Intervention in patients with antide pressant treatment in primary care

Intervención en pacientes con tratamiento antidepresivo en atención primaria

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Abstract

Introduction: Not adherence to antidepressant therapy remains a significant challenge to quality depression care.
Objective: to determine the effectiveness of an intervention to improve early adherence among patients prescribed antidepressants.
Methods: In primary care practices, a randomized clinical efficacy study was conducted at 2 sites between January 2018 and December 2021.
Results: At 6 weeks, PIPT participants had improved 30.2% from baseline (95% CI, 21.7 to 38.8).
Conclusions: The PIPT intervention was most effective in helping patients achieve adequate adherence during the critical early adherence period.

Keywords: adherence, treatment, depression, antidepressants, primary care source: DeCS
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Resumen

Introducción:La falta de adherencia a la terapia antidepresiva sigue siendo un desafío importante para la atención de la depresión de calidad.
Objetivo: determinar la efectividad de una intervención para mejorar la adherencia temprana entre pacientes con prescripción de antidepresivos
Método:Se realizó un estudio de eficacia clínica aleatorizado en 2 sitios entre enero de 2018 y diciembre de 2021 en prácticas de atención primaria
Resultados:a las 6 semanas, los participantes del PIPT habían mejorado un 30,2 % desde el inicio (IC del 95 %, 21,7 a 38,8).
Conclusiones:La intervención PIPT fue más efectiva para ayudar a los pacientes a lograr una adherencia adecuada durante el período crítico de adherencia temprana.

Palabras clave: adherencia, tratamiento, depresión, antidepresivos, atención primaria fuente: DeCS

Introduction

Nonadherence to antidepressant therapy remains a significant challenge to quality depression care. Nonadherence rates among older adults range from 29% to 40%. Most depression treatment is provided in primary care, and higher rates of nonadherence to antidepressants are documented compared with psychiatry sites[(1)]. Although nonadherence is problematic throughout treatment, the first six weeks of treatment are a particularly critical period for promoting adherence, with increased risks of treatment dropout, relapse, medication discontinuation, vulnerability to suicide, and increased financial burden among those who exhibit early nonadherence to antidepressants. In addition, there is evidence that appropriate early antidepressant dosing and good adherence are associated with recovery from depression and may improve long-term outcomes for patients with depression[(2)].

Key risk factors for nonadherence include age, comorbid conditions, beliefs about treatment, and concerns about adverse events. In the elderly, additional risk factors may include patient variables such as lack of a medication routine, retention of discontinued medications, prescription mix, and multiple storage locations[(3)].

Although older adults face structural barriers (e.g., medication costs, and distance between home and doctor's office), negative attitudes are often the most important factors affecting adherence[(4)].Perceived stigma predicts poorer medication adherence and treatment discontinuation among older people with depression. In addition, low perceived symptom severity is associated with worse adherence,and even when distress is recognized, many older adults feel they should not need mental health help[(5)].

The Treatment Initiation and Participation Program (TIPP) is a brief psychosocial intervention designed to improve adherence to pharmacotherapy in patients with depression. The program helps patients address barriers, identify the benefits of treatment, and feel empowered to manage their medication regimen and communicate effectively with the physician[(6)].

For this 2-site randomized clinical trial of PIPT effectiveness, we focused on the critical early adherence period among middle-aged and older adults with newly initiated antidepressant treatment for depression by their primary care physician (PCP). The authors hypothesized that PIPT participants would be more likely to have at least 80% adherence to their antidepressant medication at 6 and 12 weeks after the prescription was provided compared with participants who received treatment as usual. In addition, we hypothesized that PIPT participants would have a greater reduction in depressive symptoms compared with participants receiving treatment as usual. Finally, we explored whether greater adherence in the PIPT and treatment as usual groups was associated with decreased depression at 24 weeks.

Method

A randomized clinical efficacy study was conducted at two sites between January 2018 and December 2021 in primary care practices in the city of Ambato. Trained staff reviewed each medical record for inclusion eligibility (e.g., newly prescribed antidepressants for treatment of depression) before contacting patients. To capture early adherence decisions among a wide range of patients, staff cold-called all eligible patients to assess their interest in the study within ten days of the prescription date. Patients who expressed interest were met in person by research staff for a more in-depth discussion of the study, written informed consent, and baseline assessment. Meetings were held at the primary care office or nearby research offices. Participants who met eligibility criteria during the baseline assessment were randomized 1 to 1 (stratified by site) to receive the PIPT

intervention in addition to antidepressant monitoring provided by their MAP or usual treatment monitoring provided by the MAP. This study was approved by the Universidad Regional Autónoma de Los Andes (UNIANDES).

PIPT sessions were conducted within the first six weeks of pharmacotherapy. In addition, research assessments were collected at 6, 12, and 24 weeks to evaluate the impact of PIPT on adherence and depressive symptoms.

Patients aged 55 years or older were eligible; this age cutoff was designed to include middle-aged adults who might be more similar to older adults in terms of medical burden or socioeconomic disadvantage. All patients had recently been prescribed an antidepressant by their MAP specifically for depressive symptoms. Patients were excluded if they had (1) active suicidal tendencies; (2) current substance abuse, bipolar disorder, or psychosis; (3) significant cognitive impairment; (4) terminal illness or current chemotherapy; or (5) inability to communicate

The PIPT intervention included 5 steps: (1) review symptoms and antidepressant regimen and conduct a barrier assessment; (2) define a personal goal that could be achieved with adherence; (3) provide education about depression and antidepressant therapy; (4) collaborate to address barriers to treatment participation; and (5) create an adherence strategy and empower the older adult to speak directly to the MAP about treatment

Adequate antidepressant adherence was defined as 80% adherence to ensure that most doses are taken to achieve a biological effect (e.g., therapeutic level).For this project, the goal was a sustained period of early adherence, defined as self-reported adherence of 80% or greater at the 6- and 12-week assessments.

Sociodemographic, functional, or clinical differences were assessed by t and χ 2test comparisons. In addition, in separate logistic regression models, the authors examined differences between groups in achieving 80% adherence to antidepressants at weeks 6 and 12 and a combined measure of adherence at weeks 6 and 12. Database and statistical data processing were performed and analyzed in SPSS 26 software (SPSS Inc., Chicago, IL, USA).

Results

Of the 607 patients who met the initial study inclusion criteria, 277 (45.6 %) consented and 231 were randomized to receive the PIPT intervention in addition to their antidepressant and MAP care (115 [49.8 %]) or treatment as usual with MAP (116 [50.2 %]). Primary outcome data were collected at 6 weeks from 211 participants (91.3 %), 200 at 12 weeks (86.6 %), and 199 at 24 weeks (86.1 %). There were no significant differences in retention rates by treatment group, sex, race/ethnicity, age, site, or educational level.

Nonadherence rates were highest among participants in the treatment as a usual group throughout the study period. Participants in the PIPT group were 5 times more likely to be adherent to their antidepressant at week 6 (odds ratio [OR], 5.54; 95 % CI, 2.57 to 11.96; χ^2 1 = 19.05; P <. 0.001) and almost three times more likely at week 12 after controlling for study site (OR, 2.84; 95 % CI, 1.47 to 5.50; χ^2 1 = 9.60; P = 0.002) compared with participants in the treatment as usual group. A combined measure of 80 % adherence at 6 and 12 weeks showed that PIPT participants as a group were three times more likely to be adherent at both 6 and 12 weeks combined (OR, 3.27; 95 % CI, 1.73 to 6.17; χ^2 1 = 13.34; P < 0.001) (Table 1). The effect of PIPT on the combined adherence measure was also greater than treatment as usual (OR, 2.2; 95 % CI, 1.1 to 4.3; χ^2 1 = 0.8; P = 0.03) within the subgroup of persons with mild to moderate depressive symptoms.

Table 1. Logistic regression predicting adherence by PIPT site and intervention.

Adherence to follow-up,	AIC	PIPT	Treatment as usual

(week)							
		O R(95%IC)	χ2	Valueof P	O R(95%IC)	χ2	Valueof P
	204.76	5,54 (2,57-11,96)	19.05	<.001	3,48 (1,70-7,13)	11.60	.001
	231.28	2,84 (1,47-5,50)	9.60	.002	2,82 (1,47-5,41)	9.78	.002
	228.06	1,49 (0,78-2,85)	1.48	.22	2,71 (1,41-5,24)	8.85	.003
6 y 12	244.18	3,27 (1,73-6,17)	13.34	<.001	3,30 (1,76-6,19)	13.80	<.001
6, 12 y 24	248.38	2,79 (1,50-5,19)	10.50	.001	3,90 (2,10-7,25)	18.58	<.001

Source: statistical analysis, p≤ 0.05 Abbreviations: AIC, Akaike information criterion; OR, odds ratio; PIPT, Program Initiation to Treatment and Participation.

Group symptom improvement rates for the total sample did not differ significantly over time (time per treatment: F 2377 = 1.03, P = 0.36). However, PIPT participants showed significant improvement (24.9 %) in depressive symptoms at 6 weeks (95 % CI, 13.9 to 35.9; t 337 = 4.46, adjusted P < 0.001), whereas treatment as usual participants showed less robust nonsignificant improvement. improvement (10.7 %) (95 % CI, -0.01 to 21.4; t 337 = 1.96, adjusted P = 0.05). Participants in the PIPT group showed additional improvements in depressive symptoms that were not statistically significant throughout the study. Treatment as usual participants showed a 12% improvement at 12 weeks (95% CI, 2 to 23; t 337 = 2.32; adjusted P = .04), with no further reduction in depressive symptoms. In a post hoc analysis of participants with mild to moderate depression severity at baseline assessment, both PIPT and treatment as usual participants improved throughout the study with no significant differences between groups. However, at 6 weeks, PIPT participants had improved 30.2 % from baseline (95 % CI, 21.7 to 38.8), whereas among treatment as usual participants, improvement was less robust (23.8 %) (95 % CI, 15.5 to 32.1). Improvement in depressive symptoms, measured as percent change from baseline, did not change significantly as a function of 80 % compliance status (at weeks 6 and 12) and treatment arm (time per treatment per compliance interaction: F 2363 = 2.28, P = .01). However, participants in both groups who were 80 % compliant at weeks 6 and 12 had a 15 % greater improvement in depressive symptoms throughout treatment (95 % CI, -0.2 to 30; t 369 = 1.93, P = .051) after controlling for the study site.

Discussion

In this community-based effectiveness trial among adults aged 55 years or older who had been prescribed pharmacotherapy for depression in primary care, patients who participated in PIPT were likelier to adhere to their medication than participants who received treatment as usual. The 5-fold increase in adherence during the first 6 weeks of care supports the clinical utility of PIPT in improving early adherence. The increased adherence among PIPT participants was further sustained during the first 3 months of care. Although PIPT did not significantly improve overall depression, the PIPT group showed a significant early reduction in depressive symptoms. These findings were replicated in participants with mild to moderate depression at baseline.

To our knowledge, few previous interventions have effectively improved adherence among adults with depression, despite its importance in quality care and potential to reduce the personal and societal costs of depressive

disorders[7,8].Research has documented that antidepressant prescribing rates in primary care are increasing, and adherence to antidepressant medication is associated with decreased mortality and reduced likelihood of suicidal ideation at 1-year follow-up. In a randomized cluster trial, shared decision-making was found to help select an antidepressant and improve patient satisfaction but was not effective in improving adherence[9,10].Programs focused on increasing patient activation to maximize participation and engagement in care have had a limited impact on retention. In 2014, the most recent update of the Cochrane review of adherence research concluded that additional adherence interventions are needed, given their influence on treatment outcomes[11].To our knowledge, PIPT is the only brief intervention that explicitly targets early adherence by working directly with the patient to reduce barriers, increase perceived benefits, and promote a personalized antidepressant adherence strategy[12,13]. This patient-centered approach can help address the informal cost-benefit analysis that significantly increases adherence. These findings also support the relationship between early adherence and improvement in depression.

The present study found no significant impact of PIPT on depression compared to treatment as usual. There was an early response to depression among the PIPT group, but both groups improved over time. There is emerging evidence of the differential impact of antidepressant medications on the trajectory of depression as a function of symptom clusters and the benefit of looking beyond symptom severity to predict treatment response[14,15].Targeted treatments and improved adherence could improve depression outcomes, as appropriate dosing remains a challenge for depression treatment, especially in primary care, which remains the largest provider of mental health services for older adults[16]. Recent research has documented that depression remains poorly managed in primary care, especially compared to other chronic diseases[17,18].

There are limitations to this study. First, we cannot account for factors outside the primary care setting that may affect adherence. Second, this study uses a self-report measure of adherence. Although the adherence measure has been validated, is reliable, and does not increase attention to adherence or serve as an intervention. Different measures (e.g., electronic monitoring, pill counts, self-report) yield different information. Individuals who deny nonadherence or involuntary nonadherence may have been overlooked. In addition, the study could not include adults with cognitive impairments who may have higher rates of unintentional nonadherence by focusing on acknowledged adherence. Third, as a new intervention, the study did not use an independent evaluator to perform cross-validation of intervention fidelity. Finally, In focusing on early adherence, the authors recruited only patients whose physicians diagnosed them with depression and could be contacted within 10 days of their prescription for early decision-making[19,20].

Conclusions

The intervention was most effective in helping patients achieve adequate adherence during the critical early adherence period. Adequate adherence to antidepressants was one of the 6-month depression outcomes. Given the high rates of depression, nonadherence, and use of primary care as a mental health service, large-scale implementation of a targeted adherence intervention, such as PIPT, could have a significant public health impact.

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