hematological parameters and increases the quality and expectancy of life. Despite the evident benefits of HU, there is significant inter-individual variability in pharmacological response and genetic factors seem to be associated. The aim of this study was to evaluate the individual variability of pharmacological response to treatment with HU, analyzing pharmacogenetic markers and hematological parameters of patients with not treated SCD and after treatment.

Materials and methods: 185 patients with SCD treatment (n=93) and without treatment (n=92) with HU followed at Fundação Hemominas, Belo Horizonte/Minas Gerais (MG)- Brazil were evaluated. The mean levels of hemoglobin (Hb), hematocrit, reticulocytes, global leukometry and fetal hemoglobin (HbF) were assessed before and after treatment. Patients were genotyped by real-time PCR (qPCR) for the polymorphisms G>T (rs1799983) and T>C (rs2070744) on the endothelial nitric oxide synthase (eNOS) gene, G>T (rs17399586) of arginase type 1 (ARG1) gene, A>C (rs766432) and G>A (rs4671393) of the B-cell lymphoma/leukemia 11A (BCL11A) gene, G>A (rs9960464) of the Urea Transporter (UTA) gene and A>G (rs2182008) of the Fms-related tyrosine kinase 1 (FLT1). The Ethics Committee has approved this study.

Results: The average age of patients was 15.8±11.3 years, among which 54% were men. Genotypic and allele frequencies for polymorphisms in the gene of eNOS (rs1799983: G=0.76; T=0.24; rs2070744: T=0.65; G=0.35), ARG1 (C=0.86; G=0.14), BCL11A (G=0.76; T=0.24), rs766432: A=0.76; C=0.24, UTA (G=0.61; A=0.39), and FLT1 (rs2182008: G=0.92; A=0.08) were similar in Hardy–Weinberg equilibrium and were similar to those found in other populations. In the group of patients treated with HU, those with the GT genotype for the polymorphism in eNOS gene had higher baseline Hb values when compared to GG patients (p=0.033). When patients were grouped according to HU response profile in “responders” (HbF ≥ 20%) or “non-responders” (HbF < 20%), it was found that those with the AC and CC genotypes in the BCL11A and GA gene in the UTA gene responded more effectively to drug treatment than patients homozygous for the most frequent allele. No significant influences were found related to other polymorphisms or the response to HU after analyses by logistic regression.

Conclusion: This study is pioneer in describing the frequencies of 7 polymorphisms in 5 candidate genes in a population of individuals with SCD treated with HU in the state of MG. The findings suggest that patients with the GT genotype in the eNOS gene (rs1799983) have higher Hb values and that the polymorphisms in the BCL11A (rs766432) and UTA seem to affect the hematological response to HU. Support: FAPEMIG (APQ-02608-14, PPSUSAPQ-03560-13) and UFJE.

The authors do not declare any conflict of interest

P-049 A ROADMAP FOR DELIVERING A GLOBALLY ACCESSIBLE GENE THERAPY

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Purpose: The convergence of innovative biotechnologies is propelling the field of gene therapy with consequential implications for treating and curing genetic and infectious diseases globally. Although dozens of gene therapies for a broad range of disease areas are expected to receive regulatory approval worldwide over the next decade, patients are unlikely to receive equitable access to these medical breakthroughs. In particular, the sophisticated infrastructure required to deliver gene therapies pose critical challenges for low and middle-income countries (LMICs) seeking to integrate gene therapies into resource-constrained health systems. Without critical foresight and targeted investments across LMICs, gene therapies will perpetuate global health inequity.

Materials and methods: Using gene therapies for sickle cell disease and human immunodeficiency virus (HIV) in sub-Saharan Africa as use cases, this project examined the necessary infrastructure required for effectively and sustainably delivering gene therapies in low-resource settings. Data was obtained through a series of interviews with expert stakeholders from sub-Saharan Africa, Europe, and the US. Interviewees represented multiple sectors including hospitals and community clinics, gene therapy companies, manufacturing, patient advocacy and community engagement, technical training, and global health priority setting. Interviews were supplemented with an extensive literature review.

Results: An analysis of stakeholder interviews revealed the need for core infrastructure across seven thematic areas: research; engagement and education; facilities and manufacturing; information systems, workforce, regulation; and finance. Although assessed individually, these domains are interdependent, highlighting the need to invest and co-develop across all areas simultaneously and synergistically.

Conclusion: Building the requisite infrastructure for delivering gene therapies is a multi-decade endeavour. This long horizon should not discourage immediate action; rather, it should be acknowledged and appreciated as an opportunity for strategic preparation assuring future success.

By establishing and maintaining infrastructure across several thematic areas, countries can accelerate the development and delivery of gene therapies. Throughout this process, key steps should be taken to improve outcomes:

- Engage communities early and often: The process of providing gene therapies must be patient-centred. Involving communities in the design and implementation process will lead to effective therapies that are acceptable and accessible.
- Leverage existing infrastructure: Maximizing the impact of limited resources and removing redundancy requires integrated services, multi-use facilities, and increased coordination.
- Collaborate internationally: While countries in SSA build research capacity, promote private sector innovation and commercialization, and update regulatory frameworks, international collaboration will facilitate the exchange of scientific equipment, knowledge and training, and policy.
- Improve and adapt iteratively: The success of gene therapy hinges on iterative cycles of feedback between research and clinical deployment. Infrastructure should support the ability of scientific and societal findings to inform healthcare practices and regulations.

While this study focuses on gene therapy delivery and its requisite infrastructure, considerations of health systems strengthening should remain at the forefront. The delivery of gene therapies should expand to align with health priorities set by countries (e.g., attention to non-communicable diseases). A narrow focus on gene therapies can create vertical systems of planning, management, and monitoring and evaluation that are not suited for other health areas and do not maximize the use of limited resources.

The authors do not declare any conflict of interest

P-050 UNDERSTANDING BARRIERS TO AND ENABLERS IN EMPLOYMENT FOR PEOPLE WITH SICKLE CELL DISORDERS IN ENGLAND

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Purpose: This paper reports on empirical research which was conducted in England in 2018-2020 before the COVID-19 pandemic. It involved trying to understand barriers and enablers to employment for people who have sickle cell disorder (SCD).

Materials and methods: The project worked with people with SCD, and two of their voluntary organisations, the Sickle Cell Society and OSCAR Sandwell as partners. It used a method of ‘democratic co-production’ which 54% were men. Genotypic and allele frequencies for polymorphisms G>T (rs1799983) and T>C (rs2070744) on the endothelial nitric oxide synthase (eNOS) gene, G>T (rs17399586) of arginase type 1 (ARG1) gene, A>C (rs766432) and G>A (rs4671393) of the B-cell lymphoma/leukemia 11A (BCL11A) gene, G>A (rs9960464) of the Urea Transporter (UTA) gene and A>G (rs2182008) of the Fms-related tyrosine kinase 1 (FLT1). The Ethics Committee has approved this study.

Results: The average age of patients was 15.8±11.3 years, among which 54% were men. Genotypic and allele frequencies for polymorphisms in the gene of eNOS (rs1799983: G=0.76; T=0.24; rs2070744: T=0.65; G=0.35), ARG1 (C=0.86; G=0.14), BCL11A (G=0.76; T=0.24), rs766432: A=0.76; C=0.24, UTA (G=0.61; A=0.39), and FLT1 (rs2182008: G=0.92; A=0.08) were similar in Hardy–Weinberg equilibrium and were similar to those found in other populations. In the group of patients treated with HU, those with the GT genotype for the polymorphism in eNOS gene had higher baseline Hb values when compared to GG patients (p=0.033). When patients were grouped according to HU response profile in “responders” (HbF ≥ 20%) or “non-responders” (HbF < 20%), it was found that those with the AC and CC genotypes in the BCL11A and GA gene in the UTA gene responded more effectively to drug treatment than patients homozygous for the most frequent allele. No significant influences were found related to other polymorphisms or the response to HU after analyses by logistic regression.

Conclusion: This study is pioneer in describing the frequencies of 7 polymorphisms in 5 candidate genes in a population of individuals with SCD treated with HU in the state of MG. The findings suggest that patients with the GT genotype in the eNOS gene (rs1799983) have higher Hb values and that the polymorphisms in the BCL11A (rs766432) and UTA seem to affect the hematological response to HU. Support: FAPEMIG (APQ-02608-14, PPSUSAPQ-03560-13) and UFJE.

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