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Duloxetine and care management treatment of older adults with comorbid major depressive disorder and chronic low back pain: results of an open-label pilot study

Jordan F. Karp[1,2,3,6], **Debra K. Weiner**[3,4,6,7], **Mary A. Dew**[1,3,5], **Amy Begley**[1,3], **Mark D. Miller**[1,3], and **Charles F. Reynolds III**[1,2,3]

[1]Advanced Center for Intervention and Services Research for Late Life Mood Disorders, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[2]the John A. Hartford Center of Excellence in Geriatric Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[3]Department of Psychiatry, University of Pittsburgh School of Medicine and Graduate School of Public Health, Pittsburgh, PA, USA

[4]Department of Medicine, University of Pittsburgh School of Medicine and Graduate School of Public Health, Pittsburgh, PA, USA

[5]Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA

[6]Department of Anesthesiology, University of Pittsburgh School of Medicine and Graduate School of Public Health, Pittsburgh, PA, USA

[7]Geriatric Research Education and Clinical Center, VA Pittsburgh Healthcare System, Pittsburgh, PA, USA

Abstract

Objective: In older adults, major depressive disorder (MDD) and chronic low back pain (CLBP) are common and mutually exacerbating. We predicted that duloxetine pharmacotherapy and Depression and Pain Care Management (DPCM) would result in (1) significant improvement in MDD and CLBP and (2) significant improvements in health-related quality of life, anxiety, disability, self-efficacy, and sleep quality.

Design and Intervention: Twelve week open-label study using duloxetine up to 120 mg/day + DPCM.

Setting: Outpatient late-life depression research clinic.

Patients: Thirty community-dwelling adults >60 years old.

Outcome Measures: Montgomery Asberg Depression Rating Scale (MADRS) and McGill Pain Questionnaire-Short Form (MPQ-SF).

Results: 46.7% (n = 14) of the sample had a depression remission. All subjects who met criteria for the depression remission also had a pain response. 93.3% (n = 28) had a significant pain response. Of the subjects who met criteria for a low back pain response, 50% (n = 14) also met criteria for the

Correspondence to: J. F. Karp, MD, karpjf@upmc.edu.

depression remission. The mean time to depression remission was 7.6 (SE = 0.6) weeks. The mean time to pain response was 2.8 (SE = 0.5) weeks. There were significant improvements in mental health-related quality of life, anxiety, sleep quality, somatic complaints, and both self-efficacy for pain management and for coping with symptoms. Physical health-related quality of life, back pain-related disability, and self-efficacy for physical functioning did not improve.

Conclusions: Serotonin and norepinephrine reuptake inhibitors like duloxetine delivered with DPCM may be a good choice to treat these linked conditions in older adults. Treatments that target low self-efficacy for physical function and improving disability may further increase response rates.

Keywords

depression; pain; geriatric; back pain; clinical trial

Introduction

Among older adults, major depressive disorder (MDD) and chronic low back pain (CLBP): (1) are highly comorbid, (2) are risk factors for one another, (3) slow each others' rate of remission, and (4) increase each others' risk of recurrence (Garron and Leavitt, 1983; Atkinson *et al*., 1988; Herr *et al*., 1993). The interaction between MDD and CLBP in older adults can lead to a cycle of demoralization (Jacobsen *et al*., 2007), physical and psychosocial disability (Lenze *et al*., 2001), and exacerbated medical and psychiatric comorbidity (Von Korff and Simon, 1996). When both conditions are present, treating them to complete response is critical to break this cycle. Although these interactions have been observed for decades, to our knowledge there have been no trials aimed at treating both conditions in older adults with a single pharmacological intervention.

Duloxetine is a serotonin norepinephrine reuptake inhibitor (SNRI) that is approved for the treatment of MDD (Detke *et al*., 2002) and reported to be safe and effective for depressed older adults (Wohlreich *et al*., 2004; Raskin *et al*., 2007; Karp *et al*., 2008). It is also the only antidepressant approved for the treatment of diabetic peripheral neuropathic pain (DPNP) and fibromyalgia, and has been observed to improve chronic back pain in mixed aged adults without depression (Skljarevski *et al*., 2009). Tricyclic anti-depressants also have dual serotonin and norepinephrine reuptake inhibition, and have been observed to improve pain more quickly than depression (Max *et al*., 1992). We know of no studies of tricyclics for older adults living with both major depression and a pain condition. Because duloxetine (1) has analgesic properties and (2) is probably safer than tricyclics for use in older patients (Bryson and Wilde, 1996), we selected this agent for an open pilot study in older adults living with both MDD and CLBP. Duloxetine was administered as the psychopharmacologic component of a Depression and Pain Care Management (DPCM) intervention.

The first hypothesis we tested was that compared to baseline, after 12 weeks of open-label treatment with duloxetine + DPCM, older adults living with comorbid MDD and CLBP would have clinically significant reductions in both depression and low back pain. Our second hypothesis was that compared to baseline, after 12 weeks of treatment there would be significant improvements in health-related quality of life, pain-related disability, self-efficacy for chronic pain, sleep quality, and somatic complaints. Finally, consistent with findings observed with tricyclics, we predicted that the observed time to response would occur sooner for low back pain than depression.

Methods

Subjects

The study setting was a university-based clinic for the treatment of depression in elderly patients. The study was conducted after approval from the university's institutional review board. Subjects were recruited from primary care practices and from our specialty mental health clinic for older adults with mood disorders. Recruitment also occurred by word of mouth, referrals from clinicians, advertisements, and presentations to lay groups of older adults and their families.

The participants were at least 60 years of age; met the criteria of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), for current MDD (nonpsychotic and nonbipolar), as determined according to the Structured Clinical Interview for DSM-IV Axis I Disorders, version 2.0 (SCID, Spitzer *et al*., 1995); and had a score of at least 15 on the Montgomery Asberg Depression Rating Scale (MADRS, Montgomery and Asberg, 1979) (scores can range from 0 to 60, with higher scores indicating more severe depression). They were required to score at least 20 on the Folstein Mini-Mental State Examination (MMSE, Folstein and Folstein, 1975). A wider range of MMSE scores was accepted to increase the generalizability of our findings to a geriatric sample that included individuals with mild cognitive impairment. Participants were excluded if they had ever received a diagnosis of dementia (this was corroborated with family members and medical records if dementia was considered). Participants were required to endorse CLBP of at least moderate severity, more days than not, for at least the previous 3 months (Rudy *et al*., 2007). All patients provided written informed consent.

Participants were excluded if they had a SCID lifetime diagnosis of bipolar disorder, schizophrenia, schizoaffective, or other psychotic disorders, a history of alcohol/drug abuse within the past 3 months, or a history of non-response or non-tolerance to duloxetine. Subjects were also excluded if they reported ‘red flags’ suggesting acute superimposed upon chronic pain (e.g., herniated disk, vertebral fracture, infection, *cauda equina* syndrome, or other spine emergency). All subjects agreed to not begin any new analgesic or other pain-relief interventions (e.g., physical therapy, acupuncture, spinal injections, massage, chiropractic manipulation, cognitive behavioral therapy) during their participation in the protocol. They were permitted to continue analgesics (Table 1) or other somatic treatments for pain being taken upon study entry.

Between January 2006 and April 2007 we screened 52 subjects, 40 of whom provided informed consent and met inclusion and exclusion criteria. Thirty-two subjects agreed to participate (Figure 1). Thirty subjects received at least one dose of duloxetine and are included in these analyses. Of these 30 subjects, 28 completed the study.

Assessments

We evaluated subjects' demographic information and history of both depression and low back pain before starting treatment with duloxetine. At the time of study enrollment, all subjects had a physical examination, electrocardiogram, and labwork (e.g., complete blood count, chemistry and hepatic panel, and thyroid stimulating hormone). Medications (analgesic and non-analgesic) were assessed at study entry and at every study visit.

Depression—The severity of depression was assessed with the MADRS (Montgomery and Asberg, 1979) at every study visit. The reliability and validity of the MADRS has been established in older depressed patients with (Koenig *et al*., 1989; Arranz and Ros, 1997) and

without (David *et al*., 2001; Podea and Chenderes, 2007) medical comorbidity. Inter-rater reliability was maintained at an ICC of >0.90. Clinician raters were not blind to treatment.

Pain—We measured pain intensity with the McGill Pain Questionnaire-Short Form (MPQ-SF, Melzack, 1987) which has been validated in community dwelling older adults with CLBP (Gangliese and Melzack, 1997). Subjects were asked to focus on their low back pain when completing the MPQ-SF. The MPQ-SF was completed at every study visit and assessed pain intensity for the past 7 days.

Comorbid medical burden—We used the Cumulative Illness Rating Scale adapted for use with geriatrics (CIRS-G, Miller *et al*., 1992) at study entry to assess medical burden. The CIRS-G can be successfully applied in both medically and psychiatrically impaired older adults, with good inter-rater reliability and face validity (Miller *et al*., 1992). Inter-rater reliability was maintained at an ICC of 0.96. History of spine surgery was also documented at baseline.

Quality of life—The Medical Outcome Survey (Ware *et al*., 1993) (SF-36) was developed as a generic measure of perceived health status, and it was administered at baseline and week 12. The SF-36 provides self-reports of mental and physical functioning. Published reliability of the physical and mental component subscales are 0.92 and 0.88, respectively (Ware *et al*., 1994).

Disability—Back-specific disability was assessed with the Roland Morris Disability Questionnaire (Roland and Morris, 1983), a scale developed to measure disability specifically in patients with low back pain, and validated in older adults (Roland and Morris, 1983; Weiner *et al*., 1996). This self-report assessment was administered at baseline, week 6, and week 12. Published internal consistencies for the Roland Morris range from 0.87 to 0.95 (Stratford and Binkley, 2000; Turner *et al*., 2003).

Anxiety—The anxiety subscale of the Brief Symptom Inventory (BSI) was completed at baseline, week 6, and week 12. The BSI was derived from the Symptom Checklist-90-Revised (SCL-90-R) (Peveler and Fairburn, 1990). Published internal consistency for the anxiety subscale of the BSI is 0.91 (Derogatis, 1993).

Sleep quality—The Pittsburgh Sleep Quality Index (PSQI) (Buysse *et al*., 1989) was completed at baseline, week 6, and week 12. The PSQI assesses sleep quality and disturbances over the past 4 weeks. A global PSQI score >5 has been shown to distinguish good and poor sleepers. Published internal reliability for the seven component subscales of the PSQI is 0.83 (Buysse *et al*., 1989).

Self-efficacy—Self-efficacy is a strong predictor of disability in chronic pain patients in general and in those with CLBP in particular (Grembowski *et al*., 1993). The Chronic Pain Self-efficacy Scale (CPSS, Anderson *et al*., 1995) was administered at baseline, week 6, and week 12. The CPSS is a 22-item questionnaire designed to measure chronic pain patients' perceived self-efficacy to cope with the consequences of chronic pain. The three domains of self-efficacy that are assessed are self-efficacy for: (1) pain management, (2) physical functioning, and (3) coping with symptoms. We have calculated Cronbach as of 0.91 for the total score, 0.67 for pain management, 0.90 for physical function, and 0.87 for coping with symptoms suggesting good internal consistency.

Somatic complaints—The Udvalg for Kliniske Under-sogelser (UKU) Side Effects Rating Scale (Lingjaerde *et al*., 1987) was designed to capture the side effects of psychotropic medications. The UKU was administered at every visit. The UKU side-effect rating scale

contains 48 items, which are rated on a Likert scale of 0–3 for degree of severity. The items are split into the categories of psychic, neurologic, autonomic, and others. The traditional use of the UKU includes asking subjects to rate the likelihood of the causal relationship of endorsed items with the study medication as 'improbable', 'possible', or 'probable'. In our use of the UKU, we do not obtain perceptions on the likelihood of the side effects to be associated with the study medication. This allows repeated observations of somatic concerns frequently endorsed by patients with depression or pain. Inter-rater reliability was maintained at an ICC of 0.91.

Intervention

All antidepressants and over-the-counter psychoactive medications (e.g., diphenhydramine for insomnia) were discontinued in a tapered fashion over 1–2 weeks concurrent with the start of duloxetine + DPCM. Participants unable to discontinue benzodiazepine therapy were converted to an equivalent dose of lorazepam (generally 0.5–2 mg/day). If insomnia was not managed by lorazepam, the lowest effective dose of zolpidem was permitted. Subjects were allowed to continue taking analgesics (prescribed and over-the-counter) that were prescribed at pre-study doses throughout participation in the study. Subjects agreed to not start new analgesics or increase the dose of currently prescribed analgesic medications throughout the course of the study. Medications were assessed at every clinical contact.

To decrease the risk of treatment-emergent side effects, duloxetine was started at 30 mg/day for the first 7 days. The dose was then increased to 60 mg/day. Subjects were seen weekly for the first 6 weeks and then every other week. DPCM, conducted by psychiatric nurses and masters and Ph.D.-level psychologists who were supervised by geriatric psychiatrists, consisted of education about geriatric depression and CLBP, a careful review of symptoms of depression, low back pain, and side effects using the MADRS (Montgomery and Asberg, 1979), MPQ-SF (Melzack, 1987), and UKU (Lingjaerde *et al*., 1987), respectively, and management of suicide risk. DPCM was based upon the principles of managing depression as a chronic illness as outlined in the PROSPECT (Bruce *et al*., 2004) and IMPACT (Lin *et al*., 2003) studies.

Remission

Remission from depression was defined as two consecutive MADRS scores <9. Requiring two consecutive scores at this level indicates a more meaningful, stable response. Subjects who were not depression remitters at 6 weeks had the dose of duloxetine increased to 90 mg/day. At week 8, those subjects who still had a MADRS score >9 had the dose increased to the maximal dose of 120 mg/day. Depression remission criteria guided the dosing of duloxetine. However, we also tracked low back pain *response* at every scheduled visit. CLBP response was defined as an improvement from baseline of the MPQ-SF by at least 30%. This degree of improvement has been determined to be the minimal clinically important improvement in pain outcome trials (Farrar *et al*., 2001a,b). We also examined rate of pain response using an improvement criteria of 50%.

If a subject was determined to be a depression remitter by week 6, but later converted to a nonremitter (i.e., MADRS >9), the dose of duloxetine was increased to 90 mg/day. For those subjects, if after 2 weeks at 90 mg/day the MADRS was still >9, the dose was then increased to 120 mg/day. Subjects were seen weekly for the first 6 weeks and then every other week.

Statistical analysis

Prior to any analysis, the data were examined for normality of distribution and for the presence of outliers. Descriptive statistics (mean, standard deviation, median) were generated for the clinical and demographic variables collected at baseline. To address our first question

concerning whether there were reductions in levels of both depression and low back pain after 12 weeks of open-label treatment with duloxetine, we used paired *t*-tests to compare baseline *versus* final (12 week) assessment data. In categorical response of main outcomes (depression and low back pain) at week 12, scores were imputed based on mixed models using random slope and intercept. In these analyses, only subjects categorized as completers were included. To address our second question regarding whether there were improvements in health-related quality of life, pain-related disability, self-efficacy for chronic pain, sleep quality, and somatic complaints, we used paired *t*-tests to compare baseline *versus* final assessment data. We used the Hommel method (Hommel, 1988) (PROC MULTTEST: SAS Institute) to control for multiple tests. The Hommel method, a modified Bonferroni correction, is valid when the hypothesis tests are independent or when they are non-negatively associated (Sarkar and Chang, 1997). To address our third question regarding time to response for both depression and low back pain, we used Kaplan Meier survival analysis to calculate time to response. In the survival analyses, we treated non-completers as censored observations.

Results

Table 1 lists the demographic and clinical characteristics of the sample. The average age was 71.4 and 70% of the subjects were female. The median MADRS score at baseline was 22.0. This was at least the second depressive episode for 60% of the subjects. The median duration of this depressive episode was 52.0 weeks. The median MPQ-SF score at baseline was 13.0.

The median maximal dose of duloxetine was 90.0 mg/day. The median duration on this maximal dose was 41.0 days. At baseline 50% of the subjects were taking opioids and 63.3% were taking nonsteroidal anti-inflammatory medications (NSAIDs).

The median Roland Morris Disability Questionnaire score was 14.0. The medical burden of the sample was high, reflected by the CIRS-G score of 11.6 (SD = 4.7) and the elevated average BMI of 30.3 (SD = 8.1). In addition, 36.7% of the subjects had a history of spine surgery (e.g., laminectomy, lumbar fusion, foraminectomy).

Question 1: are there reductions in *both* depression and low back pain after 12 weeks of open-label treatment with duloxetine + DPCM?

46.7% ($n = 14$) of the sample had a depression remission, defined as two consecutive MADRS scores <9. The mean change in the MADRS was −11.7 (median = −12.5, SD = 6.5) ($t = -9.6$, df = 27, $p < 0.001$, Cohen's d effect size = 1.81). All of the subjects who met criteria for depression remission also met criteria for pain response. All subjects who remitted sustained their improvement with a MADRS <9 at week 12 except for one participant who scored 10.

Pain response was defined as a 30% decrease in the MPQ-SF; 93.3% ($n = 28$) of the sample met this criteria for response. The mean change in the MPQ-SF was −6.0 (SD = 1.9) ($t = -4.03$, df = 27, $p < 0.001$, Cohen's d effect size = 0.76). Of the subjects who met the 30% improvement criteria for low back pain response, 50% ($n = 14$) also met criteria for depression response. Using a more stringent 50% improvement criteria for low back pain response, 60% of subjects (18/30) improved by week 12.

Question 2: are there improvements in health-related quality of life, pain-related disability, self-efficacy, sleep quality, and somatic complaints?

The change scores between baseline and exit from the study were calculated for *a priori*-designated clinically relevant variables (Table 2). There were significant improvements in mental health-related quality of life, anxiety, sleep quality, and side effects. There was

improvement in all domains of the CPSS except for self-efficacy for physical function. Physical health-related quality of life (measured with the SF-36) did not change.

Question 3: will low back pain respond before depression?

The mean time to depression response was 7.6 (SE = 0.6) weeks (Figure 2). The mean time to low back pain response was 2.8 (SE = 0.5) weeks (Figure 2). Although all subjects reported low back pain of at least moderate intensity to enter the study, seven of the subjects had relatively low MPQ-SF scores of <10, suggesting relatively less severe low back pain. Therefore, we also examined the time to response for those 23 subjects with more pain at baseline (e.g., MPQ-SF score >10). Using this more stringent criteria of low back pain severity, the mean time to pain response in this group was 2.2 (SE = 0.3) weeks. We also examined time to response using a 50% improvement from baseline as criteria for response. Using this more stringent response criteria, 27 subjects responded, and the mean time to response was 2.8 (SE = 0.7) weeks.

Discussion

This is the first treatment study of older patients living with comorbid major depression and CLBP in which both conditions improved during open-label treatment with duloxetine + DPCM. Despite the majority of subjects having recurrent depression and prolonged index episodes, almost 50% of the subjects experienced a significant depression response. This response rate is similar to that of depressed older adults switched to duloxetine after non-response to optimal treatment with escitalopram (Karp *et al*., 2008). The average time to depression response is also similar to the 7.9 weeks observed in a study of older adults treated with open-label paroxetine (Karp *et al*., 2005). It appears that duloxetine + DPCM treatment of depressed older adults living with CLBP may be associated with similar response rates and time to response of depressed older adults who are not living with CLBP.

It is noteworthy that all of the subjects who met criteria for depression remission also met criteria for low back pain response. This is in contrast to the observation that among the 93.3% of subjects who met criteria for low back pain response, only 50% met criteria for depression remission. As predicted, on average, improvement in low back pain occurred more rapidly than improvement in depression. Indeed, even after excluding subjects with less severe low back pain and using a more stringent 50% criteria for response, the time to pain response was still less than 3 weeks. This finding is consistent with the observed time to pain improvement with tricyclic antidepressants for neuropathic pain (Lipman, 1996) (of which CLBP in older adults often has a component (Weiner *et al*., 2006)). While this association is likely bidirectional, the timing of improvement may suggest the possibility of a cascade of events such as behavioral activation, improved sleep quality, and decreased social isolation, all of which may lead to improved mood. Another possible explanation for the observed sequence of improvement is that there are distinct neurophysiologic temporal signatures for the effect of duloxetine on depression and pain. While hypothetical, duloxetine perhaps modulates the lateral (sensory–discriminatory) structures of the ‘pain matrix’ before medial (affective–cognitive–evaluative) components (Tracey and Mantyh, 2007).

The degree of medical comorbidity, assessed with the CIRS-G, was higher (mean = 11.6) than several other studies of late-life depression, where the average CIRS-G scores ranged from 3.7 to 10.0 (Reynolds *et al*., 1999; Adeoye *et al*., 2003; Taylor *et al*., 2004; Lyness *et al*., 2006; Reynolds *et al*., 2006; Chapman *et al*., 2007). A possible explanation for the higher medical comorbidity, other than the requisite CLBP, is that comorbid depression and CLBP are associated with less self-care and less activity, both of which can result in or exacerbate medical conditions such as hypertension, diabetes, arthritis, and obesity (Lorig *et al*., 1999; Ciechanowski *et al*., 2000). There has been increased attention to the link between depression

and obesity (Kloiber *et al*., 2007). Among older adults, it is possible that CLBP may play a role in this relationship. It should also be noted that chronic pain in older adults is associated with lower self-rated health (Reyes-Gibby *et al*., 2002), and that self-rated health is associated with enhanced morbidity and mortality (Ferraro and Kelley-Moore, 2001).

The number of subjects prescribed a benzodiazepine at study entry (36.7%) was similar to other observations of benzodiazepine use in depressed older adults (Valenstein *et al*., 2004). This level of use is supported by observed PSQI and BSI scores which suggest impaired sleep quality (Buysse *et al*., 1989) and high anxiety levels (Andreescu *et al*., 2007), respectively. We observed statistically significant and clinically meaningful improvements in both sleep quality and anxiety over the course of treatment. Future work is planned to evaluate the sequence of improvement during treatment of these linked conditions: depression, pain, anxiety, and sleep quality.

The total score of the CPSS and all of the subscales except for physical function improved during treatment with duloxetine. The baseline CPSS total score was 53.6 (SD = 18.6). In a recent study of non-depressed older adults living with CLBP, the average CPSS total score was 81.8 (SD = 15.1) (Rudy *et al*., 2007). A likely reason for the lower CPSS scores in our sample (suggesting lower self-efficacy) is because of the comorbid major depression. Low self-efficacy is a risk factor for poor outcomes in both the pain and depression literature (Seligman, 1972; Maciejewski *et al*., 2000; Wells-Federman *et al*., 2002; Turner *et al*., 2005; Woby *et al*., 2007). Improving self-efficacy by treating depression may have a positive effect on pain outcomes. Given that pain improved more than depression, one may theorize that self-efficacy for physical function would also improve during treatment. These preliminary findings, however, suggest that self-efficacy for physical functioning may be more closely linked with depression than with pain severity.

There are several limitations to this analysis. It is likely that subjects' (and assessors') expectations inflated the rate of response in this open-label trial. Indeed, the placebo response rate of both depression and pain trials is generally around 30% (Deyo *et al*., 1990; Walsh *et al*., 2002). In addition, DPCM is not an inert intervention. DPCM included the provision of ongoing and frequent support and education about depression and low back pain, encouraging medication adherence, and attending to frequent complaints of insomnia with the judicious use of lorazapam and recommendations for improved sleep hygiene. It is probable that improvement resulted from combination treatment—as well as spontaneous improvement in both depression and/or CLBP unrelated to duloxetine + DPCM. Descriptions of spontaneous response rates in older depressed patients and CLBP patients are needed to put open-label findings into perspective. To the best of our knowledge, such data have not been reported. In addition, the relatively small size of the sample may have resulted in unstable estimates of response rates. Given the limited number of ethnic minorities represented in this sample, application of these findings may not be relevant for non-European American patients. Future studies with more racially diverse sampling are currently underway. Another limitation of these findings is that we did not have medical or surgical data to substantiate the various causes of CLBP. For example, some causes of CLBP such as myofascial pain and spinal stenosis may have been more responsive to treatment with duloxetine than sacroiliac joint syndrome or vertebral fractures (i.e., skeletal and joint etiologies). Finally, we did not measure fear avoidance, a construct associated with both chronic pain and disability (Kovacs *et al*., 2007); this information would have enhanced our description of the sample.

In conclusion, our open-label data suggest that duloxetine (up to 120 mg/day) + DPCM may be a rational choice for the treatment of older adults living with comorbid depression and CLBP. Treating these linked conditions with a dual mechanism agent that is delivered with supportive care management has several advantages to treating them separately. Among these are safety

(polypharmacy and the increased risks of side effects and adverse events are minimized), and increased adherence (fewer pills, fewer missed doses). While we did not explore change in co-prescribed analgesic use in this project, future work will explore the pharmacoeconomics of treating both depression and CLBP with combination duloxetine + DPCM. While feelings about having a mental illness were not assessed, (i.e., stigma associated with depression (Griffiths *et al*., 2008)), we hypothesize that the stigma of receiving treatment for a psychiatric condition may be reduced when linked with a physical condition such as low back pain. The lack of statistically significant improvements in back-related disability, self-efficacy for physical function, and self-perceived physical health, however, suggests that duloxetine + DPCM may not be adequate to optimize outcomes for about 50% of these patients. Treating both conditions to complete response and remission is critical since symptoms of both depression and low back pain are risk factors for the recurrence of each other (Reid *et al*., 2003). Non-pharmacologic interventions that specifically improve disability and self-efficacy for physical functioning (i.e., behaviorally activating treatments such as Problem Solving Therapy (Arean *et al*., 2008), functional rehabilitation programs, and physical therapy) which can reduce learned helplessness and improve physical conditioning—may be indicated for those patients who do not respond to first line treatment with duloxetine + DPCM. We are planning double blind placebo controlled work that integrates antidepressant pharmacotherapy such as duloxetine with behavioral treatments to further guide rationally-selected treatment options for these complex patients.

Key points

- In older adults, major depression and CLBP are frequently comorbid, mutually exacerbating, and risk factors for one another.
- These open-label data suggest that duloxetine at doses of up to 120 mg/day, delivered with DPCM, may be a rational treatment choice for older adults living with comorbid depression and CLBP.
- Treatment of these linked conditions with duloxetine + DPCM may result in improvement in low back pain before improvement in depression.

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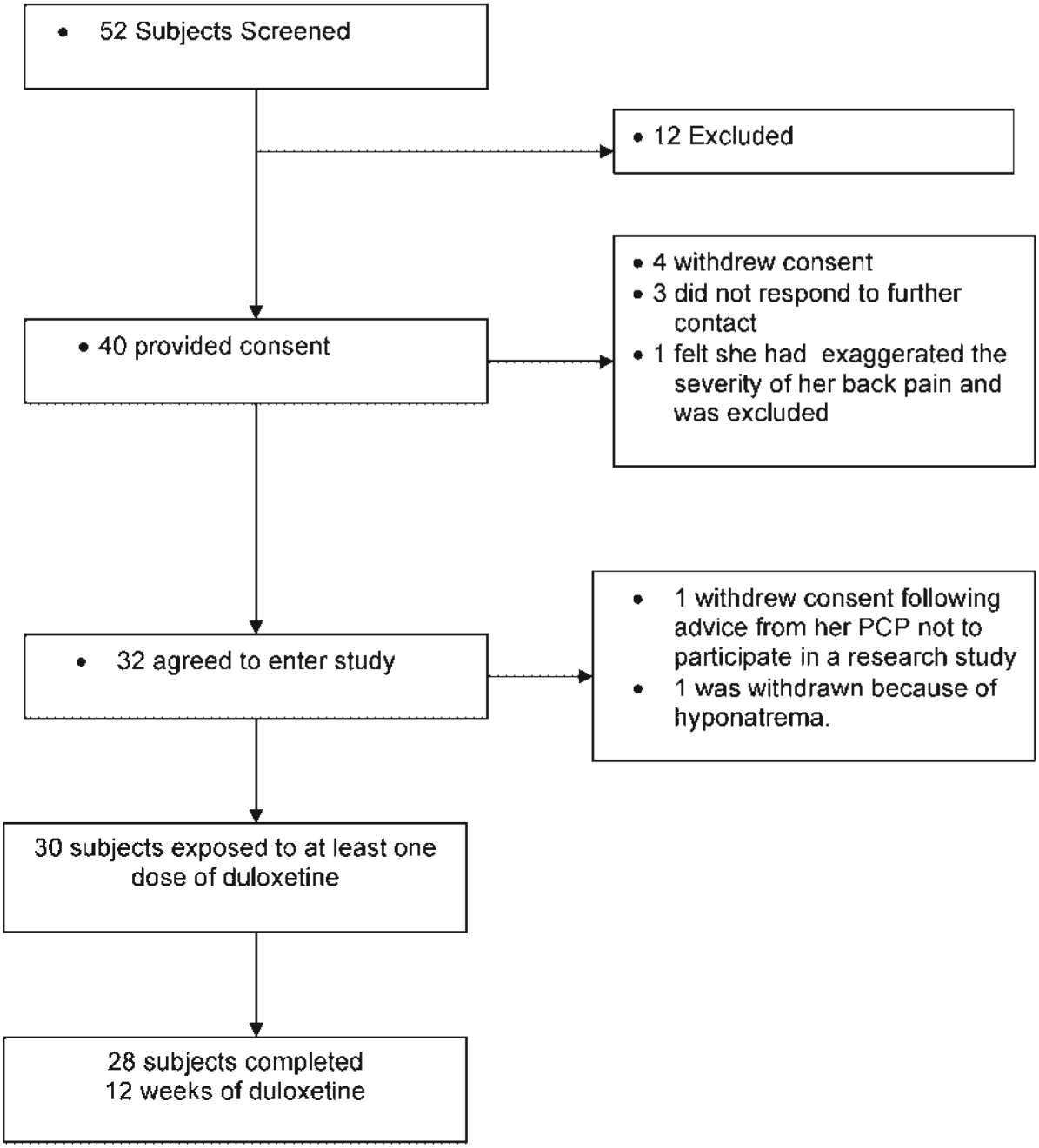

Figure 1.
Consort figure illustrating subject flow through the study.

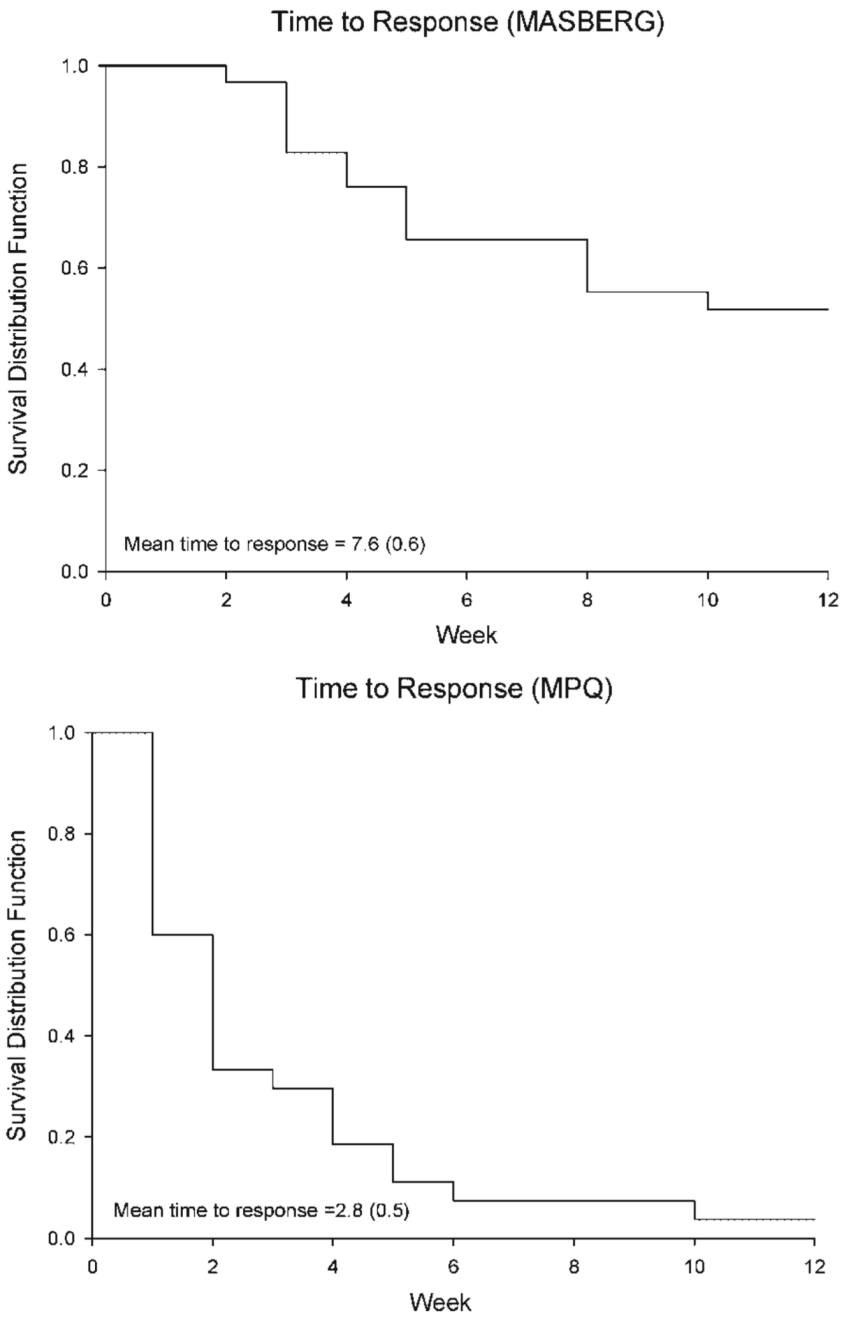

Figure 2.

The top curve shows the mean time to depression response, defined as 2 Montgomery Asberg Depression Ratings Scale scores <9. The lower curve shows the mean time to low back pain response, defined as an improvement on the McGill Pain Questionnaire (short form) by at least 30%.

Table 1

Baseline demographic and clinical characteristics (*n*=30)

Variable	Mean (SD)	Median	Theoretical range
Age	71.4 (7.61)	70	>60
% Female	70% (*n*=21)	—	—
% European American	97% (*n*=29)	—	—
Montgomery Asberg Depression Rating Scale	22.1 (5.5)	22.0	0–60
Duration of depression (weeks)	158.1 (253.6)	52.0	—
% Recurrent depression	60.0 (*n*=18)	—	—
Age at first depressive onset	51.3 (21.6)	52.5	—
McGill Pain Questionnaire-Short Form total score	13.5 (6.1)	13.0	0–45
Roland Morris Disability Questionnaire	13.2 (5.0)	14.0	0–24
% With history of spine surgery	36.7 (*n*=11)	—	—
Cumulative illness rating scale—geriatrics (total)	11.6 (4.7)	12.0	0–52
Brief symptom inventory—anxiety subscale	1.1 (0.8)	0.8	0–4
SF-36 physical component subscale (*n*=29)	34.8 (9.7)	34.3	—
SF-36 mental component subscale (*n*=29)	32.3 (10.2)	30.6	—
UKU side effects scale total (somatic complaints)	13.3 (5.0)	12.5	0–138
Mini Mental State Examination	28.5 (1.3)	29.0	0–30
Pittsburgh Sleep Quality Index	9.9 (4.5)	10.5	0–21
% Taking opioid analgesics	50.0 (*n*=15)	—	—
% Taking non-steroidal anti inflammatory analgesics (NSAIDs)	63.3 (*n*=19)	—	—
% Taking benzodiazepines	36.7 (*n*=11)	—	—

Table 2

Change during treatment

	N	Mean (SD)	*t*, *p*-value	Adjusted *p*-value (Hommel Method)	Cohen's d Effect size
Montgomery Asberg Depression Rating Scale	28	−11.7 (6.5)	−9.60, <0.001	<0.001	1.81
McGill Pain Questionnaire-Short Form	28	−6.0 (7.9)	−4.03, < 0.001	<0.003	0.76
Brief symptom inventory—anxiety subscale	22	−0.5 (0.8)	−2.93, 0.008	0.032	0.63
Roland Morris Back Pain Questionnaire	28	−1.8 (4.6)	−2.01, 0.05	0.16	0.38
SF36 physical component subscale	28	0.6 (6.4)	0.50, 0.62	0.62	0.10
SF-36 mental component subscale	28	13.8 (13.0)	5.63, < 0.001	<0.001	1.06
Pittsburgh Sleep Quality Index	28	−3.3 (3.4)	−5.05, < 0.001	<0.001	0.95
UKU side effects scale total score (somatic complaints)	27	−2.5 (4.6)	−2.80, < 0.01	0.038	0.54
Chronic pain self-efficacy scale					
Total self-efficacy score	26	10.8 (13.2)	4.21, < 0.001	0.002	0.83
Self-efficacy for pain management	26	16.2 (20.7)	3.97, < 0.001	0.003	0.78
Self-efficacy for physical function	26	5.4 (20.9)	1.31, 0.20	0.40	0.26
Self-efficacy for coping with symptoms	26	13.7 (13.5)	5.19, < 0.001	<0.001	1.02