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Original Article

Pharmacotherapy Follow up in Mental Health: Which Outcomes Change in a Short Period?

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ABSTRACT

Objectives: Investigate the outcome changes in patients with depression and anxiety during a pharmacotherapy follow up service, in a short period. **Materials and Methods:** A randomized and controlled trial of 70 adults was developed in Psychosocial Care Centers in Brazil. Patients in the intervention group received pharmacotherapy follow up service according over a 4-month period. The control group received traditional service. After the 4-month period, patients of the control group were invited to participate for another four months receiving pharmacotherapy follow up service (control group post-intervention). The primary outcomes (medication adherence, anxiety and depression rates, quality of life) and the variations between groups were compared. **Results:** The evaluation of the control group data showed no statistically significant difference for parameters. However, in relation to adherence to pharmacotherapy, there was a statistically significant difference in the intervention group, between consultations 1 and 3 and consultations 1 and 4. For the clinical parameters (depression and anxiety) and humanistic (quality of life), there was no difference between the intervention group consultations. For the patients in the control group post-intervention (consultations 1 to 4), when compared to moment 4 of the control group, the levels of depression decreased between the moment 4 control group and the moments of the pharmaceutical appointment 2, 3 and 4. **Conclusion:** This study points out that these patients should take much more time being followed up, in order to improve the clinical and humanistic outcomes. Also, standardized documentation and records have to be provided in this pharmaceutical service.

Key words: Clinical Pharmacy, Medication Adherence, Mental Disorders, Mental Health, Outpatient Psychiatry, Pharmacist.

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INTRODUCTION

The last years, pharmacists' roles have gradually evolved from focusing mainly on dispensing medications to embracing a patient-centered approach in pharmacotherapy management.[1] In the face of the global burden of mental disorders, international institutions have supported and encouraged the introduction of pharmacists into multidisciplinary health care teams in mental health.[2-4]

Studies show new pharmacists acting in mental health within multidisciplinary teams, such as in the early detection of mental health conditions, developing care plans and pharmacotherapy follow up.[5-8] There are studies of patients with mental illness showing that pharmaceutical care contribute to the achievement of therapeutic goals like medication adherence, treatment satisfaction, reduction of depressive and anxiety symptoms.[9-12] However, many have not utilized controlled designs;[13] moreover, most of the few studies have been derived from developing countries.[14,15]

In Brazil, there are no recommendations in official government documents that guarantee the presence of the pharmacist in mental health teams.[16] Therefore, is necessary investigate the impact of the pharmacist interventions using replicable care models in mental health. Thus, the aims of the study were to investigate the clinical and humanistic outcomes in patients with depression and anxiety during a pharmacotherapy follow up service in a short period.

MATERIALS AND METHODS

Local and type of study

Primary Health Care Services are linked to Psychosocial Care Centers (CAPS) in a network of the Brazilian Public Health System.[17] The CAPS are the main outpatient care units for users of mental health services, in which the majority offer only the medication dispensing service to patients.

The applied research model was randomized controlled trial in according in which there was a "control group" (CG) and an "intervention" group (IG). The collection period for patients CG and IG was one month (August 2016). The randomization was determined in groups by simple random allocation by random draw, carried out in sealed and numbered envelopes. The IG received the pharmacotherapeutic follow-up service (PFS) from the pharmacist researcher for a period of four months (one meeting per month), with application of the questionnaires of the clinic and humanistic parameters (September 2016; December 2016). Those randomized to CG received the application of the questionnaires of the same parameters the IG for future comparison along of four months (September 2016; December 2016). After the cycle of the CG, some participants were collected (January 2017), randomly drawn again and invited to participate for another 4 months receiving PFS, called CGPI (control group post-intervention; January 2017; May 2017). Thus, the total study time was the period August 2016 until May 2017.

Population and selection of patients

This study used sample size calculation, taking into account the population of the municipality.[18] At the end of the study in the CG, sample calculations were performed again to infer a minimum number in which we could apply a PFS for another 4 months (CGPI).

The target patients were primarily those previously diagnosed with depression and/ or anxiety disorders, according to the International Classification of Diseases, ICD10.[19] The patients invited must be adults (20–60 years old) with diagnosis of depression or anxiety disorder made at least three months before their enrollment in the study.[20] This criteria was taken in order to consider the latency period of antidepressants drugs possibly used in the treatment of these disorders.[21] Patients who accepted to participate in the study were instructed to return every thirty days. After the psychiatric consultation, they were submitted to follow-up (IG and CGPI) and application of the instruments (CG, IG and CGPI).

Data Collection

The PFS was configured according to the Dáder method, as a method for clinical monitoring of patients with the follow-up type.[22] The primary outcomes of the PFS were treatment adherence rate, anxiety and depression rates (clinical parameters), in addition to quality of life (humanistic parameters). The influence of the PFS in this outcome was assessed from specific instruments described below, which they were used to evaluated the outcomes at four time points (every consultation/ month) for treatment adherence, anxiety and depression rates and two time points (first and last consulting), for quality of life.

Instruments used

Morisky Green Levine Test

Medication adherence of treatment was assessed using a validated scale called Morisky Green Levine Scale (MGLS), a four-item self-reported questionnaire of the public domain.[23-25] Adherence was measured using the number of "yes" responses to the four high (0 yes responses), intermediate (1–2), or low (3-4).

Depression and anxiety scale

Beck Anxiety Scale (BAS): is to measure severity of anxiety symptoms.[26] Respondents are asked on a 4-point scale, ranging from 0 (not all) to 3 (severely) and the added items result in total scores that can vary from 0 to 63.

Beck Depression Scale (BDS): As a self-report inventory, is designed to measure emotional, cognitive, somatic and motivational components.[27] Each answer is scored on a scale value of 0, 1, 2 and 3, to obtain a score ranging from 0 to 63.

Quality of life- EQ-5D-3L instrument (HRQoL)

The quality of life was measured by EQ-5D-3L instrument used in the first and last consulting for each group, the EQ-5D visual analogue scale (EQ VAS).[28] This is a 0–100 scale validated in the Brazilian population, where patients are asked to indicate their overall health today.[29,30] The license for using this scale for present survey is under number L-30153.

Interviews

The interviews of consultations were carried out by the researching pharmacist and the two research assistants, who were not part of the CAPS professional team. The interval between consultations lasted one month and the first one was reserved for the questionnaire completion in all the groups, as well to the beginning of the PTF to IG and CGPI. The Figure 1 below represents the general flow chart of the services offered at CAPS.

Data analysis

The groups were compared in relation of adherence to treatment, rates of depression and anxiety (clinical parameters) and quality of life (humanistic parameters). The normality of the samples was assessed by the Shapiro – Wilk test.[31]

Regarding the clinical parameters, to check the variations between groups (CG, IG and CGPI) ANOVA 1 criterion was used, complementing with the Bonferroni post hoc test. In relation to the same clinical parameters, ANOVA 1 was also used to compare the same patients, in the last interview (4) CG with the all 4 pharmaceutical consultations (CGPI). The t-Student test was applied for the analysis of intra-group variations (CG, IG and CGPI), for the same clinical parameters in the first and last consultations and was also applied for the analysis of the change in the quality of life inter and intra groups. The data was analyzed using the BioEstat program, version 5.0 and a 95% confidence interval and a significance level of 5% were considered.

Ethics Approval

The study was designed according to the guidelines for research involving human subjects and approved by the Ethics Committee in Research of the Federal University of Ceará - *COMEPE* (*1.519.326/2016*).

RESULTS

Characteristics of CAPS and Pharmacotherapy follow up

The analitic sample consisted of 70 patients (36 CG, 34 IG), being that 18 CG patients were submitted to another 4 months of follow-up, constituting the CGPI. Figure 2 below shows the formation of the study sample. Initially, 83 patients agreed to participate in the study, with 38 randomized to IG and 45 patients to CG. During follow-up, there was a loss of 4 patients to the IG (2 dropped out of the follow-up and another 2 missed the last meeting), with a final number of 34 patients in this group. In the CG, 2 patients left the CAPS, 3 gave up participating in the research and 4 missed the last meeting, totaling 9 losses and a final number of 36 patients in this group (Figure 2).

Clinical parameters of control group

The evaluation of the CG data showed no statistically significant difference for the variables adherence, depression, anxiety (clinical parameters). That is, the consultations carried out in the CG group did not influence the alteration of these parameters.

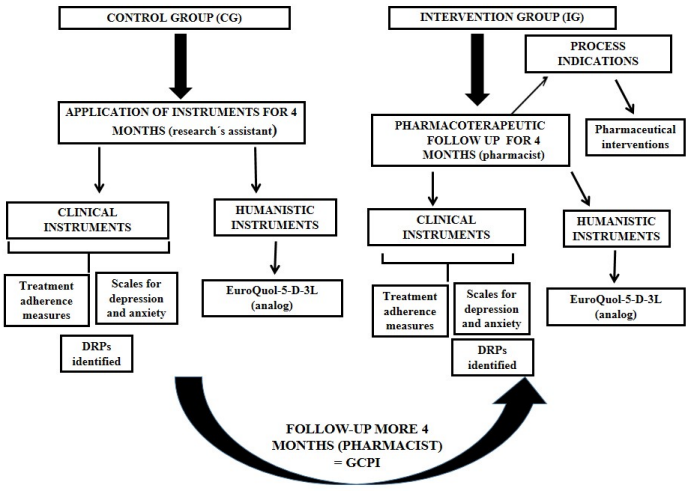

Figure 1: General flow chart of the services offered at CAPS (August, 2016; August, 2018).

Clinical and humanistic parameters of intervention group

The analysis showed that there is a statistically significant difference (F = 6.89; p = 0.0004) as to the improvement in the pattern of adherence to pharmacotherapy due to pharmaceutical intervention (Table 1, Figure 3). The Bonferroni test, a priori, detected the difference in adherence in the intervention group between pharmaceutical consultation 1 and 3 (B = 4.27; p <0.05) and between pharmaceutical consultation 1 and 4 (B = 3.39; p <0.05) (Table 2). Moreover, the number of patients in each adherence level in the intervention group, during pharmaceutical consultations, confirmed this pattern of improvement (Figure 3). For the clinical parameters of depression and anxiety and for the humanistic (quality of life), there was no difference between the IG consultations (Table 1).

Humanistic parameter (quality of life) of all groups (CG, IG and CGPI)

The analysis of intra-group quality of life (CG, IG and CGPI) at consultations 1 and 4 showed that there was no influence of the pharmaceutical consultation on the quality of life of the individuals in these groups (Table 3). In this turn, the quality of life score of same patients in the IG and CGPI was assessed at consultations 1 and 4. The analysis showed that the pharmaceutical consultation did not change the quality of life of these patients.

Clinical parameters control group x group control pos intervention

The results regarding the influence of the pharmaceutical intervention for the same patients (moments 1 to 4) in the CGPI when compared to moments 4 of the CG did not reveal a statistically significant relationship for the adherence to pharmacotherapy and anxiety levels. However, the analysis showed a statistically significant relationship for the variable depression level between the moment 4 CG and the moments of the pharmaceutical appointment 2 (F = 6.77; p = 0.008), 3 (F = 4.51; p = 0.0044) and 4 (F = 4.72; p = 0.0036) of CGPI (Table 4).

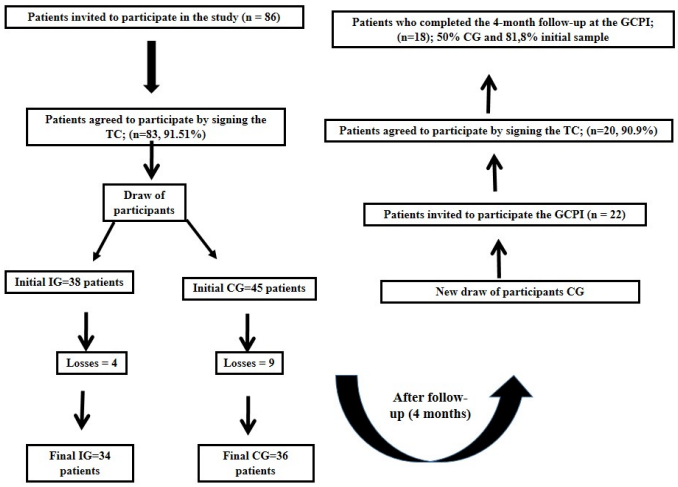

Figure 2: Formation of the study sample from the beginning to the final group (CG, IG and CGPI); CAPS (August, 2016; August, 2018).

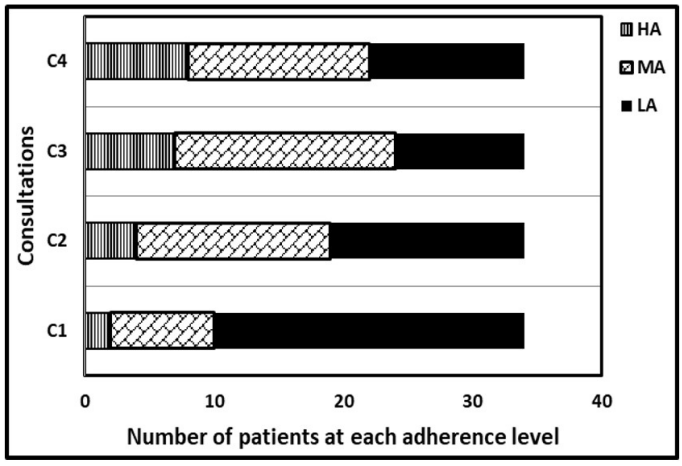

Figure 3: Number of patients at each adherence level in the intervention group during pharmaceutical consultations; n = 34, CAPS (August, 2018; December, 2018). HA = high adherence, MA = medium adherence, LA = low adherence.

DISCUSSION

In recent decades in Brazil, psychiatric hospitals ceased to be the base of the care system, giving ground to a more integrated, dynamic, open and community-based mental health care model.[17] This model takes into account the rehabilitation and psychosocial interaction, the complexity of mental health care, the multiple drug therapy and the accompanied by long-term therapeutic and occupational support.[16,17]

In this context, providing only the medication dispensing service to patients with mental disorders does not guarantee continuous support

Table 1: Differences in levels of adherence, anxiety, depression and quality of life between pharmaceutical consultations in the intervention group. CAPS, August 2016 / December 2016.

Statistical Indicator	Adhesion	Anxiety	Depression	Quality of life
SQ				
Between	19.20	584.67	732.09	2.48
Intra	122.53	32.70	13.00	776.50
GL				
Between	3	3	3	1
Intra	132	24	80	66
Medium Square				
Between	6.40	194.89	244.03	2.48
Intra	0.93	136.33	161.94	11.76
F	6.89	1.42	1.50	0.2112
p-value	**0.0004***	0.258	0.2178	0.6521

SQ = sum of squares; GL = degree of freedom; F = F test (variance); * p< 0.05

Table 2: Comparison of the level of adherence in the pharmaceutical consultations of the intervention group. CAPS, August 2016 / December 2016.

Statistical Indicator	Pharmaceutical consultation					
	1 and 2	1 and 3	1 and 4	2 and 3	2 and 4	3 and 4
Difference of means	0.50	1.00	0.79	0.50	0.29	0.20
Bonferroni	2.13	4.27	3.39	2.13	1.25	0.88
p- value	w.s.e.	<0.05*	<0.05*	w.s.e.	w.s.e.	w.s.e.

w.s.e = without statistical significance; * p< 0.05

to them, since this service offers guidance in a timely manner, without offering follow-up. Thus, the involvement of the pharmacist through the PFS service in supporting patients with psychiatric disorders becomes essential for access to rational pharmacotherapy.[32,33]

In mental health patients, the lack of insight about the disease, the complexity of the therapeutic regimen, a lack of family support, side effects, the belief that the medication is ineffective, the difficulty of medication access and remembering to take the medicine are predictors of poor adherence.[34-37] So, nonadherence to medication among patients with mental disorders must be prevented, avoiding negative clinical and economic consequences in these patients.[38-40]

In the present study, PFS improves the adherence of treatment over the course of pharmaceutical consultations. Similarly, recent studies concluded that pharmacist interventions (counseling and treatment monitoring) improved antidepressant medication adherence by 15% to 27%.[41-43] However, in their systematic review, other authors concluded that just a few studies demonstrated statistically significant differences in this issue.[38]

The successful result regarding treatment adherence may be due to motivational components of the interventions (present at all PFS meetings), with a care plan developed in partnership with the patient and with monthly goal assessments and feedbacks. Similarly, another study was successful in adherence results when conducting motivational interviews for 6 months.[44] In fact, good advice based on dialogues and understandings of each patient's perspective directly and / or indirectly improves adherence to psychiatric treatment.[45]

For the clinical parameters of depression and anxiety, there was no difference between the IG consultations. Meta-analysis of the literature containing studies of pharmaceutical interventions in depressed outpatients also showed unchanged clinical outcomes, despite the improvement in treatment adherence.[39] The accessibility that the pharmacist has in motivating and advising the patient favors the management of adherence. However, in turn, clinical improvement also depends on other factors, such as, for example, follow-up time. Indeed, study shows the need for longer periods of monitoring of depressive patients by the pharmacist in obtaining positive clinical findings.[46]

Although other studies showed a positive correlation between pharmaceutical interventions and clinical improvement of depression, there is variability in the methodology in these studies, where what is offered as treatment to the control group sometimes includes different interventions that can in themselves promote clinical improvements (bias factor not found in the present study).[47,48] This fact is reflected in a lack of adequate "shielding" in studies said to be randomized, in addition to the variability of checklists of measurement instruments for depression and anxiety disorder.[49] In fact, Ho and colleagues recognized the heterogeneity of the studies, as well as the lack of randomized controlled trials, which can compromise their internal and external validity.[38] Therefore, there is a need for a standardized pharmaceutical intervention approach for this group of patients, coupled with trials that relate adherence versus long-term clinical outcomes.

Another reason was the presence of other factors that significantly reduced the bias of the present research. Firstly, on the few studies that obtained positive clinical outcomes, the effect bias was not shielded in relation to the latency period.[45-48] The patient, at the beginning of antidepressant therapy, depending on his life context, may have his general health status altered, having the antidepressant action taking place only 4 to 6 weeks after starting treatment.[21] Thus, the effects observed during the latency period can be both the result of pharmaceutical intervention and the positive effects brought about at the beginning of therapy. Therefore, this is the first Brazilian study that measured the results of pharmaceutical intervention on the depression rate in a treatment period greater than that of latency.

Table 3: Analysis of quality of life in the control versus intervention, intervention versus control and control group post- intervention in consultations 1 and 4. CAPS, August 2016 / May 2017.

Statistical Indicator	Consultation 1				Consultation 4			
	CG	IG	IG	CGPI	CG	IG	IG	CGPI
Means	4.76	5.29	5.29	4.66	4.94	5.67	5.67	4.66
Standart deviation	2.98	3.52	3.52	3.21	3.31	3.33	3.33	3.08
t-Student	-0.7348		0.6293		-0.9209		10.646	
p- value	0.4650		0.5320		0.3603		0.2921	

CG= control group; IG= intervention group; CGPI= control group post- intervention

Table 4: Difference in adherence to pharmacotherapy, depression and anxiety in the control group (consultation 4) versus the control group post-intervention (consultations 1, 2, 3 and 4). CAPS, August 2016 / May 2017.

	Adhesion				Depression				Anxiety			
Statistical	4CG×1	4CG×2	4CG×3	4CG×4	4CG×1	4CG×2	4CG×3	4CG×4	4CG×1	4CG×2	4CG×3	4CG×4
Indicator	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI	CGPI
SQ												
Between	0.69	3.36	1.36	3.36	20.83	80.03	80.03	172.80	7.14	8.64	14.00	5.78
Intra	48.94	41.61	40.94	39.61	4727.20	4951.46	4558.46	4948.46	3034.85	3448.85	2889.00	3470.71
GL												
Between	1	1	1	1	1	1	1	1	1	1	1	1
Intra	34	34	34	34	14	14	14	14	6	6	6	6
Medium Square												
Between	0.69	3.36	1.36	3.36	20.83	80.03	80.03	172.80	7.14	8.64	14.00	5.78
Intra	1.44	1.22	1.20	1.16	337.65	353.67	325.60	353.46	505.80	574.80	481.50	578.45
F	0.48	2.74	1.13	2.88	0.4510	6.77	4.51	4.72	0.07	0.26	0.17	0.1396
P-value	0.5011	0.1030	0.2955	0.0949	0.09258	**0.0008***	**0.0044***	**0.0036***	0.9954	0.9362	0.9729	0.9838

CG= Control Group; GCPI= Group Control Post-Intervention; SQ= Sum of Squares; GL= Degree of Freedom; F =F test (variance); ***P<0.05**

Moreover, anxiety disorders are commonly associated with depression, so sometimes its symptoms are identified and measured in patients with a diagnosis of isolated depression.[45,49,50] However, it is worth noting that, in the present study, the assessment of the degree of anxiety measurement was performed only in patients who had the diagnosis in the medical record, which may have been a reducing factor in the number of participants in the statistical calculations.

Finally, the assessment instruments used to measure symptoms of depression and anxiety disorders are not for diagnostic purposes. The diagnosis of a mental disorder can only be made by a specialist doctor, depending on other complex and subjective factors. Thus, the AFT results on the rates of depression and anxiety disorders reflect the consequences of the intervention of the pharmaceutical service offered in relation to the patients' emotional state, not necessarily reflecting the transformation of their medical diagnosis.

The pharmaceutical intervention did not change the quality of life of patients. Depression and anxiety disorders have a wide impact on all aspects of the patient's life, which is not restricted only to the symptoms of the disease, but also to the greater use of medical services, to decreased productivity at work and impaired quality of life.[51] Studies that used the EQ-5D show that its measurement can be influenced by sex, age group, income, chronic conditions, as well as access to the use of health services.[28,52-54] Thus, the self-perception of the patients in the study may have been influenced by factors that were not impacted by the pharmaceutical intervention, such as social conditions and low monthly income (more than half of the individuals received up to $ 200 dollars, with a large part of this population not purchasing their drugs through the government).

Another indicator is the time factor. The present study was limited to four months of intervention due to the unavailability of auxiliary researchers. However, several studies have observed an improvement in the quality of life of patients only after intervals greater than or equal to six months of interventions.[55-58] One of the few studies that did not follow this trend was that of Wang and colleagues, who observed significant results after eight weeks.[59] Thus, it is suggested that, in order to more accurately assess the impact of pharmaceutical interventions on patients' quality of life, the association of generic and specific quality of life instruments combined with studies that consider longer follow-up times (6 months, 1 year and 2 years).[60,61]

The analysis showed that the improvement in depression levels was altered by the pharmaceutical intervention for the CGPI. The follow-up factor and the number of meetings with health professionals alone show a propensity for self-care, which reflects in results in improving depression.[39,62] In addition, when undergoing PFS, patients had access to information about your medications, as well as health education, factors directly related to health empowerment that provides improvements in self-care.[39,62]

Finally, in view of the variability in methods, designs and tools used to measure the clinical outcomes resulting from the impact of pharmaceutical interventions, it is recommended that future studies are dedicated to investigating, developing and agreeing on standardized measures for monitoring of the patients in this group.[62]

CONCLUSION

Although with limitations, this research collaborates greatly in the literature on the clinical and humanistic outcomes of Pharmacotherapy follow up in patients with depression and anxiety. The study showed that PFS in a short period of time (4 months) improves level of adherence over the course of pharmaceutical consultations. The effect on others clinical parameters (depression and anxiety rates), as well as the humanistic parameters (quality of life) requires further study and suggest more time of intervention (over 6 months). Furthermore, there is a significant improvement in relation to the clinical parameters of depression in patients who receive these pharmaceutical services after their participation in the control group. Recommendations as the pharmacist's training in mental health in CAPS should also be examined with regard to their ability to communicate skills, health education as well as other specific aspects related to the mental health area, such as motivational and / or behavioral interventions. Indeed, public policies to increase the number of pharmaceutical professionals in the CAPS, as well as their mandatory presence in these establishments are also necessary. Thus, this study reinforces the need to establish others solid controlled trials for future comparisons in relation the outcomes using more appropriated measurement instruments (specific in the area), with the period of follow up more than 4 months of duration and comparing the effect of intervention in different times (for example: 6 months, 1 year and 2 years).

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CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

ABBREVIATIONS

CAPS: Psychosocial Care Center; **CG:** Control Group; **IG:** Intervention Group; **PFS:** Pharmacotherapeutic Follow Up.

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