Brief Report

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Evaluation of pharmacotherapy in sickle cell disease in an Afro-Colombian community: A cross-sectional analytical study in San Basilio de Palenque, Bolívar

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SUMMARY: Sickle cell disease (SCD) is an orphan and extremely rare condition in Colombia and worldwide. However, a significant number of cases were identified in San Basilio de Palenque, Bolívar, enabling a pharmacotherapeutic follow-up study. This population represents a genetic bottleneck with limited admixture, making it crucial for further genetic and clinical research. Despite being largely unexplored due to lack of awareness and state neglect, SCD persists in this community. This study aimed to characterize and follow up pharmacotherapeutically on patients with SCD and traits. An observational, cross-sectional analytical study was conducted in 20 patients, assessing sociodemographic factors, pharmacotherapeutic follow-up, and pharmaceutical interventions. Results showed that 75% of patients were female, and 40% were homozygous. The most commonly used medications included folic acid, analgesics (paracetamol, tramadol, naproxen, codeine, ibuprofen, morphine), L-glutamine, and enalapril. Pain from vaso-occlusive crises and hemolytic episodes was the main reason for analgesic use. Notably, 62% of homozygous patients were not receiving baseline treatment with hydroxycarbamide, increasing their risk of complications. Addressing this gap through pharmaceutical interventions was one of the study's key contributions. In conclusion, this research highlights the need for a multidisciplinary approach to optimize treatment and improve the quality of life of affected patients. Given its genetic significance, San Basilio de Palenque represents a unique setting for further studies on SCD.

Keywords: hemoglobinopathy, sickle cell disease, pharmacotherapeutic follow-up, mutation, pharmaceutical intervention

1. Introduction

Sickle cell disease (SCD) is an orphan and extremely rare condition worldwide that originated in Africa as a protective mechanism to counteract malaria (*1,2*). Recognized as a public health problem by the World Health Organization since 2008, worldwide there are 300,000 children with hemoglobinopathies where 83% present SCD. In Colombia, it affects 20,000 children each year, especially in regions such as Bolivar, Valle del Cauca and Atlántico (*2*). The migration of the population from Africa to northern Colombia brought with it the genetic inheritance of SCD, being San Basilio de Palenque the place where part of that population settled. Currently there are about 3,500 people, of which it has not been determined exactly how many present both the condition and the trait. This information should be managed by regulatory entities such as the district administrative department of health (DADIS). However, the lack of knowledge contributes to the fact that SCD continues to grow along with the population due to the lack of diagnostics and timely education in the community; through pharmaceutical care, The sociodemographic characterization of the population was initially carried out and subsequently the pharmacotherapeutic follow-up of patients was carried out through the DADER method, which allows to have a pharmaceutical report that includes the patient's history, prescribed medications, clinical information, therapeutic results and recommendations to the patient; this allows to follow up any patient, in any health care setting, in a systematized, continuous and documented manner (*3,4*).

Considering the above, this study aimed to characterize and conduct a pharmacotherapeutic follow-up of patients with SCD in the town of San Basilio de Palenque (Bolívar), given their unique genetic heritage. The significant presence of SCD in this rural Colombian population makes it a compelling subject for the

scientific community and local authorities. Additionally, this study sought to implement adherence strategies to optimize treatment and improve patients' quality of life.

2. Patients and Methods

The low prevalence of SCD, a rare disease, significantly limited the sample size and made patient selection difficult. To address this limitation, we opted for non-probabilistic convenience sampling in the corregimiento of San Basilio de Palenque. The inclusion criteria focused on patients diagnosed with SCD and sickle cell trait, while those who did not give informed consent or had other hemoglobinopathies were excluded. The research was divided into three stages.

2.1. Stage 1: Patient selection and sociodemographic characterization

The first stage was the sociodemographic characterization of the population of the corregimiento of San Basilio de Palenque. Once the diagnosis of hemoglobinopathy was confirmed, an informed consent form was issued, which allowed patients to participate or not in the study; in the case of pediatric patients, their parents or guardians were responsible.

Those who agreed to participate in the study were given a comprehensive survey. This survey included a range of questions, from basic demographic information to more specific queries about the participant's condition and treatment. The thoroughness of the survey ensured that we gathered a comprehensive set of data for our study.

Patients with sickle cell traits were included in the genetic diagnosis, because they presented symptoms similar to homozygous patients, and it was decided to carry out pharmacotherapeutic follow-up.

2.2. Stage 2: Pharmacotherapeutic follow-up

This service was approached comprehensively, addressing both patients' health problems and their prescribed medications, with a focus on assessing the necessity, effectiveness, and safety of pharmacotherapy. Consequently, the next phase of this study involved presenting and offering pharmaceutical care to the characterized population using the DADER pharmacotherapeutic follow-up method, a validated approach developed at the University of Granada to identify, prevent, and resolve drug-related problems and negative outcomes associated with medication (*5*). Patients were given the option to accept or decline participation. Once enrolled, the first interview was scheduled to establish their pharmacotherapeutic history, with clinical documentation playing a crucial role. This process provided insight into the management of SCD by hematologists overseeing patient care. Following this, each clinical case was analyzed to evaluate the patient's current condition, identify specific needs, and address both medication-related and non-medication-related problems.

2.3. Stage 3: Pharmaceutical interventions

Upon completion of the data collection stage, a multidisciplinary group composed of hematologists, psychologists, some DADIS officials, and pharmaceutical chemists established interventions according to the criteria of each professional. These interventions were executed through a strategic action plan. Subsequent interviews confirmed that this approach significantly improved the quality of life of the patients.

2.4. Ethical considerations

The study adhered to strict confidentiality and ethical guidelines. Participants provided informed consent and were assured of minimal risk. Results were handled confidentially and used solely for research purposes.

All guidelines as per declaration of Helsinki and good clinical practice guidelines were followed

2.5. Statistical analysis

After completing the data collection stage, a database was created using Microsoft Excel to carry out descriptive statistics through tabulations and graphs. Subsequently, the Python programming language was used with the Matplotlib tool to generate Figure 1 and Figure 2.

3. Results and Discussion

In Colombia, about 20,000 children are born annually with SCD which highlights the importance of studies such as this one, especially in specific populations such as that of the township of San Basilio de Palenque, Bolivar due to its genetic inheritance. The lack of accurate data on the prevalence of SCD in Colombia by the governmental entities in charge of generating case reports represents a significant obstacle for the implementation of effective public policies aimed at this population. This lack of information, added to the generalized lack of knowledge about the condition on the part of patients increases the risk that numerous cases go undiagnosed and unreported to the health system. A literature study conducted in 2017 suggests that the prevalence of sickle cell hemoglobinopathy could reach 12% in Afro-Colombian communities (*3*).

Table 1 shows the sociodemographic characteristics of the patients included in the study, with a total of 20 people during the period 2022-2023, of which 75% were female and 25% male, given that SCD is a genetic disease determined by a specific mutation and not by factors related to sex or gender. The distribution found

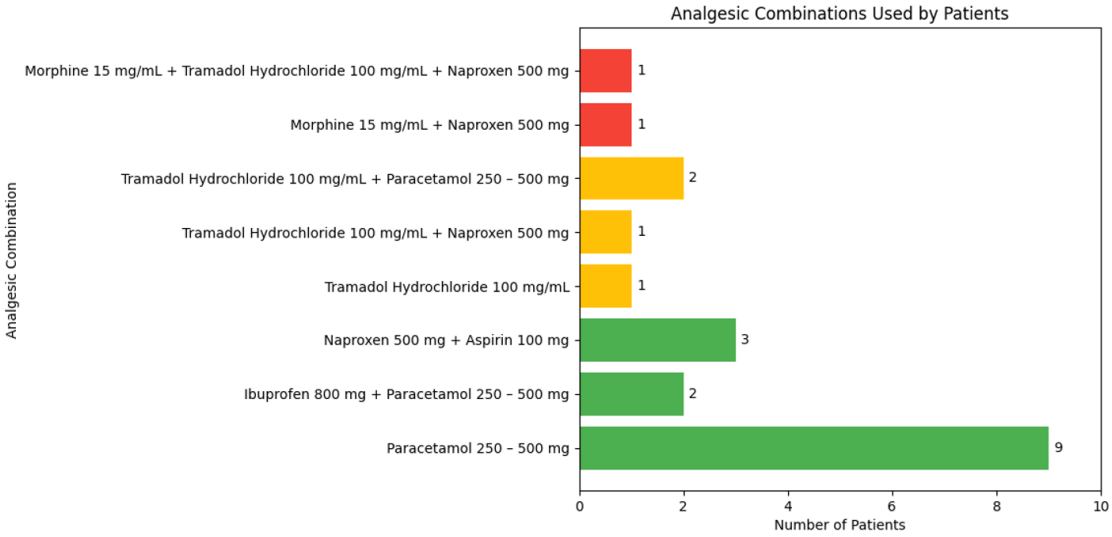

Figure 1. Medications used by patients to attenuate pain during crises. Green: Non-opioid analgesics (NSAID), Yellow: Weak opioids and NSAID and Red: Strong opioid and NSAID.

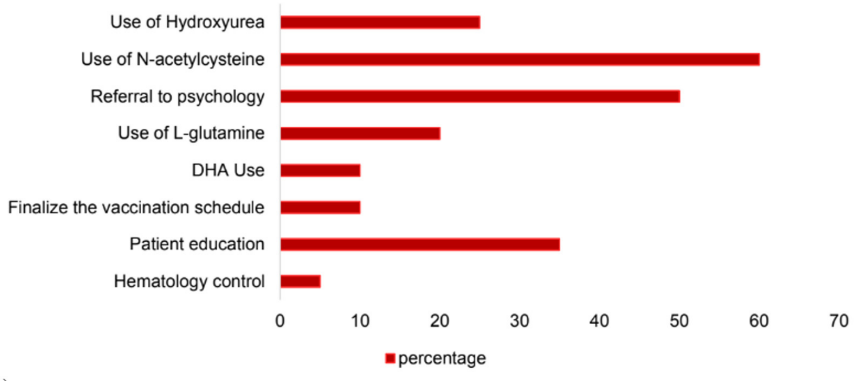

Figure 2. Multidisciplinary interventions implemented in the population of San Basilio de Palenque, Bolivar.

in this sample is random, as for the characteristics of hemoglobinopathy 40% were homozygous, that is, they presented the mutation in both alleles and 60% were heterozygous, mutation in one allele. Among the common diseases in the home it was found that 100% of patients have had respiratory complications and 80% gastrointestinal problems.

According to the results found, for the youngest patients, still in kindergarten (10% of the total), information was prioritized for the caregivers since they are the ones who spend the most time with them. In the case of children in primary school (30%) and high school (50%), visual resources such as animated diagrams were used to explain the disease clearly and concisely, as well as the preventive measures to follow to avoid episodes of crisis through simple steps such as keeping hydrated, constant hand washing, avoiding exposure to the sun, avoiding exposure to high temperatures, reducing physical activity in the event of changes such as changes in the color of the cornea to a more yellow color or the skin, notifying a responsible adult in the event of painful abdominal palpation or swelling of the upper and lower limbs, and emphasizing the importance of adherence to pharmacological treatment (*6*).

On the other hand, the DADER method categorizes DRPs into three main groups: unmet needs, efficacy and safety problems. Table 2 shows the DRPs found in the community under study, where 62% of homozygous patients at the beginning of the study did not receive the basic drug, and as regards to safety, it was found that they consumed painkillers indiscriminately to cope with the discomfort of crisis episodes and comorbidities.

Considering the above, it is necessary to take into account the treatment guidelines for SCD established by the Spanish Society of Hematology and Hemotherapy, where the basic treatment is Hydroxyurea 500 mg (HU). This is an antineoplastic drug that inhibits the M2 subunit of ribonucleotide reductase, blocking DNA synthesis and restructuring. It is used as a pharmacological inducer of fetal hemoglobin in SCD patients, inducing the synthesis of nitric oxide (NOS) and decreasing arginase in red blood cells and plasma,

leading to an increase in nitric oxide production, which is important for vasodilation. Also included is Folic Acid 1 or 5 mg, with the aim of stimulating the bone marrow to produce red blood cells at a faster rate, as these cells have a short lifespan in SCD (*7*).

Table 3 refers to the main reasons for which patients are admitted to hospital centers. In this case, the frequency of crises at the beginning of the study was five, and at the end, two. For headaches, six patients presented pain at the beginning and two at the end. To visualize significant changes, the patient should structure new habits in their lifestyle.

Upon obtaining these results, pain management was analyzed using the World Health Organization analgesic ladder, which consists of three steps, each tailored to different levels of pain intensity. The first step involves the use of non-opioid analgesics, such as paracetamol, for the relief of mild to moderate pain. When pain intensifies, the ladder recommends the second step, which combines weak opioids with other medications for improved control. Finally, for severe pain, strong opioids such as morphine are used.

As shown in Figure 1, patients from the district of San Basilio de Palenque were identified at the first step of the analgesic ladder; eight patients were taking paracetamol in 250 mg and 500 mg doses as their primary analgesic, either alone or in combination with 600 mg of ibuprofen. At the next level, three patients were identified as using weak opioids, such as tramadol hydrochloride 100 mg/mL, often in combination with other analgesics such as naproxen 500 mg or paracetamol 250 mg and 500 mg.

Figure 1 illustrates the use of analgesics and their combinations, ranging from the minimum level, such as the use of paracetamol 250 mg, to the highest combinations involving strong opioids, such as morphine 15 mg/mL + tramadol hydrochloride 100 mg/mL + naproxen 500 mg.

The above indicates that the patients used the three analgesic options allowed according to the intensity of the pain. For this reason, a specialized pharmaceutical professional in the field of pharmaceutical care was invited to guide the patients and caregivers on the proper use of analgesics and the potential consequences of their prolonged use over time, as in the case of opioids, which initially cause tolerance but over time can lead to dependence. Similarly, the prolonged use of paracetamol can cause liver damage because it undergoes extensive hepatic metabolism through three main pathways: conjugation with sulfate and glucuronic acid, and oxidation mediated by cytochrome P450 2E1. The drug follows the conjugation pathways, generating inactive metabolites that are excreted through the renal route. However, a small fraction is transformed into N-acetyl-p-benzoquinone imine (NAPQI), a hepatotoxic reactive metabolite, which causes liver damage (*8*).

Figure 2 shows the most frequent pharmacological interventions, with a high percentage of patients receiving hydroxyurea and N-acetylcysteine. The use

Table 1. Sociodemographic characterization of patients in San Basilio de Palenque, Bolivar

Characteristics	Percentage
Sex	
Female	75%
Male	25%
Age	
2–30	60%
31–58	40%
Characteristics of hemoglobinopathy	
Homozygous	40%
Heterozygotes	60%
Level of schooling	
Nursery	10%
Primary	30%
High school	50%
Technologist	10%
Common diseases	
Gastrointestinal	80%
Respiratory	100%

Table 2. Identification of problems related to medications in patients included in the study in the town of San Basilio de Palenque, Bolivar

PRM ID	Description
NEED (Untreated health problems)	62% of homozygous patients (mutation in two alleles) were not receiving Hydroxycarbamide 500 mg base treatment at the beginning of the study.
SAFETY (Self-medication)	65% of patients used paracetamol 250 and 500 mg consistently, 15% used weak opioid analgesics such as tramadol hydrochloride 100 mg/mL, and 15% used potent opioids such as morphine 15 mg/mL.

Table 3. Frequency of crises and headaches in patients immersed in the study at the beginning and at the end of the study

Measure	Start of the Study		End of the Study	
Frequency of Crisis	With Crisis	No Crisis	With Crisis	No Crisis
	5	3	2	6
Headache	In Pain	Painless	In Pain	Painless
	6	6	2	10

of L-glutamine was also significant, although to a lesser extent. These data suggest that pharmacological management is a mainstay in the treatment of this condition.

Pharmacotherapeutic monitoring allowed an assessment of the individual status of each patient. Such assessment was communicated to other health professionals; and this allowed for improving the quality of life of patients. In Figure 2, such multidisciplinary interventions are presented, as is the case of the hematology team which authorized access to Hydroxycarbamide 500 mg to patients adjusting the dose according to weight. HU is a key drug to prevent vaso-occlusive crises in patients with SCD. A 2009 study showed that, after implementing HU in 30 patients, mainly men, the number of transfusions and crises was significantly reduced, thus decreasing hospitalizations (*9*).

Complementary treatments for SCD include antioxidants. L-glutamine is an essential amino acid for the synthesis of NAD, a coenzyme involved in oxide reduction reactions in the body. When oxidative stress occurs in red blood cells, L-glutamine consumption increases to maintain glutathione levels (*10*). In the case of N-acetyl cysteine, it is transformed into L-cysteine, which in turn increases glutathione and decreases the oxidative stress of the red blood cell by bibliographic documentation (*10*).

Patients with SCD are more vulnerable to bacterial and viral infections due to a condition called functional asplenia, which is the loss of spleen function, affecting their ability to fight infections. In addition, they have alterations in other parts of their immune system. For this reason, the infections they develop are usually more severe and require more aggressive treatment. To prevent these infections, it is recommended that all patients be vaccinated and antibiotics such as penicillin administered, especially to children under five years of age (*11*). Under this premise, the pediatric patients in this study were vaccinated through the support of territorial entities such as DADIS and companies that financed the study.

Based on the observed results and the physiology of SCD, it was considered necessary to take into account the process of accelerated red blood cell production, known as erythropoiesis, which increases the body's demand for folate. To compensate for this deficiency and reduce anemia-related symptoms, patients with SCD should take regular folic acid supplements at doses of 1 to 5 mg (*12*). L-glutamine at 5 g is also used as a supplement, as lymphocytes — key cells of the immune system — primarily rely on glutamine for their function. In addition to serving as an energy source, glutamine helps protect these cells from damage caused by oxidative stress. Therefore, it plays a key role in preventing vaso-occlusive and hemolytic crises in these patients.

Clinical research has positioned HU as a reference treatment for SCD. A local study conducted in Barranquilla between 2012 and 2013 with 129 patients evidenced that the use of HU 500 mg compared to Folic Acid 1 mg was associated with a significant decrease in the frequency of seizure episodes in patients (*13*).

Figure 3 shows the family tree of an extended family from San Basilio de Palenque, which reveals a pattern of inheritance of SCD through multiple generations. The genealogical tree presented shows the inheritance patterns of the genetic condition under study, differentiating between homozygous and heterozygous individuals. Conventional genetic symbology is used: circles for females, squares for males, and colors to represent the characteristic of the hemoglobinopathy (red: homozygous; red and white: heterozygous; white: non-carrier). The numbers assigned to each allow identification of the patients included in the pharmacotherapeutic follow-up. Family relationships are represented by lines (solid: siblings; dotted: partners). Marital separations (transverse line).

Finally, the family tree of this family from San Basilio de Palenque provides valuable insight into the transmission of SCD through multiple generations. The extensive family network clearly identifies the autosomal recessive inheritance pattern and reveals the disease's clinical heterogeneity. In addition, the inclusion of unaffected relatives allows for the estimation of the mutant allele's frequency in the population and the assessment of the impact of modifying factors on phenotypic expression. That allows us to perform an analysis of past generations, confirming the origin of the homozygous or heterozygous characteristic, which in the present time allows the health professional to perform genetic counseling to the population to prevent the condition from continuing to spread and to present alternatives to those suffering from the condition that allows them to lead a relatively normal life.

4. Conclusion

The research highlights the need for a multidisciplinary approach to optimize treatment and improve the quality of life for affected patients, as evidenced by the monitoring of analgesic use, which can help prevent future medication dependency and the progressive deterioration of organs involved in the process. On the other hand, the study successfully characterized and conducted pharmacotherapeutic follow-up of patients with SCD and sickle cell traits, which allowed for a positive impact on patients and their families in the comprehensive management of their diagnostics. Moreover, due to its genetic significance, San Basilio de Palenque represents a unique setting for future studies on SCD.

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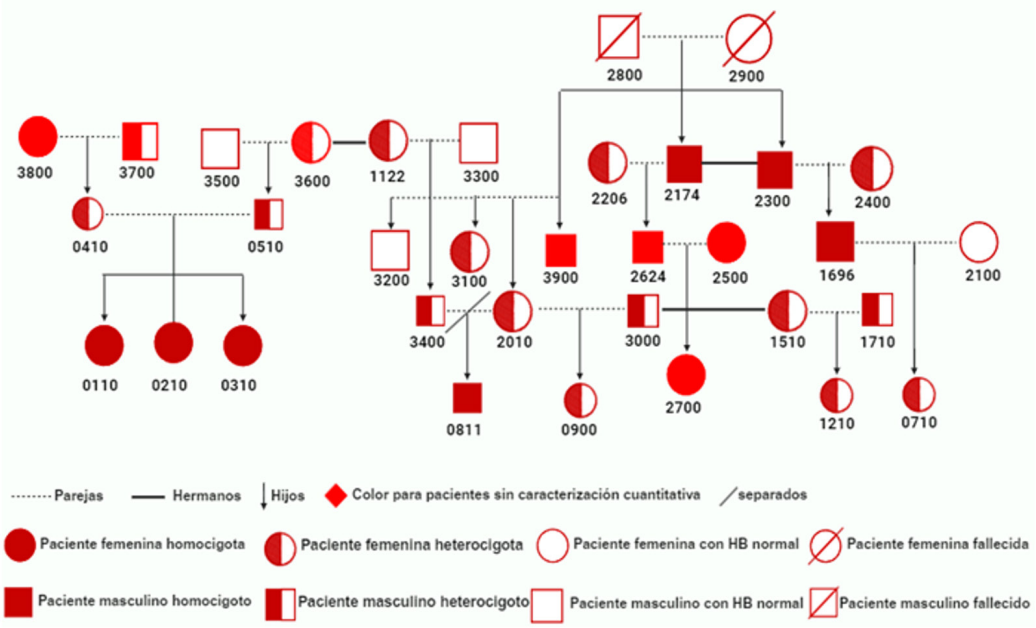

Figure 3. Family tree constructed using the data provided by the families as a result of pharmacotherapeutic monitoring.

Therapeutics research group, released funds for transportation, stationery, food, and supplies for the proper execution of the project's objectives.

Conflict of Interest: The authors have no conflicts of interest to disclose.

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