

Clinical case report

Therapeutic adherence and patient management in schizophrenia during outpatient pharmacotherapeutic follow-up: A case report

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SUMMARY

Therapeutic adherence and patient management in schizophrenia during outpatient pharmacotherapeutic follow-up: a case report

Introduction. Social stigmas and the constraining effects of chronic antipsychotic therapy are factors influencing low therapeutic adherence. This study presents a case with a favorable prognosis after seven months of pharmaceutical monitoring at a specialized public outpatient mental health center. **Case report.** The subject is a 29-year-old man diagnosed with schizophrenia (ICD F20.0), who recently experienced a psychotic episode with both positive and negative symptoms. The patient exhibited non-adherence to prescribed medications, including haloperidol, risperidone, nortriptyline, and diazepam, with no reported psychological therapy. Baseline objective data revealed a body mass index below reference values, and borderline blood pressure and capillary blood glucose levels. During consultations, pharmacotherapy-related problems (PRF) were identified, such as low therapeutic adherence, drug interactions, inappropriate administration frequency, inadequate treatment duration, and significant adverse reactions. Pharmaceutical interventions included health education, therapeutic adjustments in collaboration with the prescriber, and referrals to other services. Ultimately, psychometric scales confirmed

medication adherence and improvement in depressive and anxious symptoms. **Discussion.** Pharmacotherapeutic monitoring proved significantly relevant, facilitating not only the detection but also the resolution of PRF while fostering health improvement. **Conclusion.** In this context, it enabled the management of therapeutic efficacy and safety, thereby increasing the patient's prospects for greater social integration.

Keywords: Pharmacotherapeutic monitoring; Therapeutic adherence; Schizophrenia

RESUMEN

Adherencia terapéutica y manejo del paciente con esquizofrenia durante el seguimiento farmacoterapéutico ambulatorio: Reporte de caso

Introducción. Los estigmas sociales y los efectos limitantes de la terapia antipsicótica crónica son factores que influyen en la baja adherencia terapéutica. Este estudio presenta un caso con pronóstico favorable tras siete meses de seguimiento farmacéutico en un centro ambulatorio público especializado en salud mental. **Reporte de un caso.** El sujeto es un hombre de 29 años diagnosticado con esquizofrenia (CIE F20.0), que recientemente experimentó un episodio psicótico con síntomas tanto positivos como negativos. El paciente presentó incumplimiento de los medicamentos prescritos, incluidos haloperidol, risperidona, nortriptilina y diazepam, sin que se informara terapia psicológica. Los datos objetivos basales revelaron un índice de masa corporal por debajo de los valores de referencia, y niveles de presión arterial y glucosa en sangre capilar en el límite. Durante las consultas se identificaron problemas relacionados con la farmacoterapia (FRP), como baja adherencia terapéutica, interacciones medicamentosas, frecuencia de administración inadecuada, duración inadecuada del tratamiento y reacciones adversas significativas. Las intervenciones farmacéuticas incluyeron educación sanitaria, ajustes terapéuticos en colaboración con el prescriptor y derivaciones a otros servicios. Al final, las escalas psicométricas confirmaron la adherencia a la medicación y la mejoría de los síntomas depresivos y ansiosos. **Discusión.** El seguimiento farmacoterapéutico resultó significativamente relevante, facilitando no sólo la detección sino también la resolución de la PRF y fomentando la mejora de la salud. **Conclusión.** En este contexto, permitió gestionar la eficacia y seguridad terapéutica, aumentando así las perspectivas del paciente de una mayor integración social.

Palabras clave: Monitoreo farmacoterapéutico; adherencia terapéutica; Esquizofrenia

RESUMO

Adesão terapêutica e gerenciamento de um paciente com esquizofrenia durante Acompanhamento Farmacoterapêutico ambulatorial: relato de caso

Introdução. Os estigmas sociais e os efeitos limitantes da terapêutica crônica com antipsicóticos são fatores que condicionam a baixa adesão terapêutica. Aqui apresentamos um caso com prognóstico favorável após sete meses de acompanhamento farmacêutico num centro ambulatorial público especializado em saúde mental. **Relato de caso.** Trata-se de um homem, 29 anos, com diagnóstico de esquizofrenia (CID F20.0), em episódio recente de surto psicótico, e evolução de sintomas positivos e negativos. Paciente não aderente à prescrição de haloperidol, risperidona, nortriptilina e diazepam, sem relato de terapia psicológica. Dados objetivos basais revelaram índice de massa corporal abaixo dos valores referenciais e pressão arterial e glicemia capilar limítrofes. Nos atendimentos foi possível identificar problemas relacionados à farmacoterapia (PRF), como baixa adesão terapêutica, interações medicamentosas, frequência de administração e tempo de duração do tratamento inadequados e reações adversas importantes. As intervenções farmacêuticas consistiram em educação em saúde, ajustes terapêuticos em consentimento com prescriptor e encaminhamentos para outros serviços. Ao final, através de escalas psicométricas, foi possível constatar adesão medicamentosa e melhora nos sintomas depressivos e ansiosos. **Discussão.** O acompanhamento farmacoterapêutico demonstrou significativa relevância, uma vez que viabilizou não somente a detecção, mas também a resolução de PRF, ao mesmo tempo em que

fomentou a melhoria da condição de saúde. **Conclusão.** Nesse contexto, possibilitou o manejo da eficácia e segurança terapêutica o que, por sua vez, aumentou as perspectivas do paciente para uma maior integração social.

Palavras-chave: Acompanhamento farmacoterapêutico; Adesão terapêutica; Esquizofrenia.

1. INTRODUCTION

Schizophrenia is a severe and disabling psychotic disorder that affects approximately 1% of the global population, involving emotional, cognitive, and behavioral alterations [1]. It manifests through positive symptoms such as delusions, hallucinations, disorganized speech, and behavior, as well as negative symptoms like affective impoverishment and lack of motivation [2]. These symptoms are associated with social stigmas and prejudices, further hindering patients' socialization and exacerbating factors that contribute to low adherence to therapies [3].

Therapeutic adherence can be defined as the degree to which an individual's behavior, concerning medication usage, aligns with recommendations agreed upon by a healthcare professional [4-6]. According to the World Health Organization, only half of patients with chronic diseases are considered adherent [6]. Factors contributing to low adherence encompass social and economic issues, as well as those related to therapy, the disease, the patient, and healthcare system-related factors [5, 6].

Patients with psychiatric disorders are more prone to not adhere to medication therapy due to a lack of understanding about their clinical condition and pharmacological treatment [7]. This low adherence reduces treatment effectiveness, leading to increased hospitalizations, reduced quality of life, higher healthcare costs, and suicide cases [7]. In the case of schizophrenia, studies reveal a non-adherence rate of 63-74% among patients [8].

From this perspective, patients should be regularly monitored, and clinical pharmacists can play a vital role in patient care by detecting, resolving, and preventing PRF. In this regard, we describe the successful management of a patient with schizophrenia during pharmacotherapeutic monitoring at a specialized public mental health outpatient center in Brazil.

The pharmacotherapeutic monitoring followed the clinical method adapted from the Ministry of Health of Brazil (Figure 1) [9]. In the anamnesis, an adapted pharmaceutical consultation script was employed to conduct an anthropometric evaluation, encompassing measurements such as weight, abdominal circumference, capillary glucose, and body mass index (BMI). Additionally, a scalometric evaluation was performed to measure the severity of anxiety and depression symptoms, as well as medication adherence using the General Anxiety Disorder (GAD-7) [10], Patient Health Questionnaire (PHQ-9) [11], and Medication Adherence Measure (MAT) [12], respectively. The GAD-7 and PHQ-9 have a cutoff value of 10, and a MAT score above 5 classifies the patient as adherent to pharmacological therapy. Patient monitoring occurred remotely through telephone communication and text messages via WhatsApp®.

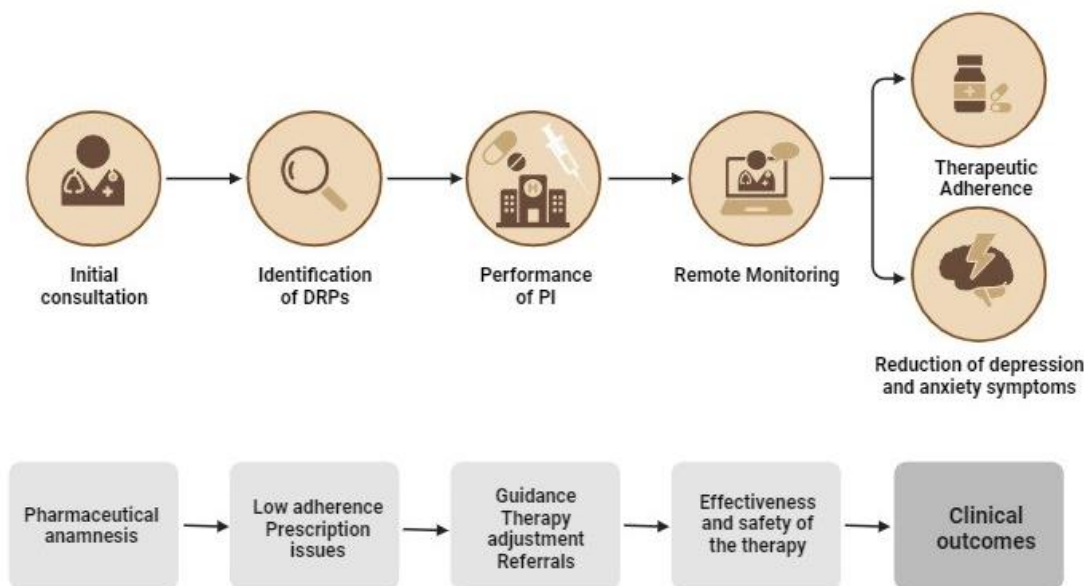


Figure 1: Steps of pharmaceutical care conducted for the management of a patient with schizophrenia. PI: pharmaceutical intervention; DRPs: Drug-Related Problems

2. CASE REPORT

A 29-year-old man, diagnosed with schizophrenia (International Statistical Classification of Diseases and Related Health Problems - ICD F20.0) 12 years ago, began treatment at the Child Psychosocial Care Center at the age of 17, where he remained for five years, and was later transferred to an adult psychiatric outpatient clinic. He commenced pharmaceutical monitoring in February 2022 due to issues of low therapeutic adherence, the need to monitor therapy effectiveness, and a recent history of a psychotic outbreak with aggression and the progression of some positive and negative symptoms. The consultations were attended by the patient's mother, who also served as his caregiver.

Regarding sociodemographic data, the patient reported being single, unemployed, having an incomplete elementary education, and residing with his mother. Concerning lifestyle, he denied alcohol and tobacco use and did not engage in physical exercises. He claimed to have good dietary habits; however, he was currently experiencing food refusal.

During the consultation, the patient's mother reported that since childhood, he had exhibited signs and behaviors suggestive of hallucinations, had difficulties in walking and speaking, experienced bullying at school, and had his first psychotic outbreak at the age of 17. During this period, he frequently ran away from school and home, being considered missing for a period. The patient denied having been diagnosed with other illnesses, and with regards to the family history, he had no knowledge of relatives with mental health issues.

With respect to the current history, approximately a week before the initial appointment, he presented extreme irritability and aggression, to the extent of physically assaulting his mother, who had to call the Mobile Emergency Care Service (SAMU). He was then transported to the psychiatric hospital, where he remained under observation for several hours. At the hospital, he expressed feelings of emotional exhaustion. The patient and his mother were facing financial difficulties, both unemployed, with no income and no support network, as his father had passed away the previous year due to a coronavirus infection.

During the first pharmaceutical consultation, the patient was still recovering from the psychotic outbreak, displaying signs of irritability and occasional aggression. He reported complaints of muscle pain, headaches, insomnia, and blurred vision. Delusional ideas, thinness (BMI 17.54 Kg/m²), and bradykinesia were observed during the consultation. The patient did not have recent laboratory tests and mentioned not having any for over a year. Anthropometric and scalometric data are described in Table 1.

Table 1. Clinical parameters verified during the first and last pharmaceutical consultation and therapeutic goal established according to guidelines.

PARAMETERS	FIRST CONSULTATION	LAST CONSULTATION	GOAL ⁽¹³⁻¹⁵⁾
BP (mmHg)	120X80	120X80	Ideal: 120/80 mmHg
BGT (mg/dL)	104	107	Ideal: Less than 140 mg/dL
Weight (Kg)	61,3	64,6	Ideal: Between 65 and 87 Kg
BMI (Kg/m ²)	17,54	18,50	Ideal: Between 18.5 - 24.9 Kg/m ²
WC (cm)	71	75	Ideal: Less than 94 cm
PHQ-9	21	12	Ideal: Below 10
GAD-7	18	8	Ideal: Below 10
MAT	4,28	5,43	Ideal: Above 5

BP: blood pressure; BGT: blood glucose test; BMI: body mass index; WC: waist circumference; PHQ-9: Patient Health Questionnaire; GAD-7: Generalized Anxiety Disorder; MTA: Measure Therapeutic Adherence.

Regarding medication use, the patient denied self-medication, the use of herbal teas, or other therapeutic options. The details of prescribed medications and dosing regimens assessed at the beginning of pharmaceutical monitoring are described in Figure 2. At this point, polypharmacy with psychotropic drugs, drug interactions, inappropriate dosing frequency of nortriptyline, extended diazepam use, and limiting adverse reactions were identified, such as extrapyramidal effects of antipsychotics in the absence of central anticholinergics.



Figure 2. Medications used continuously at the beginning and end of Pharmaceutical Care.

The caregiver and the patient could not accurately report the exact duration of benzodiazepine use but estimated it to be approximately two to three years. In addition to this, there was observed low adherence to psychotropic therapy, with reports of dose increases, reductions, and frequent omissions by the patient's own decision. The PHQ-9 (21) and GAD-7 (18) scores indicated severe symptoms of depression and anxiety, partly attributed to low medication adherence (MAT 4.53) (Table 1).

The pharmacist carried out interventions to optimize the therapy, suggesting the discontinuation of haloperidol and the continuation of risperidone as monotherapy to the prescribing physician. It was also suggested to initiate the use of biperidene, an anticholinergic drug to reverse extrapyramidal effects, adjust the dosing frequency of nortriptyline to once daily, and gradually discontinue diazepam. Given the medical refusal to discontinue haloperidol, a request was made for a change in the pharmaceutical form from solution to tablets (due to the patient's complaint about the unpleasant taste of the medication). Furthermore, the patient and caregiver were reinforced on the importance of adherence and adherence to the medical prescription.

In addition to interventions for psychotropic therapy adjustment, the pharmacist provided counseling on general health, including the promotion of healthier measures such as physical exercise, a balanced diet, increased water intake, and the provision of referral letters to other services, such as general practitioners, ophthalmology, nutrition, psychology, and social services. A table describing the medications and dosing times, educational material (leaflet on medication adherence), and a list of free psychology services were also created and made available.

To assess the patient's clinical progress, goals were established throughout the monitoring process based on reference standards established in the literature [13-15] (Table 1). During remote monitoring, reports on sleep quality, appetite/food intake, bowel function, signs of persecution, hallucinations, irritability, social interaction, and complaints of adverse reactions were tracked. Remote contact was primarily through the patient's mother, who, in the first two appointments, reported that the patient was very sleepy, tearful, verbalizing that "his life had no importance," with statements such as "feeling very alone, without friends, and without employment".

In the fifth remote appointment, the complaint of sialorrhea was reported. After investigation and confirmation with the patient, it was discovered that he was using haloperidol incorrectly and taking extra doses instead of biperidene. The caregiver and the patient were again educated about the proper use of medications, emphasizing treatment goals.

In the 7th and final consultation, conducted in person, the patient showed substantial improvements in the assessed parameters. He reduced the severity of anxiety and depression symptoms by 55.5% and 42.8%, respectively, as measured by psychometric scales, and displayed a slight weight gain and an increase in abdominal circumference, progressing from underweight to normal weight. He became adherent to pharmacological therapy, demonstrating behavioral improvement, expressing a willingness to share family activities and routines, reducing thoughts of worthlessness, decreasing irritability, aggression, and delusional ideas. Furthermore, he showed an interest in physical activity and no longer experienced sialorrhea.

This case report is part of a study approved by the Ethics Committee of the Federal University of Bahia under CAAE: 28844820.3.0000.8035; #3,978,405/2020.

3. DISCUSSION

This narrative discusses psychotropic therapy adherence and the management of a patient diagnosed with schizophrenia during pharmaceutical monitoring at a psychiatric outpatient clinic. Through this approach, it was possible to identify and address Medication-Related Problems (MRPs), create a care plan that included monitoring, goal setting, and pharmaceutical interventions, primarily related to health education, therapy adjustments, and referrals. Collectively, the coordination of these steps resulted in a positive prognosis for the patient.

The pharmaceutical monitoring lasted for 7 months, including two in-person consultations (initial and final) and four remote monitoring sessions. Of the pharmaceutical interventions carried out, the prescribing physician chose not to discontinue haloperidol. Still, the dosing frequency of risperidone was reduced to twice daily, biperidene was added, diazepam was discontinued, and the dosing frequency of nortriptyline was adjusted to daily use. The therapy at the end of the monitoring period consisted of haloperidol 5 mg/day, risperidone 3 mg twice daily, biperidene 2 mg twice daily, and nortriptyline 25 mg/day (Figure 2).

Monotherapy for schizophrenia is recommended by the Clinical Protocol and Therapeutic Guidelines (PCDT) provided by the Brazilian Ministry of Health [16]. The evidence base for polypharmacy with psychotropic drugs in schizophrenia treatment is generally scarce, but it can be justified in certain clinical situations. However, the risk-benefit should be evaluated, and adverse effects should be carefully monitored [17].

Due to polypharmacy, the patient had the potential for interactions between haloperidol and risperidone, haloperidol and diazepam, and haloperidol and nortriptyline, with a potential risk of anticholinergic effects and central nervous system depression. The appropriate course of action was therapy monitoring and the interventions that were carried out, according to Lexicomp® [18].

The assessment of medication adherence can be ascertained through objective methods, such as clinical outcome measurements, dose counting, pharmacy records, and electronic monitoring of drug administration. These methods have the potential to more accurately measure treatment adherence, but often involve higher costs [19]. On the other hand, subjective methods involve the evaluation of patient behavior and the collection of information about medication use. Typically, these methods utilize questionnaires, which, although subject to biases, allow for tracking and predicting patients' medication usage patterns [19].

In this study, the Medication Adherence Measurement Scale, validated by Borba et al. (2018), was chosen to assess the patient's adherence to mental health treatment [20]. Non-adherence by the patient was identified, and several factors may be related to this lack of adherence, including individual patient characteristics, prescribed medications, and the interaction between the patient and healthcare services [6]. Additionally, the patient's clinical condition may contribute to the lack of interest and discipline in following pharmacological therapy. Consequently, interventions were carried out, involving guidance and counseling on the disease and treatment, as well as the provision of educational materials.

The observed increase in medication adherence following the monitoring period may have been achieved through these interventions, as well as the intention to minimize treatment complexity. Studies support the association between the number of medications and their impact on patient adherence [21-23]. Encouraging the reduction of the number of medications, when possible, not only promotes adherence but also helps reduce adverse effects, lower healthcare costs, and enhance medication rationalization.

In this perspective, the discontinuation of benzodiazepines has been discussed and emphasized in the scientific literature. It is recommended that benzodiazepines be limited to a period of 2 to 4 weeks to avoid the risk of dependence [24]. In contrast to current literature, the patient had been using diazepam for about two to three years without positive results for insomnia and anxiety.

Furthermore, diazepam is not the first-line drug for insomnia because it has a long duration of effect and can lead to metabolite accumulation, increasing the likelihood of interference with REM (Rapid Eye Movement) sleep, rebound drowsiness, dizziness, and falls [25]. In par-

allel with the gradual diazepam withdrawal process, the patient received guidance for participation in psychotherapy sessions, considering that approaches that include psychological interventions offer positive results in the treatment of insomnia [26, 27].

The importance of pharmaceutical activities, including pharmacovigilance, was highlighted in this specific case, where the identification of adverse drug reactions (extrapyramidal reaction and sialorrhea) resulting from haloperidol use was conducted. To determine the likelihood of haloperidol causing these Adverse Drug Reactions (ADRs), the Naranjo Probability Scale was used [28] (Table 2). The score obtained for extrapyramidal reaction was 5 points, indicating this reaction as probable due to haloperidol use, reinforced by the inclusion of biperidene.

Table 2. Naranjo Probability Scale with questions, corresponding point values, and score interpretation adapted for the patient to determine the probability of haloperidol causing extrapyramidal syndrome and sialorrhea.

Questions	Yes	No	Unknown/Not Applicable	Sum of Scores Extrapyramidal syndrome	Sum of Scores Sialorrhea
1. Is the adverse reaction expected for this drug?	+1	0	0	+1	+1
2. Did the reaction occur after drug administration?	+2	-1	0	+2	+2
3. Did the reaction improve when the drug was discontinued?	+1	0	0	0	0
4. Did the reaction reappear upon drug re-administration?	+2	-1	0	0	0
5. Are there alternative causes? (e.g., underlying disease)	-1	+2	0	-1	-1
6. Does the reaction reappear with the introduction of a placebo?	-1	+1	0	0	0
7. Is the plasma concentration at a toxic level?	+1	0	0	0	0
8. Did the reaction increase with a higher dose or decrease with a lower dose?	+1	0	0	+1	+1
9. Has the patient experienced a similar reaction previously with a drug from the same therapeutic class?	+1	0	0	+1	0
10. Was the reaction confirmed by any objective evidence?	+1	0	0	+1	+1
			Total	5	4

Scoring for the Naranjo Algorithm: > 9 = definite; 5-8 = probable; 1-4 = possible; 0 = doubtful.

Regarding sialorrhea, the score was 4 points, suggesting that this could have been triggered by haloperidol use, further reinforced by the disappearance of the reaction after reducing the dose of the suspected medication (Table 2). Studies addressing this topic have emphasized the critical role of pharmacists in managing medication-induced adverse reactions, including their contribution to improved treatment adherence [7, 29, 30].

A significant approach that demonstrated relevance for the patient's successful management was the screening of specific health conditions. The PHQ-9 and GAD-7 scores observed

at the beginning of pharmaceutical monitoring were high, representing severe depression and anxiety, respectively. These comorbidities are found among patients with schizophrenia, with prevalence rates of up to 50% for depression and 38% for anxiety [29]. In these situations, depressive symptoms not only increase the level of suffering of the negative affective state of schizophrenia but are also associated with more frequent psychotic episodes, longer illness duration, substance misuse, poor quality of life, and suicide risk [31, 32].

By using these scales as monitoring tools, it was possible to conduct well-founded interventions and assess the effectiveness of the approaches implemented during the patient's clinical course. Thus, the contribution of the clinical pharmacist proved to be of paramount importance, enabling the recovery of symptoms in a patient diagnosed with schizophrenia after a psychotic outbreak period.

4. CONCLUSION

Pharmaceutical monitoring played a crucial role in reducing symptoms, encouraging adherence, as it addressed the patient's needs while interacting with a multidisciplinary team. In this context, pharmaceutical monitoring not only enabled the monitoring of the effectiveness and safety of pharmacological therapy but also referrals to other clinical healthcare services. Besides the aspects directly related to therapy, the monitoring had a positive impact on the patient's mental health, offering new prospects for social integration. Experiencing improvements in his condition, the patient showed an increased ability to engage in social activities and establish interpersonal connections, ultimately enhancing his quality of life and emotional well-being.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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