Assessment of the Effectiveness of Pharmacotherapy Follow-up in Patients Treated for Depression

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ABSTRACT

BACKGROUND: Several studies have established the effectiveness of pharmaceutical care (PC) in patients with heart failure, diabetes, hypertension, and dyslipidemia. However, there are few studies using standardized methods, e.g., randomized controlled trials, to assess the effectiveness of pharmacotherapy follow-up (PF) in patients with depression.

OBJECTIVE: To assess the effectiveness of PC via PF according to the Dáder Method in female patients diagnosed with depression.

METHODS: Sixty-eight patients were selected and randomly allocated to groups, stratified by age, type of medication, severity of depression, and presence of recurrence and/or relapse. Patients in the intervention group (IG) received clinical pharmacy intervention at monthly visits over a 3-month follow-up period. The control group (CG) also received monthly visits from the pharmacist, but PF intervention was not performed.

RESULTS: A comparison of the effects of usual treatment (CG) and PC (IG) on depressive symptoms showed a statistically significant difference between groups, with a median reduction in Beck Depression Inventory score (Δ) of 2.5 points in the CG and 13.5 points in the IG. Similarly, statistically significant results were observed for anxiety symptoms, with a median reduction in Beck Anxiety Inventory score (Δ) of 3.5 points in the CG and 13.0 points in the IG. The patients who underwent PF showed a high level of satisfaction with the service.

CONCLUSION: The PF is well accepted and effective in treating depressed patients, as indicated by the reduction of the depressive and anxious symptoms.

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What is already known about this subject

- The disabling burden of neuropsychiatric conditions is almost the same for males and females, but the major contributing causes are different. While depression is the leading cause for both males and females, the burden of depression is 50% higher for females than males. Females also have a higher burden from anxiety disorders, migraine, and Alzheimer's and other dementias. In contrast, the male burden for alcohol and drug use disorders is nearly 7 times higher than that for females and accounts for almost one third of the male neuropsychiatric burden (WHO, 2004).
- Since the concept of pharmaceutical care was introduced in the United States about 20 years ago, this initiative has become a dominant form of practice for thousands of pharmacists around the world (Berenguer et al., 2004). Currently, pharmaceutical care is understood to be the pharmacists' provision of medication-

related treatment to patients and the responsibility to monitor their pharmacotherapy to help them obtain the maximum benefit from the pharmacological treatments. Indeed, an awareness of the problem resulting from the use of medicines exists, and numerous studies reflect that drug use control is necessary since there is an important relationship between morbidity/mortality and pharmacotherapy (Berenguer et al., 2004).

- Guidelines for the treatment of depression recommend weekly interviews with the doctor in the first 4 to 6 weeks of treatment because they improve the patients' outcome and promote better compliance to treatment (Schulberg et al., 1998; APA, 2010). During this period, there is a need to monitor the response to antidepressants, side effects, adherence, and suicide risk (Schulberg et al., 1998; Fleck et al., 2009; APA, 2010). However, it is known that, in practice, Brazilian patients who use the public health system are not monitored as recommended in the guidelines (Neves, 2011). Thus, the pharmacist would be the suitable professional to monitor patients through pharmaceutical care, working with the doctor.
- It has been observed that the use of pharmacists in the mental health system is in its early stages, and few studies have been developed outside the United States with the objective of demonstrating the importance of the pharmacist on the mental health team (Razali et al., 1995; Shaw, 2000; Prats and Cebrián, 2002; Castelló, 2002; Ceresér et al., 2009). There are few randomized controlled trials, 3 of them were developed in the United States (Finley et al., 2003; Capoccia et al., 2004; Adler et al., 2004) and 2 in the Netherlands (Brook et al., 2003; Brook et al., 2005), which do not specify the method used in pharmaceutical care.

What this study adds

- Pharmacotherapeutic follow-up (PF) by the Dáder Method has been used in several countries (Spain, Brazil, Colombia, Bogotá, and Portugal) to monitor the pharmacological treatment of various diseases (Chemello et al., 2011; Fontana et al., 2003; Ceresér et al., 2009; Amariles et al., 2004; Muñoz et al., 2006; Afonso et al., 2012). However, to date, this methodology had not been evaluated to monitor the treatment of patients with depression. Despite many papers on the effectiveness of a collaborative model where the pharmacist works with other health professionals in treating depressed patients, there is variability in follow-up methods used, which tends to hinder the comparison between the results obtained (Finley et al., 2003).

What this study adds (continued)

- This is the first randomized controlled trial about pharmaceutical care in patients with depression, using a standardized method, which was developed outside the context of developed countries (U.S. and Netherlands).

Depression is a chronic and recurrent disorder, among the 20 most disabling diseases worldwide, and the burden of disability is 50% greater among females.¹ The prevalence of depression among females is 2- to 3-fold higher than in males.² In Brazil, drug therapy is considered the first therapeutic choice for depression; however, pharmacotherapy is associated with such problems as adverse reactions, drug interactions, and lack of compliance.³⁻⁴ In this regard, pharmacists may be able to improve treatment results by supplying such services as patient education, selecting the most appropriate drugs and doses, improving treatment compliance, monitoring treatment effectiveness, and identifying and handling adverse effects.⁵⁻⁸ The effectiveness of pharmacists' actions in mental health care is an increasing focus of scientific investigation.⁹⁻¹⁰

The effectiveness of pharmaceutical care (PC) in patients with heart failure, diabetes, hypertension, and dyslipidemia has been demonstrated in several studies.¹¹⁻¹⁷ A recent meta-analysis, which was published in 2010 and included 198 studies mostly conducted in the United States, showed that pharmacists' actions had favorably influenced therapeutic outcomes and provided humanitarian results for several clinical conditions. The authors of the meta-analysis suggested that pharmacists should be included on health care teams because they might improve the quality of the assistance provided to patients with several diseases.¹⁸

Pharmacotherapy follow-up (PF) is a PC modality that seeks to monitor and assess pharmacotherapy in patients on a regular basis to improve the results of treatment. However, there have been no follow-up studies of patients with depression, based on standardized methods.⁹

The Dáder Method is a simple approach that permits PF with any patient in any assistance setting and in a documented, systematic, and continuous manner.¹⁹ This method may be adapted to any situation and used to follow up pharmacological treatment for any disease. Studies that have employed the Dáder Method have shown its effectiveness in several diseases, but there are no data on patients being treated for depression.²⁰⁻²²

Due to the worldwide advancement of PC and the need to assess its effectiveness in female patients with depression, the present clinical trial sought to employ and assess the Dáder Method of PF. Our hypothesis states that the Dáder Method is effective and results in the clinical improvement of depressive and anxious symptoms.

Methods**Study Setting and Sample Recruitment**

The present study was conducted at the outpatient clinic of Alzira Velano Hospital, University of Alfenas (UNIFENAS). This outpatient clinic includes several specialties, including psychiatry and psychology. The average number of patients seen per week is 80, with various disorders such as schizophrenia, depression, bipolar, and anxiety disorders. This clinic lacks a pharmaceutical service to distribute the medications to patients. All patients with depression are seen by a psychiatrist at least 3 times during the first months of treatment (specifically, on the first consultation and at follow-up visits 40 days and 2 months later).

Patients diagnosed with depression based on *International Classification of Diseases, 10th Edition* (ICD-10) diagnostic criteria who were treated at the above-mentioned outpatient clinic were referred by the psychiatrist to the pharmaceutical assistance service, which was set up in the clinic by researcher Luciene Alves Moreira Marques, and were selected by Marques. The patients were recruited according to the following inclusion criteria: female gender, age 18 to 65 years, a diagnosis of depression at the initial stage of treatment (first treatment, no previous antidepressant), or who were prescribed a new antidepressant.

Exclusion criteria were: insurmountable difficulties in scheduling visits (lack of a telephone line or living in rural area or in a neighborhood that was difficult to access), BDI < 11 points, dependence on illicit drugs, schizophrenia diagnosis, and the presence of patent cognitive impairment that might affect the patient's ability to complete the research instruments. Such diagnoses were performed by the psychiatrist and were indicated in the patients' clinical records. The cognitive impairment was determined by the behavior of the patient when answering the screening questionnaire.

The allocation of individuals to the control (CG) and intervention (IG) groups was performed via random sampling stratified according to age, medication type, severity of depression, and the presence or absence of recurrence according to Bernoulli's method.

Intervention Design

A total of 68 patients diagnosed with depression were selected and subjected to triage, consisting of the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), and the Dáder Method questionnaire¹⁹ (Figure 1). These instruments were completed at a date and time agreed upon with each patient, either at their home, at the PC room of Federal University of Alfenas, or at the outpatient clinic; most patients (85.2%) were assisted at their homes. The clinical pharmacist called each patient on the telephone for a brief explanation of their condition, proposed the pharmacotherapy follow-up service, and scheduled the first visit. Instruments were completed at the first visit after obtaining the informed consent of the subject.

FIGURE 1 Experimental Design: Intervention Group (IG), Control Group (CG), and Pharmacotherapy Follow-up (PF)

DNO = drug-related negative clinical outcomes; DRP = drug-related problem.

After the first visit, 4 patients were excluded because they did not score higher than 11 on the BDI, and 6 others were excluded because of insurmountable difficulties in scheduling visits (lack of a telephone line or living in rural area or in a neighborhood that was difficult to access). The 58 remaining participants were allocated to the control and intervention groups according to stratification by age (18 to 65 years); severity (mild/moderate/severe), based on the BDI; medication type (tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs], other); and whether they were new cases (first treatment) or recurrences. After the onset of follow-up, 6 patients withdrew (reasons cited included lack of interest, replacement of allopathic treatment with homeopathic treatment, and change of psychiatrist), and 4 others were excluded after 3 consecutive failed attempts to schedule visits.

According to the Dáder Method, the patients in the IG received PF visits approximately every 30 days; the intervals between visits could be shorter according to the patient's

needs. These patients were given oral and written information about the treatment and educational lectures about disease and treatment; interventions with the psychiatrist were performed as needed. At the same time, the patients in the CG were visited monthly to answer inventories (BDI and BAI) but did not receive any orientation or intervention that might have altered their response to treatment. The study lasted 3 months, and due to ethical reasons, PF was offered to the patients in the CG during the following 3 months. Five patients in CG, for ethical reasons, received some timely pharmaceutical guidance. However, this approach has not been characterized as the intervention according to the Dáder Method, and they were maintained in the CG.

Data Collection

Data were collected between April 2010 and January 2012 using the following methods:

a) Beck Depression and Anxiety Inventories (BDIs and BAIs). The BDI is a self-assessment scale composed of 21 items addressing symptoms and behaviors with an intensity varying between 0 and 3. The items include sadness, pessimism, failure feelings, lack of satisfaction, guilty feelings, punishment feelings, self-dislike, self-critical feelings, suicidal thoughts, crying, social withdrawal, indecisiveness, distorted body image, inhibition of work, sleep disorders, irritability, lack of appetite, somatic concerns, fatigue, and loss of interest in sex. The BDI has been widely validated in Brazilian clinical and population samples,²³ with the following cut-off points for different intensities of depressive symptoms: minimal (0 to 11), mild (12 to 19), moderate (20 to 35), and severe (36 to 63).

The BAI was developed to assess the severity of anxious symptoms in depressed patients. The BAI includes 21 items that correspond to common symptoms of anxiety. The total scores can vary between 0 and 63, and the cut-off points are the same as those of the BDI.

All the participants completed the BDI and BAI at beginning and end of the study. Although the patients had some level of schooling, a portion of them were unable to complete the questionnaires without the researcher reading it to them.

b) Assessment of patient satisfaction with pharmaceutical assistance and pharmaceutical care. The Pharmacy Services Questionnaire was formulated in 2002 to assess customers' satisfaction with the pharmaceutical assistance provided at pharmacies.²⁴ This instrument was designed for use in population samples, the primary health care setting, and with outpatients. Both the version validated for Brazilian Portuguese²⁵ and the original version contain 20 items, which are assessed using 5-point Likert scales as follows: 5, excellent; 4, very good; 3, good; 2, fair; and 1, poor.

The Portuguese version of the Pharmacy Services Questionnaire was adapted (certain questions did not apply to the context of our study) for use in the present study. This questionnaire included 15 questions to be answered on a Likert-type scale and 3 yes/no dichotomic questions. This instrument was administered to the participants after the PF ended by a researcher other than the one who performed the PF. The researcher completed the questionnaire at each participant's home, and interviews lasted an average of 10 minutes. All patients in the CG and IG responded to the Pharmacy Services Questionnaire after completing the follow-up.

Intervention Method

a) Pharmacotherapy follow-up. The Dáder Method of pharmacotherapeutic follow-up was developed by "Grupo de Investigación en Atención Farmacéutica de la Universidad de Granada." This method develops a pharmacotherapeutic history based on information about health problems and the patient's pharmacotherapy. From the information contained in

the history, the pharmacist draws up the patient's situational state, which lets them see the "big picture" about their health and their treatment at different times, and evaluates the results of pharmacotherapy. As a result of the evaluation and analysis of the situational states, the pharmacist sets up a plan of action with the patient, where they will register all pharmaceutical interventions, with the goal of enhancing or preserving the health of the patient. Although the Dáder Method establishes basic rules for performing PF, this method is adaptable to many environments.

The Dáder Method was the procedure chosen for PF19, and the method was applied by a pharmacist (female) with professional experience. The same professional attended training courses in this method (57 hours) and has extensive experience using the method.

The pharmacotherapy history form was administered to both groups at the beginning of the study; however, the full method was only applied to the IG.

The service was offered to patients by telephone, and the first visit was scheduled for the date and time most convenient for each patient. After the aims of the study were explained, the participants signed an informed consent form, and the interview began. At the first visit, the questionnaire, Beck inventories, and the pharmacotherapy history form for the Dáder Method were administered. Most of the interviews were conducted at the patients' homes and lasted an average of 1 hour and 30 minutes. At the end of the pharmaceutical consultation, the second meeting was scheduled (1 month after the first interview or sooner when pharmacotherapy-related problems were identified).

The aim of the Dáder Method was to identify drug-related problems (DRPs) and drug-related negative clinical outcomes (DNOs). The DRPs are "those situations where the use of the drug causes or may cause a negative clinical outcomes associated with drug." The DNOs are situations associated with the use or misuse of drugs. These are classified into 6 categories according to the III Consensus of Granada (2007): (a) untreated health problems, (b) effect of unnecessary medications, (c) qualitative ineffectiveness of drugs, (d) quantitative ineffectiveness of drugs, (e) qualitative unsafety of drugs, (f) quantitative unsafety of the drug.

After the problems related to pharmacotherapy were identified, the patients were duly informed about the problems, and pharmaceutical intervention was performed via oral and/or written communication between the pharmacist and patient or between the pharmacist, patient, and doctor. All interventions were recorded on the intervention form. Interventions included strategies to improve compliance with treatment, orientation regarding the disease and the patient's medications, dose adjustment, substitutions of antidepressants, and the addition of medications, among other features. A portion of the interventions included the prescribing physician's participation.

The aim of the third visit was to assess the results of the intervention or multiple interventions. Pharmaceutical interventions included both actions designed to solve problems and health education actions—advice on hygienic and dietary habits—using oral and/or written communication as tools.

The assessment of the results of the pharmaceutical interventions took place after a period that was predefined with each subject to establish whether her problems had been solved.

Ethical Issues

Before any procedure was applied, the present study was subjected to and approved by the Research Ethics Committee of the Federal University of São Paulo (UNIFESP) protocol 1668/09 and registered at Clinical Trials, ID: NCT01571973. Each participant received a written document explaining the voluntary nature of participation, the right to withdraw at any time without losing medical treatment or follow-up assistance at the Vila Esperança outpatient clinic, the procedures to be performed, the possible risks, and the confidentiality in the use of information. The patients who agreed to participate were asked to sign an informed consent form.

Statistical Analysis

We calculated the sample size needed to detect a 4-point difference in BDI scores between the case and control groups after 3 months of follow-up with a test power of 70%, a 95% confidence interval, a constant correlation of 0.05 for the same patient's BDI scores at the 3 assessment time-points, and a standard deviation of 7.5. The 4-point difference in BDI was based on previous studies.² The sample size thus calculated was 30 patients per group.

Quantitative data were analyzed descriptively via summary measures (means and standard deviations) for continuous variables (such as BDI scores) and by means of absolute and relative frequencies for categorical variables using the Fisher exact test and G test. To compare outcomes between groups, the Mann-Whitney test was used. Data normality was tested by the Shapiro-Wilk test ($P < 0.05$). Bioestat 5.0 software was used, and significance was established at 5%. The effect size was calculated by means of an equation (average of the IG effect – average of the CG effect/standard deviation).

Results

The average age of the CG was 44.2 ± 13.9 years, and most patients were Catholic (80.76%) and married (65.4%). In the IG, the average age was 40.8 ± 12.2 years, and most patients were “other” religion (59.1%) and married (72.7%). Patients from both groups belonged to the same social class. Table 1 describes the remainder of the sociodemographic data for the patients in both groups.

The average number of medications used by the patients in the CG was 1.5 ± 0.6 ; for the IG, it was 1.7 ± 0.8 . The drugs

TABLE 1 Sociodemographic Data for the Study Participants

	Control Group n = 26	Intervention Group n = 22	P Value ^a
Age range			
18 to 39 years, n (%)	10 (38.5)	11 (50.0)	0.56
40 to 65 years, n (%)	16 (61.5)	11 (50.0)	
Marital status			
Married, n (%)	17 (65.4)	16 (72.7)	0.75
Not married, n (%)	9 (34.6)	6 (27.3)	
Schooling			
Until 9 years, n (%)	12 (46.2)	13 (59.1)	0.40
More than 10 years, n (%)	14 (53.9)	9 (40.9)	
Occupation			
Homemaker, n (%)	8 (30.8)	11 (50.0)	0.23
Other, n (%)	18 (69.2)	11 (50.0)	
Religion			
Catholic, n (%)	21 (80.8)	9 (40.9)	0.06
Other religion, n (%)	5 (19.2)	13 (59.1)	

^aFisher exact test. $P < 0.05$.

most commonly used by patients in both groups were SSRIs (Table 2). Most patients in the control (76.9%) and intervention (68.2%) groups had started antidepressant treatment within the last 60 days. Three patients were receiving concurrent psychotherapy, 2 in CG group and 1 in IG.

The groups were similar at baseline for depressive symptoms ($P = 0.17$) and for anxious symptoms ($P = 0.18$). BDI score reductions (Δ) of 2.5 points in the CG and 13.5 points in the IG groups were observed. Similar results were observed for anxiety symptoms, with BAI score reductions (Δ) of 3.5 points in the CG and 13.0 points in the IG. A comparison of the effect of the usual treatment (CG) and pharmaceutical care (IG) on depressive symptoms using the Mann-Whitney test revealed a statistically significant difference ($P = 0.0275$). The Mann-Whitney test revealed significant differences with respect to anxious symptoms ($P = 0.0194$, Figure 2 and Table 3). The effect size was 0.64 for the depressive symptoms and 0.68 for the anxious symptoms, considered a medium effect.²⁶

After 3 months of follow-up, 7 of the IG patients exhibited minimal symptoms of depression (i.e., entered remission, with $BDI < 11$ points) versus 4 of the CG. There was an 80% reduction of cases of severe depression in the IG and 60% for the CG and 53.4% reduction in moderate depression in the IG versus 7.7% in the CG.

A total of 57 DNOs were detected in 88% of patients, 64.9% of which were solved by the pharmacist's intervention. The most frequent DNO was quantitative ineffectiveness (compliance or a drug dose that could still be adjusted), followed by nonquantitative ineffectiveness (due to personal characteristics).

The most general interventions were performed by the

TABLE 2 Data for the Pharmacological Treatment of Patients in the Control and Intervention Groups

	Control Group n = 26	Intervention Group, n = 22	Test	P Value < 0.05
Treatment data				
Treatment time before starting the study (days), median	30	60	Mann-Whitney	0.53
Antidepressants				
Tricyclic agents (TCAs), n (%)	5 (19.2)	7 (31.8) ^a	G test	0.57
Selective serotonin reuptake inhibitors (SSRIs), n (%)	14 (53.8)	13 (59.1)		
Other, ^b n (%)	7 (26.9)	4 (18.2)		
Adjuvant drugs				
Other nonanti-depressant drugs, ^c n (%)	4 (15.4)	4 (18.2)		
Benzodiazepines, n (%)	10 (38.5)	8 (36.4)		
Case type				
New (first episode), n (%)	6 (23.1)	7 (31.8)	Fisher exact test	0.53
Relapse, n (%)	20 (76.9)	15 (68.2)		
Severity of depression				
Mild	8 (30.8)	4 (18.2)	G test	0.59
Moderate	13 (50.0)	13 (59.1)		
Severe	5 (19.2)	5 (22.7)		

^aThere were patients who used more than one antidepressant.

^bVenlafaxine, bupropion, mirtazapine.

^cHypnotic-sedatives, mood stabilizing anticonvulsants (topiramate, lamotrigine).

TABLE 3 Median Beck Inventory Scores of Patients in the Control and Intervention Groups at the Beginning and the End of the Study

	Baseline	3 Months	Delta (Baseline- 3 Months)	P Value (CG x IG)
SCORE BDI				
Control group (CG)	23	20.5	2.5	P=0.0275
Intervention group (IG)	28	14.5	13.5 ^a	
SCORE BAI				
Control group (CG)	24	20.5	3.5	P=0.0194
Intervention group (IG)	29	16	13 ^a	

^aStatistically significant, $P < 0.05$.

BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory.

pharmacist through pharmacist-patient verbal communication (47.4%). Of the proposed interventions, 16.7% were not accepted by the prescriber or by the patient.

A pharmacist does not have prescriptive authority. Thus, the

FIGURE 2 Median Beck Inventory Scores of Patients in the Control and Intervention Groups at the Beginning and the End of the Study

A: Median Beck Depression Inventory (BDI) scores

B: Median Beck Anxiety Inventory (BAI) scores

^aBaseline compared with 3-month follow-up in Intervention Group. Statistically significant, $P = 0.0275$ for depressive symptoms and $P = 0.0194$ for anxious symptoms in Intervention Group.

pharmacist made suggestions of interventions to a physician, such as substitute medication, increase compliance, modify the dose, add medication, alter the mode of use and administration, remove a medication, modify the therapeutic plan, and modify posology. Interventions that involved only the pharmacist and the patient were providing counseling pertaining to the unwanted side effects that patients may experience at the beginning of treatment with antidepressants, counseling on the latency period of antidepressants, counseling patients and their families about depression and treatment with medication, encouraging the patient to follow the treatment and suggesting the inclusion of nonpharmacological measures, such as psychotherapy, physical activity, or other manual activities that could assist the treatment.

TABLE 4 Instrument Items Assessing Patient Satisfaction with Pharmacotherapy Follow-up and the Average Scores that the Patients Attributed to Each Item (minimum: 1, maximum: 5)

Questions: How do you rate . . .	Mean $\pm$ SD
1. The pharmacist's availability to answer to your questions?	4.72 $\pm$ 0.58
2. The professional relationship between the pharmacist and you?	4.85 $\pm$ 0.42
3. The pharmacist's ability to warn you about problems you might have with your medications?	4.52 $\pm$ 0.96
4. The explanation the pharmacist provided about the action of your medications?	4.48 $\pm$ 1.00
5. The pharmacist's interest in your health?	4.74 $\pm$ 0.77
6. The help the pharmacist supplied about the use of your medications?	4.59 $\pm$ 0.93
7. The pharmacist's efforts to solve the problems you have with your medications?	4.61 $\pm$ 0.83
8. The responsibility the pharmacist assumes regarding your treatment?	4.78 $\pm$ 0.47
9. The orientation the pharmacist provided on how to take your medications?	4.43 $\pm$ 0.96
10. The pharmacist's answers to your questions?	4.72 $\pm$ 0.75
11. The pharmacist's efforts to maintain or improve your health?	4.76 $\pm$ 0.60
12. The privacy in your discussions with the pharmacist?	4.83 $\pm$ 0.49
13. The pharmacist's efforts to ensure that your medications will have the expected effect?	4.61 $\pm$ 0.80
14. The explanation the pharmacist gave about the possible adverse effects of medications?	4.57 $\pm$ 0.96
15. The time the pharmacist offers to spend with you?	4.74 $\pm$ 0.65

Regarding the satisfaction questionnaire, the first domain includes questions regarding the availability of the pharmacist and his relationship with the patient and the quality of their responses. The mean score obtained in these responses was greater than 4.0 (Table 4). The second domain (management therapy) consisted of items referring to aspects of cognitive services provided by the pharmacist more strongly related to pharmaceutical care. Among them are the interest, commitment, and responsibility assumed by the pharmacist in solving problems of treatment and improvement/maintenance of patient health; quality of recommendations given by the pharmacist; the privacy service; and the availability of time to spend with the patient. Similarly to the first field, the mean score was higher than 4.0, indicating a high satisfaction. For ethical reasons, after completion of the randomized clinical trial, the CG received PF. Thus, the results presented here reflect the satisfaction of both groups (IG and CG).

When asked whether they would continue their visits to the pharmacist or receive additional pharmacist visits, most patients (95.8%) answered affirmatively. When asked whether they would ask their doctor to work with the pharmacist and whether they would recommend the pharmaceutical service to friends and relatives, all patients answered affirmatively.

Discussion

The effectiveness of the Dáder Method in the PF of patients can be assessed according to the clinical and patient satisfaction results. The comparison of the effects of the usual treatment (CG) and pharmaceutical care (IG) on depressive symptoms exhibited a statistically significant difference between the groups ($P=0.0275$). Similar results were obtained regarding anxious symptoms ($P=0.0194$).

As well as the statistically significant difference between

groups regarding the depressive symptoms after 3 months, the patients in the IG also exhibited important clinical improvements.

In addition, the improvement of the anxious symptoms exhibited a statistically significant difference between groups. The intervention group exhibited significantly greater improvement, which might be due to the better pharmaceutical assistance they received during treatment. It is possible that the psychosocial support that the pharmacist provided and the trust-based relationship that was established were crucial in reducing the patients' anxiety. Although we have no specific instrument to measure a trust-based relationship (patient-pharmacist), assessment of satisfaction suggests this fact. The patients attributed high marks (4.85 ± 0.42 and 4.83 ± 0.49 , respectively) when asked: "How do you evaluate the pharmacist's professional relationship with you and how do you evaluate privacy in conversations with the pharmacist?"

In addition to the trust-based relationship that was established, assistance at home and the time made available for each interview might have encouraged the patients to describe their problems with pharmacotherapy as well as their psychosocial problems. This additional encouragement may have been the differential factor in the present study. Capoccia et al. (2004) did not find a significant difference between groups, even after 1 year of follow-up performed via telephone calls.⁶ Importantly, the present study was performed by a single clinical pharmacist; thus, the variability in the behavior toward patients was reduced. Even though each pharmacist has been trained to apply the PF (Dáder Method), each can do it with small differences because the clinical reasoning is not equal for all professionals. Interventions may be different and are the results of these measures. Therefore, in research, use of a single pharmacist could decrease the

measurement bias. In the study of Adler et al. (2004), several clinical pharmacists performed the PF of 533 patients over a 6-month period and achieved no statistically significant difference between groups.²⁶

Our study showed that PF performed by pharmacists over the first 3 months of treatment for depression is relevant for the production of better clinical results. Over that period, patients can develop undesirable effects that might threaten the continuance of treatment. This period is when the body adapts to the medication, and the disease itself might contribute to the patients' discontinuation of treatment. However, follow-up must not be interrupted at the end of this period because other problems can emerge later, especially lack of compliance and discontinuance of treatment.²⁷

The average age of the patients of both groups in the present study was similar to that reported by other published studies.^{26,28}

Considering both control and intervention groups together, 72.91% of the patients had already exhibited more than 1 episode of depression, which is in keeping with the 63.5% rate reported by Adler et al. (2004). In a study on follow-up that lasted 15 years, 85% of 380 patients who recovered from an episode of major depression exhibited at least 1 recurrence during the study. Among those who remained well for 5 years after the initial treatment, 58% exhibited recurrence over the following 10 years.²⁹ That study also identified significant predictors of recurrence, which included female gender, never having been married, previous episodes of depression, and 1 long depressive episode before admission.²⁹

Our results indicated that the patients had high levels of satisfaction with the services performed by the clinical pharmacist, which agrees with the findings of other studies.³⁰⁻³³ The questions that scored highest were those related to the patient's trust in the pharmacist. Regarding the yes/no dichotomous questions, more than 95% of the answers were affirmative. The patients stated that they would like to continue receiving the pharmacist's assistance, would recommend it to friends and relatives, and would ask the doctor to work with the pharmacist. Armando et al. (2005) found similar results.³² The type of pharmacist-patient relationship established in the present study may have been a factor that contributed to the observed results.

Limitations

Two limitations of the present study were the restriction of follow-up to only 3 months since other pharmacotherapy-related problems, such as lack of compliance, can occur after this period and threaten the success of treatment and the limited number of subjects. Thus, further studies assessing the effectiveness of the pharmacist's participation over longer follow-up periods are needed. A further limitation was the fact that the sample consisted only of female participants; for this

reason, our results may not be generalizable to males, who might exhibit different responses to PF.

Conclusion

We conclude that PF, performed according to the Dáder Method, is both well accepted by and effective in patients treated with antidepressants, as indicated by a reduction in their symptoms of depression and anxiety.

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DISCLOSURES

The authors report no conflicts of interest regarding this study. Study concept and design were contributed by Marques, Noto, and Galduróz. Marques had primary responsibility for data collection, with assistance from Oliveira and Fernandes; data interpretation was primarily the work of Marques, with assistance from Beijo, Noto, Oliveir, and Fernandes. The manuscript was written primarily by Marques, with assistance from Noto and was revised by Marques, Noto, Galduróz, and Beijo.

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