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ORIGINAL ARTICLE

Treatment of minor depression in older adults: A pilot study comparing sertraline and exercise

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Abstract
The purpose of this study was to conduct a pilot clinical trial to test the feasibility and efficacy of an exercise program and anti-depressant treatment compared with usual care in improving the emotional and physical functioning of older adults with minor depression. Participants were 37 older adults with minor depression who were randomized to exercise, sertraline, or usual care; 32 participants completed the 16-week study. Outcomes included measures of both emotional (clinician and self-report) and physical (observed and self-report) functioning. There were trends for the superiority of the exercise and sertraline conditions over usual care in improving SF-36 mental health scores and clinician-rated depression scores. Individuals in the exercise condition showed greater improvements in physical functioning than individuals in the usual care condition. Both sertraline and exercise show promise as treatments for late-life minor depression. However, exercise has the added benefit of improving physical functioning as well.

Introduction

Minor depression, characterized by depressive symptoms, which do not fulfill the severity requirement for major depression is the most common type of depression experienced by older adults (Beekman, Copeland, & Prince, 1999). In a recent Dutch community-based sample, Beekman and colleagues reported a 10% prevalence of minor depression compared with only a 2% prevalence of major depression in that sample. This is consistent with Tannock and Katona's (1995) findings that the incidence of minor depression increases with age. According to DSM-IV (American Psychiatric Association, 1994), minor depression is characterized by depressed mood or anhedonia and 1–3 of the following symptoms over a two-week period: appetite disturbance, sleep disturbance, psychomotor agitation or retardation, loss of energy, feelings of worthlessness or guilt, difficulty concentrating, and recurrent thoughts of death.

Minor depression is associated with a number of adverse health outcomes. It is a risk factor for major depression (Kessler, Zhao, Blazer, & Swartz, 1997) and is associated with increased numbers of chronic diseases (Beekman et al., 1997), functional limitations (Beekman et al., 1997), increased severity of medical illness (Barefoot & Schroll, 1996; Koenig, 1997), increased service utilization (Callahan, Hui, Nienaber, Musick, & Tierney, 1994; Cuijpers, de Graaf, & van Dorsselaer, 2004; Wagner et al., 2000), and increased risk of mortality (Barefoot & Schroll, 1996; Enzell, 1984; Murphy, Monson, Olivier, Sobol, & Leighton, 1987; Penninx et al., 1999a). In addition to functional limitations, physical disability is also a consequence of both minor and major depression. The risk for onset of disability in persons with late-life depression is significantly higher than in older adults without depression, and is similar or even greater than the risk for disability associated with other chronic illnesses (Penninx, Leveille, Ferrucci, van Eijk, & Guralnik, 1999b). Furthermore, number of depressive symptoms is associated with increasing impairment in activities of daily living (Langa, Valenstein, Fendrick, Kabeto, & Vijan, 2004). Among those older adults with 1–3 symptoms of depression, 30% reported difficulty with at least one activity of daily living (ADL) and 27% reported difficulty with at least one instrumental activity of daily living (IADL). Depression is not only linked to self-report measures of disability, but it is related to greater declines in

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observed physical functioning, such as reduced walking speed (Penninx et al., 1998; Penninx, Deeg, van Eijk, Beekman, & Guralnik, 2000). Two large studies have found that integrating pharmacotherapy and psychotherapy into the primary care setting reduces symptoms among older adults with minor depression (Unutzer et al., 2002; Williams, Barrett, Oxman et al., 2000a). In the current study, exercise and anti-depressant medication are examined as treatments for late-life minor depression.

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed anti-depressants (Stafford, MacDonald, & Finkelstein, 2001). Although their efficacy in treating depression is similar to that of tricyclic anti-depressants, the tolerability of SSRIs is greater (Williams et al., 2000b). Two large, randomized, double-blind, placebo controlled trials have demonstrated the efficacy of sertraline for the treatment of late-life major depression (Schneider et al., 2003; Sheikh et al., 2004) and one open label study (Rosen, Mulsant, & Pollock, 2000) has demonstrated the efficacy of sertraline for the treatment of late-life minor depression. Thus, SSRIs are commonly used to treat depression and these studies provide evidence that sertraline is effective for the treatment of both major and minor depression in older adults.

The potential use of exercise as an alternative to drug treatment for depression has received considerable attention. Observational and intervention studies of young psychiatric patients suggest that aerobic exercise is superior to placebo or to no treatment in reducing depressive symptoms (Christmas & Andersen, 2000; North, McCullagh, & Tran, 1990). Among adults with major depression, exercise interventions appear to be as efficacious as antidepressant medications (Blumenthal et al., 1999; McNeil, LeBlanc, & Joyner, 1991) and psychotherapy (Freemont & Craighead, 1987; Klein et al., 1985) in reducing depression. Both psychological mechanisms (increased self-efficacy, reduced negative thought patterns; Blumenthal et al., 1999) and biological mechanisms (alterations in central norepinephrine activity, reduced activity of HPA axis, increased secretion of beta endorphins; Dishman, 1997; Galbo et al., 1990; Ransford, 1982; Rubin, 1989; Sothman & Ismail, 1984) may be responsible for the favorable effect of exercise on mood.

Blumenthal and colleagues (1999) conducted a 16-week randomized clinical trial comparing exercise, sertraline, and a combination of exercise and sertraline. They found that all three conditions were successful in reducing depression scores and there were no significant differences among the conditions. Patients in the exercise condition and the combined exercise and medication condition demonstrated significantly improved aerobic capacity from baseline while the medication group demonstrated no such change. Further support for the role of aerobic exercise in reducing depressive symptoms comes from Penninx and colleagues (Penninx et al., 2002). Using data from a single blind randomized controlled trial, they examined the effects of aerobic exercise, resistance exercise, and health education on depressive symptoms and physical functioning in a sample of older adults with osteoarthritis of the knee. Participants in the aerobic exercise condition demonstrated significant improvements in depressive symptoms compared with participants from the other two conditions, and also reported less disability and higher walking speed at follow-up than the control group.

In summary, minor depression is a common problem among older adults. In addition to its negative effects on emotional functioning, minor depression is associated with decrements in physical functioning as well. Most studies of treatment efficacy have been conducted in persons with major depression; only a few studies have tested the efficacy of treatments for minor depression in older adults. Exercise is known to be effective for improving depression. One study has demonstrated the efficacy of exercise in improving functioning in depressed older adults, while another study has shown the efficacy of a combination of exercise and medication in middle-aged persons on physical functioning. Thus, in addition to the anti-depressive effects of medication, exercise appears to have the added benefit of improving physical function. Consequently, we report the results of a pilot study based on this preliminary work and extend it to late-life minor depression. We conducted a pilot study designed as a randomized clinical trial to test the feasibility and efficacy of an exercise program and anti-depressant treatment compared with usual care in improving emotional and physical functioning in older adults with minor depression.

Methods

Participants

Participants were 37 adults aged 65 years and older who were recruited from various sources: through newsletters targeting older adults interested in participating in research, newspaper ads, flyers distributed at local nursing home facilities, and public presentations. Inclusion criteria were age ≥ 65 years and having 2–4 symptoms of depression. Exclusion criteria included cognitive impairment as evidenced by a MMSE ≤ 22 (Folstein, Folstein, & McHugh, 1975), current anti-depressant medication use, medical contraindications that would preclude random assignment (e.g., significant orthopedic problems or cardiopulmonary disease that would prevent regular aerobic exercise), current alcohol or substance abuse, bipolar disorder, and other severe psychiatric diagnoses (e.g., schizophrenia or psychosis). A total of 37 participants were

randomized to treatment: 14 to exercise, 11 to sertraline, and 12 to usual care.

Procedures

Interested individuals were screened for eligibility. The Patient Health Questionnaire-9 (Spitzer, Kroenke, & Williams, 1999) was used for the diagnosis of minor depression. Individuals rated their experience of each of the nine DSM-IV symptoms of depression on a four-point Likert scale ranging from 'not at all' to 'nearly every day'. Individuals who reported depressed mood or anhedonia as well as between 1–3 other symptoms of depression for more than half of the days over the last two weeks were considered to have minor depression. After screening for inclusion and exclusion criteria, eligible participants were randomized using a computer-generated random allocation list to one of three conditions: medication, exercise, and usual care. Assessments were made at baseline and after four months, and assessors were blinded to the condition of participants. This study was approved by the Institutional Review Board of Wake Forest University School of Medicine and all participants provided written informed consent at enrollment.

Interventions

Medication. Participants randomized to the medication condition ($n = 11$) received open-label sertraline. The initial dose was 25 mg/day during Week 1 and 50 mg/day during Week 2. The dose could be increased to 100 mg/day at Week 4 and 150 mg/day at Week 8. Study physicians had the option of changing the dosage by 25 mg increments if the patient was reporting difficulty with side effects. The maximum dosage allowed was 150 mg/day. Participants met with a study physician at baseline and weeks 2, 6, 10, and 14 to evaluate treatment response and side effects. Physicians used clinical judgment and PHQ scores to determine if therapeutic levels were reached.

Exercise. Participants randomized to the exercise condition ($n = 14$) completed a facility-based exercise regimen three days per week for 16 weeks (Messier et al., 2004). Exercise sessions lasted 60 minutes and consisted of both aerobic and resistance training. Each session consisted of a five minute warm up, 15-minute aerobic phase, 20-minute resistance training phase, 15-minute aerobic phase, and five minute cool-down period. The aerobic phases consisted of two repetitions of leg extensions, leg curls, heel raises, and step-ups. Resistance was provided by using ankle cuff weights and weighted vests. All exercise was supervised by a certified American College of Sports Medicine exercise leader and held in a group format.

Usual care. Participants randomized to the usual care condition ($n = 12$) were called at Weeks 2, 6, 10, and 14 by research staff who discussed the participant's general health status. This was done to provide some attention to the respondents in this condition.

Measures

Emotional functioning was assessed with the 17-item Hamilton Depression Rating Scale (Hamilton, 1967), the 15-item Geriatric Depression Scale (Sheikh & Yesavage, 1986), and the mental health scale of the SF-36 (Stewart, Hayes, & Ware, 1988). Physical functioning was assessed with a 23-item questionnaire of physical disability from the FAST study (Rejeski et al., 1995), the Epidemiologic Studies of the Elderly Short Physical Performance Battery (distance walked in six minutes, time to walk four meters, and time to sit and stand from a chair five times; Guralnik et al., 1994), and the physical health scale of the SF-36 (Stewart et al., 1988).

Statistical analyses

Differences in baseline characteristics across the intervention groups were examined using *t*-tests and χ^2 analyses. All treatment effects were examined using intent-to-treat analyses. A series of analyses of variance (ANOVA) were conducted to examine between group differences on the various physical and emotional outcomes at baseline and after four months. A series of ANCOVAs were also conducted to examine between group differences after controlling for baseline values on four-month change in these outcomes. Finally, for some selected outcome variables, graphs were plotted based on ANCOVA analyses with adjustment for baseline score to show group differences in the four-month change in these outcomes. Effect sizes for the interventions (exercise and medication) were calculated as the difference in the four-month change between the intervention group and usual care, divided by the standard deviation of the four-month change in both groups.

Results

The majority of the sample were in their 70s, female, white, well-educated, and had smoked at some point in their life. Baseline characteristics of the participants are presented in Table I. There were no significant differences among the participants in the three groups on these characteristics. Pre- and post-treatment scores on all measures of depressive symptoms and physical function are presented in Table II. As expected, there were no large baseline differences between groups on measures of depression severity or physical function. However, there was a significant difference for clinician-rated depression severity, with participants in the exercise

Table I. Baseline characteristics of the sample.

Characteristic	Exercise ($n=14$)	Medication ($n=11$)	Usual care $n=12$)	p
Age (M, SD)	73.5 (7.8)	76.4 (6.4)	73.9 (5.8)	0.53
Female	64%	73%	50%	0.52
White	93%	91%	67%	0.15
More than high school education	86%	82%	83%	0.97
BMI (M, SD)	27.3 (3.4)	30.7 (2.9)	30.7 (6.5)	0.11
Number of diseases (M, SD)	1.9 (1.5)	2.4 (1.4)	2.4 (1.6)	0.66
Ever smoked	57%	73%	50%	0.53
Currently drink	43%	55%	42%	0.74
MMSE (M, SD)	28.9 (1.0)	29.1 (0.9)	28.5 (1.5)	0.37

BMI, body mass index; MMSE, Mini Mental Status Exam.

Table II. Effects of treatment on depression and physical disability.

Measure	Exercise	Medication	Usual Care	$p^{\star}$
Hamilton Rating Depression Scale (score)				
Pre	12.7 (3.4)	13.7 (2.7)	9.5 (3.7)	0.02
Post	7.8 (4.3)	7.4 (4.7)	10.9 (5.8)	0.22
4-month change	−4.9 (6.6)	−6.3 (3.9)	1.5 (5.3)	0.005
GDS-15 (score)				
Pre	7.0 (3.0)	6.5 (2.9)	7.8 (4.2)	0.79
Post	4.5 (2.9)	6.1 (3.2)	6.3 (3.5)	0.40
4-month change	−2.5 (3.4)	−0.4 (4.2)	−1.6 (2.6)	0.44
SF-36 mental health component (score)				
Pre	54.1 (14.3)	61.2 (10.3)	55.8 (21.6)	0.66
Post	31.3 (13.5)	43.2 (16.7)	50.7 (25.0)	0.09
4-month change	−22.8 (16.0)	−16.3 (22.5)	−5.1 (17.4)	0.11
Six-minute walk distance (in feet)				
Pre	1528 (412)	1111 (683)	1327 (563)	0.30
Post	1576 (383)	1160 (644)	1355 (555)	0.26
4-month change	47.4 (145)	48.9 (231)	27.9 (228)	0.97
Four meter walking speed (in m/s)				
Pre	1.05 (0.25)	0.91 (0.37)	0.91 (0.39)	0.54
Post	1.12 (0.31)	0.85 (0.30)	0.92 (0.40)	0.22
4-month change	0.06 (0.1)	−0.05 (0.10)	0.01 (0.33)	0.52
Chair stand time (in seconds)				
Pre	16.2 (5.0)	18.9 (7.7)	17.7 (5.3)	0.60
Post	15.4 (6.1)	17.4 (5.3)	17.9 (5.8)	0.57
4-month change	−0.77 (4.3)	−1.59 (4.1)	0.29 (7.2)	0.76
EPESE Short Physical Performance Battery				
Pre	9.5 (2.0)	8.0 (2.4)	8.3 (3.2)	0.42
Post	9.4 (2.5)	8.1 (2.5)	8.2 (2.9)	0.50
4-month change	−0.18 (1.1)	0.13 (1.0)	−0.09 (3.2)	0.95
SF-36 physical health component (score)				
Pre	50.8 (22.7)	49.1 (23.5)	52.8 (19.2)	0.94
Post	38.9 (22.8)	43.8 (23.32)	44.3 (17.6)	0.82
4-month change	−11.9 (26.1)	−5.3 (8.0)	−8.5 (10.2)	0.76
Physical disability score				
Pre	12.5 (6.1)	11.8 (4.7)	12.3 (4.6)	0.96
Post	10.3 (4.1)	12.5 (6.3)	11.6 (3.8)	0.45
4-month change	−2.2 (2.8)	0.8 (2.3)	−0.7 (2.9)	0.08

$^{\star}p$ values are based on analyses of variance.

and sertraline groups scoring significantly higher than participants in the control group ($p=0.02$).

Participants in the exercise and sertraline conditions showed declines in clinician-rated depression severity (HRDS), while participants in the usual care condition demonstrated a slight increase in HRDS score ($p=0.005$). Similarly, there was a trend for individuals in the exercise and sertraline conditions

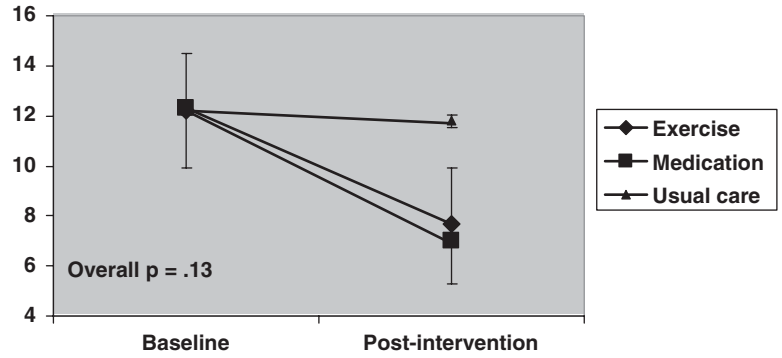

Figure 1. Impact of treatment on Hamilton Depression Rating Scale adjusted for baseline values depression. Overall $p = 0.13$; exercise versus usual care $p = 0.09$; medication versus usual care $p = 0.06$.

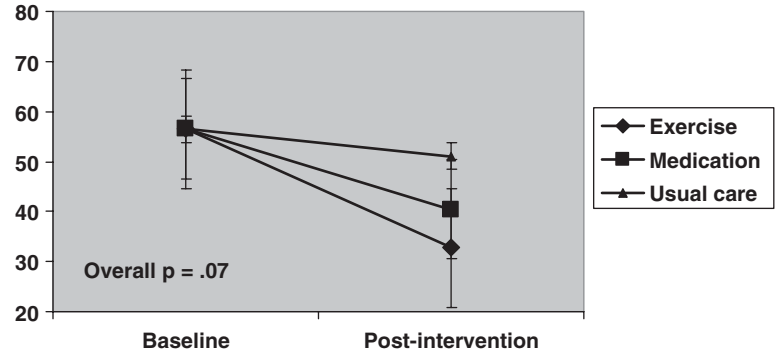

Figure 2. Impact of treatment on the mental health component of the SF-36 adjusted for baseline values of mental health. Overall $p = 0.07$; exercise versus usual care $p = 0.02$; medication versus usual care $p = 0.23$.

to experience substantial improvements in the mental health component of the SF-36 while the usual care group demonstrated only slight improvement ($p = 0.11$). All participants demonstrated a decline in self-reported depressive symptoms (GDS). With respect to changes in physical function, there was a trend for participants in the exercise condition to experience a greater improvement in physical disability score from baseline ($p = 0.08$). Participants in the usual care group experienced slight improvements in physical disability, while participants in the sertraline condition experienced slight declines. Participants in the exercise condition demonstrated improvements on all but one measure of physical function, whereas participants in the sertraline condition only demonstrated improvements on three measures of physical function.

Univariate analyses of covariance were conducted to examine the effects of the exercise and sertraline interventions on depressive symptoms and physical function while controlling for baseline symptoms and function. These adjusted analyses indicated that although the main effect of intervention condition on HRDS score was not significant ($p = 0.13$), there was a trend for both exercise and sertraline to be superior to usual care in reducing depression severity (exercise: $p = 0.09$, effect size (ES) $= 0.96$; sertraline: $p = 0.06$, ES $= 1.56$, Figure 1). There was also a trend for an effect of the intervention on the mental health component of the SF-36 (F [2, 26] $= 3.02$, $p = 0.07$), with participants in the exercise condition demonstrating significant improvement compared with participants in the usual care condition ($p = 0.02$; ES $= 0.95$, Figure 2). Finally, Figure 3 shows the trend for an effect of the intervention on physical disability (F [2, 29] $= 2.93$, $p = 0.07$), with a favorable improvement direction for those in the exercise group ($p = 0.19$, ES $= -0.22$), and a deterioration for those in the medication group ($p = 0.27$, ES $= 0.35$, Figure 3).

Discussion

This pilot study demonstrated the feasibility of performing a randomized trial of both exercise and drug therapy for the treatment of minor depression and physical disability in older adults. Participants in this study who received either exercise or sertraline demonstrated improvements in both clinician- and self-reported measures of depressive symptoms. The magnitude of improvement was similar to that reported by Rosen and colleagues (2000), who found that sertraline was effective in treating minor

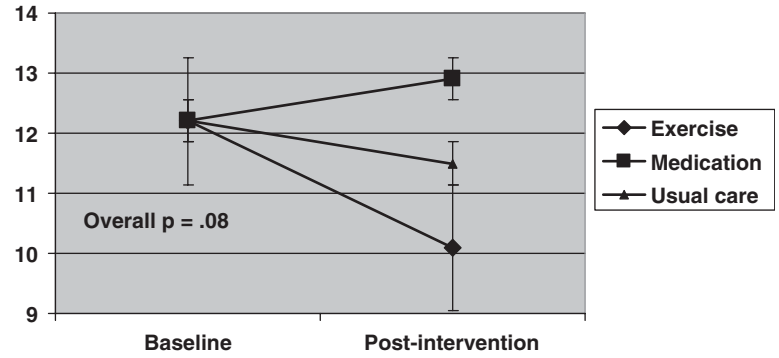

Figure 3. Impact of treatment on physical disability adjusted for baseline values of disability. Overall $p = 0.08$; exercise versus usual care $p = 0.19$; medication versus usual care $p = 0.27$.

depression in nursing home residents, and slightly less than improvements reported in studies examining the efficacy of sertraline in late-life major depression (Schneider et al., 2003; Sheikh et al., 2004). For the most part, participants who received usual care experienced small or no improvements in depressive symptoms.

Benefits of treatment on physical disability were also found. Participants in the exercise group demonstrated improvement on five out of six tasks of physical functioning while participants in the sertraline and usual care conditions improved on only three out of six tasks. There was a trend for statistical significance on physical disability for participants in the exercise versus the sertraline group. Participants in the exercise condition reported a decrease in physical disability, while participants in the sertraline condition reported an increase in disability. The pattern of results was similar with the four meter walk, with participants in the exercise condition demonstrating improvements and participants in the sertraline condition demonstrating declines. Thus, although both exercise and sertraline produced decreases in depressive symptoms, exercise appears to have a greater impact on physical disability. These findings are consistent with those of Blumenthal and colleagues (1999) who found that exercise and combination exercise and anti-depressant medication were superior to anti-depressant medication alone in improving physical functioning.

There are a number of limitations of this study. Because it was designed as a pilot study, the sample size was small and thus statistical power was weak. Although some effect sizes were large, they were not significant due to the lack of power. For example, effect sizes for the exercise and sertraline interventions on clinician-rated depressive symptoms (38.7–46.0% change) and on mental health quality of life (26.6–42.1% change) were substantial and there were small to large effects of each intervention on domains of physical functioning. The variance of the effect sizes suggests heterogeneity in participants' responses to the intervention: the intervention may have produced substantial changes in outcomes for some participants while the average effect size may only be moderate. Furthermore, even with the small sample size, there were indeed trends and significant differences for multiple outcomes. Thus, it appears that exercise and sertraline have the potential to produce significant changes in depression and physical functioning among older adults with minor depression. The generalizability of these findings may be limited by sample bias due to the recruitment strategies employed. Another limitation is that the diagnosis of minor depression was based on self-reported symptoms rather than a full clinical interview. Participant satisfaction with treatment was not assessed; however, it is likely that people were satisfied with treatment as adherence to the exercise intervention averaged 80% and only 9% of participants in the sertraline condition dropped out of the study, less than the drop out rate of a large study of sertraline for the treatment of late-life major depression (Schneider et al., 2003). Finally, the exercise intervention was center-based and findings may not generalize to home-based exercise programs.

Physical disability has been found to be consistently related to depression, both as a cause and a consequence of depression. Thus, an intervention that addresses both depressive symptoms and physical functioning is of great interest to geriatricians. The results of this study are promising and provide support for a head-to-head comparison of exercise and anti-depressants for the treatment of late life minor depression and disability. Furthermore, the possible synergistic effects of these treatments should be examined by including a condition in which both treatments are provided. Future research should also examine differential predictors of adherence and response to each treatment.

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