian, and willingness of caregivers to participate.

Exclusion criteria included: history of brain disease (stroke), unstable medical problems (severe congestive heart failure), past escitalopram failure, current alcohol abuse or dependence, or current treatment with psychotropics (except for trazadone 25–100 mg for sleep and/or lorazepam 0.5 or 1 mg for acute agitation). Cholinesterase inhibitors were allowed if the dose was stable.

All participants were started on a dose of 10 mg. At 4 weeks, the dose was increased to 20 mg if clinically necessary (no or partial improvement in symptoms). No dose adjustment was made after 4 weeks.

RESULTS

Fifteen participants were enrolled into the study. Three patients dropped out before first follow-up, due to increased insomnia, unrelated medical problems, and non-compliance. The sample was mostly female, (*n* = 8, 73%), white, widowed, educated, with a mean duration of dementia of 5.33 years (*SD* = 3.67) and depression of 2.74 years (*SD* = 3.23). CSDD scores decreased significantly (mean 9.8 point decrease over 8 weeks). There was no difference between subjects on 10 mg (mean change = −13.25, *SD* = 4.03) and 20 mg (mean change = −11.75, *SD* = 4.84) on the CSDD scores (*t*[10] = −0.532, *p* = 0.61). CGI ratings reflected 'Much' or 'Very Much' improvement in 75% at week 8. Total NPI scores decreased significantly (mean 9.94 decrease over 8 weeks). ADRQL scores improved but did not reach statistical significance. Rating on MMSE, GMHR, and ADCS did not change significantly (*p* > 0.05) (see Table 1).

Insomnia (27%), fatigue (20%), and mild tremor (20%) were the most commonly reported side effects. No medication related serious adverse events were reported.

DISCUSSION

Clinical outcomes associated with escitalopram at a dosage of 10–20 mg indicated substantial improvements in depression and behavioral problems. Week 8 depression scores were low, indicating successful treatment. At week 4, the scores were still mildly elevated, suggesting lack of placebo effect. Our study failed to find an improvement in cognition, similar to earlier findings (Munro *et al.*, 2004). Only 25% reported side-effects; a low rate given the frailty of the patient population.

Limitations of the study that affect generalizability include: small sample, open-label study design, and recruitment from specialty clinics. Despite this, the study found that it is possible to see improvement in dAD over 8 weeks, with few risks. This is the first study to demonstrate the effects and safety of an antidepressant to treat dAD. Future studies using the dAD criteria will help to validate the diagnosis and provide a common ground to generate research activities.

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