

Is Citalopram the First-Line Treatment for Late-Life Depression?

Major depressive disorder and depressive symptoms in older adults are common clinical problems encountered by geriatric psychiatrists. A recent real-world effectiveness trial of antidepressants for major depression in mixed age groups demonstrated that common antidepressant treatments may have more modest effects than was previously believed with depression remission rates of 30% following antidepressant monotherapy (1). Treatment of late-life depression (LLD) can be even more challenging given the concomitant cognitive impairment, numerous medical conditions, and polypharmacy that is common in this population.

Several guidelines have recommended citalopram as a first-line, or the first-line, treatment for LLD (2,3). Use of citalopram in older adults is extensive, indeed, 10% of nursing home residents receive citalopram, making it the second most common psychotropic in U.S. nursing homes after donepezil(4). Citalopram is often utilized as a first-line treatment for LLD as it is thought to be as efficacious and well-tolerated as other antidepressants with less potential for drug-drug interactions. However, a large, randomized, placebo-controlled trial of citalopram in LLD by Roose and colleagues (5) has called the efficacy of citalopram into question. In the study by Roose and colleagues, citalopram was no different than placebo in achieving remission of depression in a very old population. Furthermore, a recent animal model study of anticholinergic activity of medications found citalopram to have greater anticholinergic activity when compared to several other antidepressants including sertraline, venlafaxine and bupropion although it was less anticholinergic than paroxetine and tricyclic antidepressants(6).

To examine this topic in greater detail we recently completed a systematic review evaluating the efficacy and tolerability of citalopram compared to other antidepressants in LLD as part of the Evidence Based Medicine practice rounds at Baycrest Centre in Toronto. Electronic databases and reference lists were searched for all studies comparing citalopram to other antidepressants for the treatment of major depressive disorder in older adults (age \geq 65 years). The primary efficacy outcome selected for the review was depression remission (Hamilton Depression Score \leq 7 or Montgomery-Asberg Depression Score \leq 10) and the primary tolerability outcome was trial withdrawals due to adverse effects. In total, 7 seven studies were identified: 4 studies comparing citalopram to tricyclic antidepressants (2 comparing citalopram to amitriptyline, 1 with nortriptyline, 1 with desipramine), 1 study with venlafaxine as a comparator, 1 with reboxetine, and 1 study with mianserin (references available on request). In the individual studies, there were no significant differences noted between citalopram and comparators in remission of depression or trial withdrawals due to adverse effects. We are currently in the process of completing a meta-analysis of these studies.

What does this mean for clinicians? First, there are few studies of citalopram in LLD despite its widespread use and acceptance as an initial treatment for LLD. That citalopram was not better tolerated than other antidepressants, including tertiary tricyclic antidepressant medications such as amitriptyline, calls into question the presumed improved tolerability of citalopram when compared to other antidepressants. Although not directly examined in our review, the evidence for any other

antidepressant in treating LLD is likely just as limited. Future head-to-head studies of citalopram compared to other alternatives such as sertraline, venlafaxine and mirtazapine would add substantially to the existing literature and provide further guidance for clinician on the treatment of LLD.

Dallas Seitz, MD, FRCPC
Postdoctoral Fellow, Kunen-Lunenfeld Applied Research Unit
Clinical Fellow, Division of Geriatric Psychiatry
Baycrest Centre, Toronto, ON
Email: dallas_seitz@hotmail.com

References

- (1) Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, et al. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. *Am.J.Psychiatry* 2006 Jan;163(1):28-40.
- (2) Alexopoulos GS, Katz IR, Reynolds CF,3rd, Carpenter D, Docherty JP, Ross RW. Pharmacotherapy of depression in older patients: a summary of the expert consensus guidelines. *J.Psychiatr.Pract.* 2001 Nov;7(6):361-376.
- (3) Mulsant BH, Alexopoulos GS, Reynolds CF,3rd, Katz IR, Abrams R, Oslin D, et al. Pharmacological treatment of depression in older primary care patients: the PROSPECT algorithm. *Int.J.Geriatr.Psychiatry* 2001 Jun;16(6):585-592.
- (4) Centers for Disease Control and Prevention - National Center for Health Statistics. National Nursing Home Survey - 2004. <http://www.cdc.gov/nchs/nnhs.htm> .
- (5) Roose SP, Sackeim HA, Krishnan KR, Pollock BG, Alexopoulos G, Lavretsky H, et al. Antidepressant pharmacotherapy in the treatment of depression in the very old: a randomized, placebo-controlled trial. *Am.J.Psychiatry* 2004 Nov;161(11):2050-2059.
- (6) Chew ML, Mulsant BH, Pollock BG, Lehman ME, Greenspan A, Mahmoud RA, et al. Anticholinergic activity of 107 medications commonly used by older adults. *J.Am.Geriatr.Soc.* 2008 Jul;56(7):1333-1341.