

USE OF PENICILLIN V IN CHILDREN WITH SICKLE CELL DISEASE

UTILIZAÇÃO DE PENICILINA V EM CRIANÇAS COM DOENÇA FALCIFORME

USO DE PENICILINA V EN NIÑOS CON DREPANOCITOSIS

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ABSTRACT

To evaluate the use of the drug penicillin V (Phenoxymethylpenicillin) by pediatric patients with sickle cell disease in an outpatient clinic of a Children's hospital in Fortaleza, through the identification of Medication-Related Problems (DRP) and analysis of the socioeconomic profile. The study took place between March and April 2021, and was carried out using a questionnaire on the use of Penicillin V dispensed in the unit, as a form of storage and dosage. Afterwards, pharmaceutical guidance was provided and an informative folder about the medicine was delivered. 45 caregivers of children with sickle cell disease using penicillin V were interviewed, 86.7% (40) female and 13.3% (5) male. 59 non-conformities were identified regarding the use of the medication. Therefore, it is important to emphasize the importance of adequate dispensing, in order to guarantee the effectiveness and safety of the treatment.

Keywords: *Sickle Cell Disease; Rational use of Medicines; Penicillin V; Pediatrics.*

RESUMO

Avaliar a utilização do medicamento penicilina V (Fenoximetilpenicilina) por pacientes pediátricos com doença falciforme em um ambulatório de um hospital Infantil de Fortaleza, por meio da identificação de Problemas Relacionados a Medicamentos (PRM) e análise do perfil socioeconômico. O estudo ocorreu entre março e abril de 2021 e foi realizado por meio de um questionário sobre utilização de Penicilina V dispensado na unidade, como forma de armazenamento e posologia. Após, foi realizada a orientação farmacêutica e entrega de folder informativo sobre o medicamento. Foram entrevistados 45 cuidadores de crianças com doença falciforme em uso de penicilina V, sendo 86,7% (40) do sexo feminino e 13,3% (5) do sexo masculino. Identificou-se 59 inconformidades com relação ao uso do medicamento. Ressalta-se, portanto, a importância da dispensação adequada, a fim de garantir a efetividade e segurança do tratamento.


Descritores: *Doença Falciforme; Uso racional de Medicamentos; Penicilina V; Pediatria.*


RESUMEN

Evaluar el uso del fármaco penicilina V (Fenoximetilpenicilina) en pacientes pediátricos con anemia falciforme en un ambulatorio de un hospital infantil de Fortaleza, mediante la identificación de Problemas Relacionados con la Medicación (PRM) y el análisis del perfil socioeconómico. El estudio se desarrolló entre marzo y abril de 2021, y se realizó mediante un cuestionario sobre el uso de Penicillin V dispensado en la unidad, como forma de almacenamiento y dosificación. Posteriormente se brindó orientación farmacéutica y se entregó una carpeta informativa sobre el medicamento. Se entrevistó a 45 cuidadores de niños con anemia falciforme que utilizaban penicilina V, 86,7% (40) del sexo femenino y 13,3% (5) del sexo masculino. Se identificaron 59 no conformidades respecto al uso del medicamento. Por lo tanto, es importante resaltar la importancia de una adecuada dosificación, para garantizar la efectividad y seguridad del tratamiento.

Descriptorios: *Enfermedad de Células Falciformes; Uso Racional de Medicamentos; Penicilina V; Pediatría.*

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INTRODUCTION

The sickle cell disease (SCD) is an autosomal recessive genetic condition resulting from defects in the structure of hemoglobin (Hb), whether associated or not with defects in its synthesis¹. It is a group of genetic diseases characterized by a mutated form of hemoglobin - hemoglobin S (HbS), which includes sickle cell anemia (HbSS) and double heterozygosity, meaning the association of HbS with other hemoglobin variants such as HbD and HbC and interactions with thalassemia (HbS/ α thalassemia; HbS/ β + thalassemia; and HbS/ β 0 thalassemia)².

It is estimated that 4% of the Brazilian population carries the sickle cell trait (simple heterozygosity), and that 25,000 to 50,000 individuals have the disease in a homozygous state (SS - sickle cell anemia) or in the condition of compound heterozygotes or double heterozygotes (SC, SE, SD, S Beta TAL - sickle cell disease)³. The hemoglobin S gene is of high frequency throughout the Americas and in Brazil, where it is most common in the Southeast and Northeast regions. In Equatorial Africa, 40% of the population carries the gene, and sickle cell disease affects a prevalence of 2 to 3% of the population⁴.

The root cause of sickle cell disease is a single mutation in the beta-globin gene, which encodes the beta chain of sickle hemoglobin. Sickle hemoglobin tetramers polymerize when deoxygenated, damaging the sickle erythrocyte⁵.

The splenic function is compromised in sickle cell disease, leading to increased risk of bacteremia in affected children, which can progress to sepsis, septic shock, and death. However, changes in clinical practice over the years, such as neonatal screening for early diagnosis of sickle cell disease, prophylactic use of penicillin, and administration of vaccines against *Haemophilus influenzae* and *Streptococcus pneumoniae*, have resulted in a decrease in mortality from sepsis⁶.

Children with sickle cell disease up to 5 years of age should regularly use oral penicillin to prevent infections from certain types of pathogens. Thus, prophylaxis should begin around 2 or 3 months of age, using synthetic penicillin V (phenoxy-methylpenicillin in suspension), with inclusion criteria being the diagnosis of sickle cell disease and the patient's age. Unlike penicillin G, Penicillin V is effective orally because it is resistant to stomach acids. The dosage is 250mg/day for children up to 3 years old and 500mg/day for children from 3 to 5 years old, with doses administered every 12 hours³.

However, besides access to medication, it is also necessary for it to be used properly to ensure its effectiveness and safety. The WHO states that proper medication consumption occurs when patients receive medications appropriate to their health condition, in doses suitable for their individual needs, for an adequate period of time, and at the lowest possible cost for them and their community⁷.

The pharmacist plays a crucial role in reducing medication-related issues⁸. It is the pharmacist's responsibility to provide pharmaceutical guidance aimed at clarifying to the patient the benefit-risk relationship, conservation, and use of drugs and medications inherent to therapy, as well as their drug interactions and the importance of their correct handling. Additionally, pharmacists dispense medications to ensure the efficacy and safety of the prescribed therapy, while observing technical and legal aspects of

prescriptions⁹. Through dispensing services, it is possible to prevent, identify, and resolve medication-related problems¹⁰.

The concept of Medication-Related Problems originated in 1998 in Spain during the I Consensus of Granada. Years later, the concept was revised during the II Consensus of Granada in 2002, and the III Consensus of Granada in 2007. During the latter, Medication-Related Problems was defined as situations that, during the medication use process, cause or may cause the emergence of a negative outcome associated with the medication.¹¹.

The list of Medication-Related Problems (MRP), as per the III Consensus of Granada, includes: medication administered incorrectly; personal characteristics; inadequate storage; contraindication; incorrect dose, dosing regimen, and/or duration; duplicity; dispensing errors; prescription errors; non-compliance; interactions; other health problems affecting treatment; probability of adverse effects; insufficiently treated health problems; others¹¹.

Thus, this study aimed to evaluate the use of the medication penicillin V (Phenoxymethylpenicillin) by pediatric patients with sickle cell disease at an outpatient clinic of a children's hospital in Fortaleza, through the identification of Medication-Related Problems (MRP) and analysis of the socioeconomic profile.

METHODS

This is a descriptive and prospective study, based on evaluation through the application of a questionnaire to caregivers of patients using phenoxymethylpenicillin. It was conducted during the months of March and April 2021, at the outpatient pharmacy of a children's hospital. Data collection was performed by the pharmacist of the service and a pharmacy student who was completing an internship in the department.

The study population of interest comprises a total of 97 individuals, corresponding to the number of patients registered in the Hemovida Web Hemoglobinopathies System of the Ministry of Health, aimed at accessing phenoxymethylpenicillin. All patients are diagnosed with sickle cell disease and are up to five years old. Among them, 44 were female and 53 were male. Regarding the distribution of hemoglobinopathies within the studied population, Hemoglobinopathy SS was present in 72.2% of cases, Hemoglobinopathy SC in 16.5%, and other hemoglobinopathies in 11.3%.

The sample was selected using a convenience sampling method, meaning that interviews were conducted based on the caregivers' demand at the outpatient pharmacy. Data collection was carried out immediately after medication dispensation, through a questionnaire that addressed both sociodemographic and pharmacotherapeutic issues. The aim was to understand the profile of the studied population and the level of knowledge this population has about the treatment, which directly influences the success of pharmacotherapy.

The sociodemographic form aimed to delineate the social profile of both the patient and the caregiver, observing variables such as income, education level, age, employment status, and place of residence. Additionally, it sought to investigate whether these factors were related to the correct management of the medication and the degree of knowledge about pharmacotherapy. About the pharmacotherapeutic form, its objective was to assess

the caregivers' knowledge regarding pharmacotherapy and how this knowledge was applied in the proper management of the medication.

The medication-related problems assessed in this study were selected from the list established by the III Consensus of Granada, with the criterion of suitability for the studied population and the available tools for evaluation, these included: insufficiently treated health problems, inadequate storage, incorrect dose, dosing regimen, and/or duration, and personal characteristics, which in the case of the medication in question, implies the need for preparation and reconstitution.

Additionally, caregivers' knowledge regarding the purpose of treatment and the possibility of medication wastage due to improper disposal when it is still suitable for use was also evaluated, as shown in Table 1.

Table 1 – Adopted criteria for investigation of nonconformities regarding the use of phenoxymethylpenicillin

Classification of MRP according to the III Consensus of Granada	Adopted criteria
Health problem insufficiently treated	When the caregiver, for any reason, does not adhere to the use of the prescribed drug.
Inadequate storage	When the drug, after preparation, is stored in an inappropriate place, taking into account temperature and direct incidence of sunlight; or even when the drug is maintained after opened for a longer time than by the manufacturer.
Medicine waste	When the caregiver discards part of the medication because they believe it is expired after being opened, when in fact it is still within the manufacturer's established timeframe, which can result in a shortage of medication for the following days.
Dose, dosage scheme and/or inadequate duration	When the caregiver manages a different dose of the prescribed dose; or when caregiver administers the drug to the patient at different intervals from the prescribed.
Nonconformity regarding the purpose	When the caregiver is unaware of the purpose of treatment, which may compromise adherence.
Personal characteristics of the drug (need for reconstitution).	When the drug is improperly reconstituted, taking into account the amount and quality of the water added to the bottle and the temperature of the water.

Source: Own authorship.

The research respected all ethical aspects, following Resolution No. 466/12, and received approval from the Hospital Research Ethics Committee, under opinion No. 4,577,959.

RESULTS

Each interview lasted approximately 15 minutes. The information obtained was stored for subsequent statistical analysis in a Microsoft Excel 2010 spreadsheet. In cases where Medication-Related Problems (MRP) were identified, pharmaceutical guidance was provided to the caregiver regarding the correct conduct, and a folder containing information about phenoxymethylpenicillin was provided. This information included correct preparation, stability time after opening, storage location after opening, and possible adverse reactions.

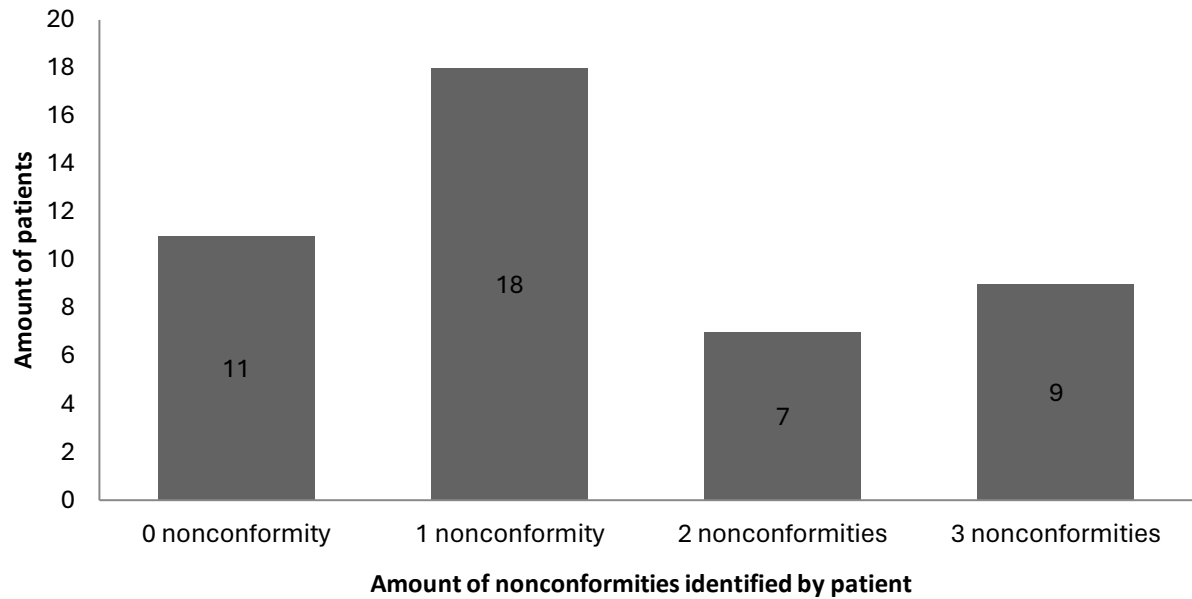
A total of 45 caregivers were interviewed, among whom 86.7% (40) were female and 13.3% (5) were male. The majority of caregivers were the patients' mothers, accounting for 80% of the respondents, followed by fathers (11.1%), grandparents (8.9%), and others (2.2%). The average age of the caregivers was 31.1 years, with the majority (52.3%) being 30 years old or younger, 42.1% between 30 and 40 years old, and 5.2% above 40 years old. Regarding family income, among those who responded to the optional question (21 out of 45), more than half (52.4%) earned up to one minimum wage. In terms of education, 60% had completed high school, and 35% had completed only elementary school. 85% of the respondents are currently unemployed. Table 2 below shows the sociodemographic profile of the research participants.

TABLE 2 - Sociodemographic characteristics of caregivers of patients with sickle cell disease using phenoxymethylpenicillin

Characteristics	Frequency
Sex (total of 45 interviewees)	F: 86.7% (39) M: 13.3% (6)
Age (total of 19 interviewees)	Under 20 years old: 0% (0) Between 21 and 30 years old: 52.6% (10) Between 31 and 40 years old : 42.1% (8) Older than 40 years old: 5.3% (1)
Kinship with the patient (total of 45 interviewees)	Mother: 80% (36) Father: 8.9% (4) Grandparent: 6.7% (3) Others: 4.4% (2)
Education (total of 20 interviewees)	Did not study: 1 (5%) Until elementary school: 35% (7) Until high school: 60% (12)
Provenance (total of 21 interviewees)	The city of Fortaleza: 28.6% (6) Interior and metropolitan region : 71.4% (15)
Family income (total of 21 interviewees)	< 1 minimum wage: 52.4% (11) 1-2 minimum wages: 28,6% (6) 3-4 minimum wages: 19% (4) More the 4 minimum wages: 0% (0)
Current work situation (total of 20 interviewees)	Employed: 15% (3) Unemployed: 85% (7)

Source: Own authorship.

Regarding pharmacotherapy, it was found that the majority of patients had at least 1 nonconformity regarding the use of phenoxymethylpenicillin (75.6%), with a total of 59 nonconformities observed in the medication's use. The graph below depicts the number of nonconformities found per patient.

Graph 1 - Number of nonconformities per interviewees

Source: Own authorship.

The majority of nonconformities were related to the knowledge about the purpose of the medication, accounting for 62.2% of the respondents. Following that, the most frequent nonconformities were regarding inadequate storage, accounting for 28.9% of the respondents.

Table 3 will provide data on the quantitative of each nonconformity.

TABLE 3 – Number of interviewees for each nonconformity		
Nonconformity	Interviewees percentage	Absolute number
Health problem insufficiently treated	2.2%	1
Inadequate storage	28.9%	13
Medicine waste	4.4%	2
Nonconformity regarding the dose, dosage scheme and/or inadequate duration	17.7%	8
Nonconformity regarding knowledge about purpose	62.2%	28
Personal characteristics of the drug (need for reconstitution)	15.6%	7
Total number of nonconformities found	-	59

Source: Own authorship.

CONCLUSION

Adherence to treatment, as well as the correct use of medications, are crucial factors for therapeutic success^{12,13}. A recent study that analyzed patients' knowledge after medical consultation and dispensation found that there were better outcomes regarding patients' knowledge about the correct usage and general aspects of prescribed medications after dispensation¹⁴. From the data obtained in this study, we can observe that a large number of caregivers of children with Sickle Cell Disease lacked knowledge about the purpose and correct use of phenoxymethylpenicillin. This deficiency in knowledge may, to some extent, compromise the expected outcomes of medication use.

A good dispensing process is necessary for patients to make proper use of medications. Lack of experience in pediatric pharmacy, among other factors, is one of the challenges faced in maintaining good dispensing practices for children¹⁵. The role of the clinical pharmacist is crucial in patient pharmacotherapy care¹⁶. In efforts to improve dispensing effectiveness, the brochure utilized as a visual and memory aid was well-received by all participants in this study.

CONCLUSION

The results of this study revealed that the majority of respondents were women with income of up to one minimum wage or unemployed. This may suggest a hypothesis of a relationship between precarious socioeconomic conditions and misinformation regarding the proper use of medications, considering the number of nonconformities related to the use of Penicillin V identified in this study.

Therefore, the presence of a pharmacist is reinforced as essential for this population, aiming to ensure effective dispensing and promoting rational medication use. This study provides insight into the relationship between the studied population and the medication in question, allowing the identification of issues that may interfere with treatment quality.

The limitations of this study include the short investigation period and the sample size, which hinder more assertive deductions regarding the subject. Therefore, it becomes essential to conduct new studies to evaluate the correct use of the medication(s) used by this population so that new strategies can be implemented to address issues in medication therapy.

REFERENCES

1. Organization WH. The selection and use of essential medicines : report of the WHO Expert Committee, 2005 [internet]. Geneva, Switzerland; 2005. [Acesso em: 21 fev. 2024]. Disponível em: <https://iris.who.int/handle/10665/43292>.
2. Alves e Luna AC, Lopes CMI, Oliveira JCS, Menezes VA. Sickle cell disease: knowledge and clinical practice of dental surgeons at Family Health Units. *Rev Gaúch Odontol*. 2020;68:e20200013. Disponível em: <http://dx.doi.org/10.1590/1981-863720200001320180027>.
3. Saúde Md. Protocolo clínico e diretrizes terapêuticas da doença falciforme [internet]. Brasil; 2018. [Acesso em: 21 fev. 2024]. Disponível em: https://www.gov.br/conitec/pt-br/midias/protocolos/pcdt_doencafalciforme_2018-1.pdf.
4. Soares LF, Lima EM, Silva JA, Fernandes SS, Silva KM, Lins SP, Damasceno BP, Verde RM, Gonçalves MD. Prevalência de hemoglobinas variantes em comunidades quilombolas no estado do Piauí, Brasil. *Cienc Amp Saude Coletiva* [Internet]. Nov 2017 [citado 23 fev 2024];22(11):3773-80. Disponível em: <https://doi.org/10.1590/1413-812320172211.04392016>.
5. Steinberg MH. Sickle Cell Anemia, the First Molecular Disease: Overview of Molecular Etiology, Pathophysiology, and Therapeutic Approaches. *Sci World J* [Internet]. 2008 [citado 23 fev 2024];8:1295-324. Disponível em: <https://doi.org/10.1100/tsw.2008.157>.
6. Baskin MN, Goh XL, Heeney MM, Harper MB. Bacteremia Risk and Outpatient Management of Febrile Patients With Sickle Cell Disease. *PEDIATRICS* [Internet]. 13 maio 2013 [citado 24 fev 2024];131(6):1035-41. Disponível em: <https://doi.org/10.1542/peds.2012-2139>.
7. Conference of Experts on the Rational Use of Drugs (1985 : Nairobi). (1987). The rational use of drugs: report of the Conference of Experts, Nairobi, 25-29 November 1985. World Health Organization. Disponível em: <https://iris.who.int/handle/10665/37174>.

8. Melo DO, Castro LL. A contribuição do farmacêutico para a promoção do acesso e uso racional de medicamentos essenciais no SUS. *Cienc Amp Saude Coletiva* [Internet]. Jan 2017 [citado 24 fev 2024];22(1):235-44. Disponível em: <https://doi.org/10.1590/1413-81232017221.16202015>.
9. Lei Nº 13.021 DE 08 DE AGOSTO DE 2014, Lei n.º 13021, 8 ago 2014 (Brasil).
10. Galato D, Alano GM, Trauthman SC, Vieira AC. A dispensação de medicamentos: uma reflexão sobre o processo para prevenção, identificação e resolução de problemas relacionados à farmacoterapia. *Rev Bras Cienc Farm* [Internet]. Set 2008 [citado 24 fev 2024];44(3). Disponível em: <https://doi.org/10.1590/s1516-93322008000300017>.
11. Farmacéutica GD. Tercer Consenso de Granada sobre Problemas Relacionados con Medicamentos (PRM) y Resultados Negativos asociados a la Medicación (RNM). *Ars Pharm*. 2007;48(1):5-17.
12. Modé CL. Atenção farmacêutica em pacientes hipertensos: um estudo piloto. 2011. 51 f. [Trabalho de conclusão de curso]. Faculdade de Ciências Farmacêuticas, Universidade Estadual Paulista; 2011. 51 p.
13. Daly CJ, Verrall K, Jacobs DM. Impact of Community Pharmacist Interventions with Managed Care to Improve Medication Adherence. *J Pharm Pract* [Internet]. 30 dez 2019 [citado 24 fev 2024];089719001989650. Disponível em: <https://doi.org/10.1177/0897190019896505>.
14. Oenning D, Oliveira BV, Blatt CR. Conhecimento dos pacientes sobre os medicamentos prescritos após consulta médica e dispensação. *Cienc Amp Saude Coletiva* [Internet]. Jul 2011 [citado 24 fev 2024];16(7):3277-83. Disponível em: <https://doi.org/10.1590/s1413-81232011000800027>.
15. Nadeshkumar A, Sathiadas G, Sri Ranganathan S. Rational dispensing of oral dosage forms of medicines to children at a teaching hospital in Sri Lanka. *BMC Health Serv Res* [Internet]. 6 maio 2020 [citado 24 fev 2024];20(1). Disponível em: <https://doi.org/10.1186/s12913-020-05246-x>.
16. Pires Grangeiro AK, de Oliveira Belém M. O papel do farmacêutico clínico na unidade de terapia intensiva adulto. *Cad ESP* [Internet]. 30 dez 2022 [citado 24 fev 2024];16(4):75-83. Disponível em: <https://doi.org/10.54620/cadesp.v16i4.798>.