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# ACOMPANHAMENTO FARMACOTERAPÊUTICO NO DESFECHO DE PACIENTE COM DOENÇA DE CROHN E MULTIMORBIDADES: RELATO DE CASO

PHARMACOTHERAPEUTIC FOLLOW-UP ON OUTCOMES FOR  
 CROHN'S DISEASE PATIENT WITH MULTIMORBIDITY: CASE REPORT

## SEGUIMIENTO FARMACOTERAPÉUTICO EN EL RESULTADO DEL PACIENTE CON ENFERMEDAD DE CROHN Y MULTIMORBIDADES: RELATO DE CASO

### RESUMO

**Introdução:** O cuidado farmacêutico auxilia o manejo de doenças como diabetes, dislipidemia, hipertensão, insuficiência cardíaca e doenças cardiovasculares, além de reduzir o risco de internações. É necessário compreender o papel e as contribuições dos farmacêuticos para o atendimento ao paciente como o objetivo de utilizar de forma mais eficaz seu conhecimento na atenção básica. **Objetivo:** Avaliar a viabilidade de acompanhamento farmacoterapêutico para pacientes ambulatoriais portadores de doença de Crohn com multimorbidades e implantar esse serviço. **Método:** As informações foram coletadas durante seis meses, em consultas farmacêuticas, complementadas com a revisão do prontuário médico sob autorização. A avaliação de problemas relacionados com medicamentos foi realizada com auxílio de software de triagem de interações e do algoritmo de Naranjo, além do índice de atividade da doença de Crohn utilizado no acompanhamento clínico. **Resultados:** Paciente de 49 anos de idade com DC, diabetes tipo 2, hipertensão e glaucoma foi acompanhada. Identificou-se reação adversa à metformina que resultou em não adesão ao tratamento, com posterior resolução do problema relacionado a medicamento após intervenção com a equipe de saúde e orientação da paciente quanto à alteração na posologia do medicamento. **Conclusão:** O acompanhamento contribuiu para a execução das corretas intervenções: educação quanto ao tratamento, mudança na posologia da terapia antidiabética e identificação de reação adversa a medicamento. O estudo também mostrou a viabilidade para implantação desse serviço farmacêutico no hospital, expandindo o serviço aos demais pacientes com doença inflamatória intestinal.

**Descritores:** Doença de Crohn, Acompanhamento farmacoterapêutico, Intervenções farmacêuticas.

### ABSTRACT

**Background:** Pharmacist care may help the management of disorders such as diabetes, dyslipidemia, hypertension, heart failure, and cardiovascular disease and reduces the risk of all-cause and heart failure hospitalizations. It is necessary to better understand their roles and contributions to patient care to more effectively use the expertise of pharmacists in primary care. **Objectives:** To assess the viability of pharmacotherapeutic follow-up for outpatients with Crohn's disease with multimorbidities and to implement this service. **Methods:** Data were collected during six months in pharmaceutical consultations, also information on medical records with due authorization. Assessment of drug-related problems was done with a drug interaction checker and Naranjo adverse drug reaction probability scale, and also Crohn's disease activity index used during clinical follow-up. **Results:** A 49-year-old female CD patient with type 2 diabetes, hypertension and glaucoma was followed-up. It was identified adverse drug reaction to metformin resulting in noncompliance with therapy, with posterior resolution of this problem after intervention with health team and patient education about change in the drug scheduling. **Conclusions:** Pharmacotherapeutic follow-up contributed to the execution of the right interventions: education regarding therapy, change in the antidiabetic drug scheduling and identification of drug adverse reaction. This case also showed the viability to implant this pharmaceutical service in the hospital, expanding it to other inflammatory bowel disease patients.

**Descriptors:** Crohn disease, Pharmacotherapeutic follow-up, Pharmaceutical interventions.

### RESUMEN

**Introducción:** El cuidado farmacéutico ayuda al manejo de enfermedades como diabetes, dislipidemia, hipertensión, insuficiencia cardíaca y enfermedades cardiovasculares, además de reducir el riesgo de internaciones. Es necesario comprender el papel y las contribuciones de los farmacéuticos para la atención al paciente con el objetivo de utilizar de forma más eficaz su conocimiento en la atención básica. **Objetivo:** Evaluar la viabilidad de seguimiento farmacoterapêutico para pacientes ambulatorios portadores de enfermedad de Crohn con multimorbidades e implantar ese servicio. **Método:** Las informaciones fueron cogidas, y complementadas con la revisión del prontuario médico con la debida autorización. La evaluación de problemas relacionados con medicamentos fue realizada con ayuda de un software de interacciones medicamentosas y de la escala de Naranjo, además del índice de actividad de la enfermedad de Crohn usada en el seguimiento. **Resultados:** Paciente de 49 años de edad con EC, diabetes tipo 2, hipertensión y glaucoma. Fue identificada reacción adversa a metformina resultando en falta de adherencia al tratamiento, con resolución del problema después de la intervención con el equipo de salud y orientación de la paciente cuanto al cambio de la posología del medicamento. **Conclusión:** El seguimiento contribuyó eficazmente a la aplicación de las intervenciones correctas: la educación sobre el tratamiento, el cambio en la dosis de la terapia antidiabética e identificación de reacción adversa al medicamento. El estudio también demostró la factibilidad para la implementación de un servicio de atención farmacéutica en el hospital, con la ampliación del servicio a otros pacientes con enfermedad inflamatoria intestinal.

**Descritores:** Enfermedad de Crohn, Seguimiento Farmacoterapêutico, Intervenciones Farmacêuticas.

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## INTRODUCTION

Crohn's disease (CD) belongs to the group of inflammatory bowel diseases (IBD) and encompasses a multisystem group of disorders with specific clinical and pathological features characterized by focal, asymmetric, transmural, and, occasionally, granulomatous inflammation primarily affecting the gastrointestinal (GI) tract. CD occurs in equal proportion in both genders and its incidence has been growing worldwide in the last decades<sup>1,2</sup>.

Health care professionals entrusted to assist patients with CD must remember that our patients are also unfortunately exposed to other health problems. We are not dealing here with the extraintestinal manifestations of CD, whose importance we recognize and that we have probably learned to manage in a satisfactory way. Neither are we concerned with the adverse effects caused by the diverse therapies applied to our patients, such as osteoporosis or infections in the immunocompromised patients, or with the long-term consequences of the anatomical and physiological alterations induced by the disease. The problem that now demands our attention relates to a series of health problems that do not have a direct relationship to CD as such, but that could alter the diagnosis, presentation and management of the intestinal disease<sup>3</sup>.

Previous studies have shown that collaborative care involving pharmacists may help the management of disorders such as diabetes, dyslipidemia, hypertension, heart failure, and cardiovascular disease and reduces the risk of all-cause and heart failure hospitalizations. To more effectively use the expertise of pharmacists in primary care, it is necessary to better understand their roles and contributions to patient care<sup>4</sup>.

A high degree of noncompliance to treatment, associated to habitual behavior and hard to predict from demographic or clinical factor, was detected in inflammatory bowel disease patients, which suggests the need for investment in patient education regarding medication use<sup>5</sup>. In light of the scarcity of studies with pharmacotherapeutic follow-up to IBD patients, this is a case report, which aimed to analyze the viability of pharmaceutical interventions for a CD outpatient with multimorbidity, as a pilot study for the implantation of a pharmaceutical care service for IBD patients in a University Hospital.

## METHODS

This study was conducted through collaboration between the department of Pharmacy of the Federal University of Piauí (UFPI) and the University Hospital at UFPI. Gastroenterologists referred a CD patient with multimorbidity to the clinical pharmacists to learn about the pharmaceutical care service and consent to service enrollment. To be eligible for this study, patient had to be over 18 years of age and have a diagnosis of CD.

The patient was followed-up by direct pharmaceutical consultations with clinical pharmacists, and had an assessment of medical records, with due authorization, to collect and register information about the diagnosis and pharmacotherapy. The consultations took place at the University Hospital at UFPI, Teresina, Brazil, during a six-month period in 10 consultations. Throughout the intervention period, the clinical pharmacists accessed and reviewed all pertinent physician notes and laboratory test values, detected Drug-related Problems (DRP) and Negative Outcomes associated with Medications (NOMs)<sup>6</sup>, including drug-drug interactions (DDI) using a screening software and adverse drug reactions by the Naranjo probability scale<sup>7</sup>, besides, interacted with prescribers on behalf of the patients as necessary.

Authors obtained ethical approval from both the Ethics Committee at UFPI (no. 510.998/C.A.A.E. 17587913.9.0000.5214) and also the University Hospital. The patient signed an informed consent form after agreeing with the follow-up and the writing and publication of this manuscript.

## RESULTS

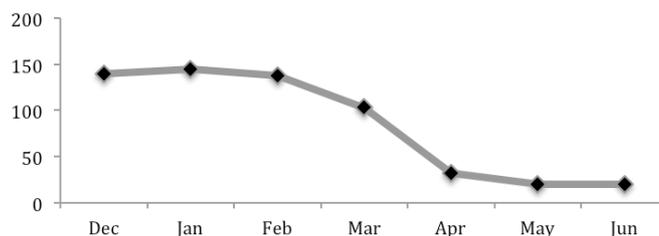
A 49-year-old white female (weight, 51.7 kg; height, 1,54 m; body mass index, 21.8 kg/m<sup>2</sup>) had a 22-year history of CD. She also had history of hypertension, type 2 diabetes and glaucoma. Allergies recorded in medical records prior to follow-up-period included "sulfa drugs", promethazine and ciprofloxacin. The patient reported taking the following medications:

Remicade® (infliximab) 300 mg IV every 8 weeks, azathioprine 50 mg PO ("per os" from latin, through the mouth) three times daily, enalapril 10 mg PO twice daily, Metformin Extended-release (MXR) 500 mg PO twice daily and timolol ophthalmic solution 0.5% once daily. The patient had not had any recent medication changes.

The following NOMs were detected during the follow-up period: untreated health problem (regarding azathioprine and metformin) and quantitative safety (regarding metformin). Patient reported that was not taking azathioprine because was not receiving it from the Pharmacy of Special Medication. No significant DDI were identified during the study according the screening software. Finally, it also was detected a DRP related to non-compliance to antidiabetic therapy due to adverse reactions, reported by the patient as nausea, and abdominal and/or general discomfort only after taking MXR with lunch but not with dinner. Because of that she stopped taking MXR with lunch by her own, taking only 500 mg once-daily with dinner. Given the above information, the Naranjo<sup>7</sup> probability scale was performed by the clinical pharmacists involved in her care, which classified the adverse drug reaction as having a probable (score 6 on the Naranjo scale) association with MXR<sup>7</sup>, after verifying the reported adverse reactions are described for metformin, appeared after beginning of the therapy and reappeared when the drug was re-administered, improved when the drug was discontinued and when the dose was decreased. It was not possible to assess the administration of a placebo neither the detection of drug in blood.

Three hematological/biochemical parameters were altered in the beginning of the follow-up-period: Glycated Hemoglobin (6.8%), Glucose (169 mg/dL) and Gamma-glutamyl Transferase (GGT) (46.4 U/L). The Crohn's Disease Activity Index (CDAI) is an important research tool used to quantify the symptoms of patients with CD. We have used the CDAI in this study to verify whether the disease was in activity or in clinical remission during the follow-up-period. The CDAI variation during the follow-up-period is presented in figure 1.

**Figure 1** - Crohn's Disease Activity Index variation of the patient during the follow-up period. December/2013 - June/2014, Teresina - Piauí.



The following pharmaceutical interventions were necessary to solve the detected NOMs and DRPs: education of the patient regarding treatment and intervention in pharmacological strategy. We requested to her endocrinologist, change in the posology of MXR, switching from twice-daily (500 mg with lunch and dinner) to once-daily (1000 mg with dinner), facilitating the administration, lowering adverse reactions and increasing compliance. The endocrinologist promptly accepted our intervention and changed the posology. The patient also showed better tolerability, as well as compliance, and achieved moderate glycemic control (Glucose 109 mg/dL) after the intervention.

The patient reported that was not receiving azathioprine for at least 3 months. We contacted the Pharmacy of Special Medication for further information about the disruption in the azathioprine supply. Azathioprine was lacking in their stock, but as soon as they solved this problem, the patient was able to receive her medication normally (Table 1).

No problems were identified regarding her treatment for glaucoma and hypertension, but the respective parameters for these disorders were followed-up and her compliance to both treatments was assessed and considered satisfactory.

**Table 1** - Pharmaceutical interventions performed by the Pharmaceutical Care service according to DRP/NOM. December - June/2014, Teresina - Piauí.

DRP or NOM according to Third Consensus of Granada <sup>6</sup>	Description	Pharmaceutical Intervention
Untreated health problem	Patient was not receiving azathioprine from the Pharmacy of Special Medication	Contacted the Pharmacy of Special Medication for information about the disruption in their azathioprine supply
Untreated health problem	Patient was not treating type 2 diabetes correctly	Education of the patient regarding treatment
Quantitative safety	Patient was experiencing adverse effects while taking MXR with lunch	Performed the Naranjo probability scale 7 and requested change in the posology of MXR to her endocrinologist

## DISCUSSION

There are many barriers to medication adherence, not only for patients with CD. The low compliance rate among patients with CD, in a multivariate analysis was not associated with any clinical or demographic factor. These findings indicate the necessity of specific educational interventions and a higher care by healthcare professionals for the use of medications by these patients<sup>5</sup>. In this specific case, the gastroenterologists were not aware about the interruption of treatment with azathioprine, and our intervention helped to clarify the situation, possibly explaining variations on the CDAI during this period.

A study<sup>8</sup> with patients with type 2 diabetes mellitus who received pharmacist-managed diabetes care demonstrated improved quality-of-life measures and met treatment goals more often than patients receiving standard care. Thus, educational materials about diabetes were a useful tool for a better understanding of the disease by the patient and the importance to correctly manage it.

Regarding metformin, it is an established treatment for diabetes with a good safety profile. Its most common adverse effects are GI. These symptoms are generally transient, resolve spontaneously, and can often be avoided by gradual escalation of dosage. However, these GI effects can negatively affect CD patients and clearly need to be avoided. The results of non-compliance to treatment due to these adverse effects can be easily verified with higher-than normal glucose and glycated hemoglobin levels. That is why our intervention regarding MXR dosage was necessary and crucial to improve medication compliance in this case. Other randomized study also showed better results with once-daily extended-release metformin at the same total daily dose<sup>9</sup>.

Studies highlight the paucity of research into interventions to improve outcomes for patients with multimorbidity, with the focus to date being on comorbid conditions or multimorbidity especially in older patients. They indicate that interventions targeted either at specific combinations of common conditions or at specific problems for patients with multiple conditions, may be more effective. Also, compared with usual care plus written education, pharmaceutical care focused on patient evaluation and follow-up in collaboration with physicians improved the achievement of therapeutic goals<sup>10</sup>.

## CONCLUSIONS

This case showed that provision of pharmaceutical care highlights the importance of the pharmacist within the healthcare team in CD management, increasing treatment adherence, patient satisfaction and reducing DRPs and NOMs. Also it was important to perform pharmaceutical interventions to better achieve therapeutic goals for the patient, considering her multimorbidity condition.

A few limitations were detected during the study, as the low applicability of Naranjo scale, impairing the correlation of the adverse reaction to metformin. The evidence level obtained with pharmaceutical interventions does not allow the extrapolation to significative results of effectiveness of the pharmacist.

However, the presented pharmacotherapeutic follow-up enabled the structuring of the service, through the application of forms for data collection, for

pharmaceutical interventions, review of drug interactions and detection of adverse drug reactions, as well as presenting this information to all the healthcare team. Thus, the study also showed the viability for the implantation of a pharmaceutical care service at the university hospital UFPI, expanding the services to other IBD patients.

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## Conflict of Interests

Authors have no conflict of interest to declare.

## Author Contributions

IHFC and RMMR collected the data and take full responsibility for the integrity of the data and the accuracy of the data analysis. All authors: data analysis, study concept and design, interpretation of data, preparation of manuscript.

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