ABHH
Associação Brasileira de Hematologia e Hemoterapia

REVISTA BRASILEIRA DE HEMATOLOGIA E HEMOTERAPIA

Editorial

Sickle cell disease - a serious problem for public health worldwide

Clarisse Lobo

Sickle cell disease is recognized as a serious public health problem worldwide, with a major impact on morbidity and mortality of the population affected by the disease.[1]

In the 1980s, a large multicenter study demonstrated that early introduction of penicillin in newborns with sickle cell anemia significantly impacted on their natural history thereby reducing mortality in the first five years of life.[2] This finding led to the introduction of hemoglobin S in neonatal screening programs in many countries worldwide depending on the ethnic composition of each population.

Years ago in Brazil, the disease was recognized by health professionals as highly prevalent.[3-5] The problem was also recognized by the Ministry of Health, which, since 2001, introduced phase II of the Brazilian program of neonatal screening, with the goal of identifying individuals with sickle cell disease.[6]

The first studies on prevalence in Brazil showed that there was a necessity of organizing a monitoring system for patients and the policy of 'Comprehensive Care for People with Sickle Cell Disease' was established.[7] This policy, conceived in Brazil, is being implanted with the participation of all the States of the country that are already performing phase II screening.

Basically composed of two guiding principles, the project initially aims to train all healthcare professionals, with the creation of a hierarchical network to look after individuals with the disease and decentralize the care of patients with low complexity by inserting them into the primary care system. The other guiding principle relates to complete access to diagnostic and therapeutic resources focused on prevention and treatment of complications. Hence, Brazil – which already had since 2002, a government ruling[8] that defined criteria for the use of hydroxyurea within the government healthcare system (SUS) – now, through this legislative pronouncement in 2010, expanded the criteria thereby placing the country among the most advanced in terms of access to this drug.[9] Through public consultation, the inclusion criteria, published in one issue of this journal, were supported by the scientific community.[10]

Despite the wide range of indications, hydroxyurea is still underused in Brazil. We believe that the reason for this is because of rejection by both professionals and patients as it is primarily a chemotherapy drug for life-long use. This rejection also occurs in other countries and can only be reversed through ongoing education of patients and the medical community.

The policy of comprehensive care highlights a need for the inclusion of transcranial Doppler (TCD) one of the examinations offered by the government healthcare system. Hence, a meeting of hematologists and neurologists from various regions of the country was held in Rio de Janeiro in May 2010, with the goal of developing criteria for the use of TCD in Brazil. These guidelines – based on the TCD study published in 1999 by Dr. Robert Adams[11] – will be adopted as another norm of the Ministry of Health that will be launched in November 2010.

Although screening was developed for the early diagnosis of individuals with sickle cell disease, there is a necessity of identifying sickle cell trait carriers. This is a benign condition with no impact on public health but with significant epidemiological importance that corresponds to individuals that are heterozygous for A and S genes. Subsequently genetic counseling should be provided for these individuals by primary healthcare professionals. Again this stresses the issue of training professionals in the government healthcare system to address health issues related to the S gene. The benign nature of the sickle cell trait must be explained to carriers.

The S gene originated in equatorial Africa (where it is present in up to 30% of the population) as a genetic modification, which is considered a positive adaptation, since it seems to protect heterozygous carriers (AS) from death due to *Plasmodium falciparum*. Its prevalence in some countries has been estimated prospectively through the results of neonatal screening programs.[12]

In the 1940s, one of the first Brazilian epidemiological studies was carried out by Maia de Mendonça in soldiers to determine the frequency of the S gene.[13] Since then, several reports from different regions of Brazil followed. In 1987, Naoum et al. published a major work of population screening in which 55,217 individuals were enrolled in 40 Brazilian cities.[14]

Subsequently, Brazilian studies on the prevalence of the sickle cell trait among blood donors corroborated data obtained from other healthy populations and showed, once again, great heterogeneity in the distribution of the gene.[15,16]

More recently, neonatal screening has been fulfilling the role of determining more precisely the epidemiological profile of the sickle cell gene in Brazil. Due to the racial mix in Brazil, this prevalence is strongly related to the percentage of African descents in each region, varying from 1/80 individuals in Rio Grande do Sul to 1/22 in Rio de Janeiro.[17] In electrophoresis of sickle cell trait blood samples, HbS represents 30% to 40% of the total hemoglobin but carriers present no significant clinical or laboratory manifestations. Life expectancy and overall mortality are not affected and there is no evidence that any limitation or treatment should be instituted in these individuals.[18]

Reports of sudden death in sickle cell trait athletes and recruits undergoing strenuous exercise, supposedly due to the heterozygosity, was later identified as being

related to inadequate physical conditioning and other previously undetected diseases.[19]

Consequently since 2007, Brazil has guidelines for sickle cell trait individuals in respect to sports and military activities.[20] The establishment of these Brazilian guidelines represented another step forward in the treatment of sickle cell disease in Brazil by reducing the invisibility of this large group of Brazilians.

By the way, invisibility is notable the history of sickle cell disease in the Americas. Remember that the first report of the disease occurred only in 1910[21] – two centuries after the arrival of the first carriers of the S gene. This year we commemorate 100 years since the description of that first case and we emphasize the importance of following the construction of an effective public healthcare policy to treat sick individuals through the government healthcare system. At least, we have an obligation to properly counsel sickle cell trait carriers as they must know their genetic heritage. Thus we again stress the need for training of the healthcare professionals responsible for this counseling for them to provide the correct genetic information, without myths or omissions. Inappropriate approaches can lead to stigmatization, which is the arbitrary creation of a negative social identity which, in turn, leads to strong sanctions against those who are stigmatized, in particular in the evolution of humanity.

References

1. Powars DR. Natural History of sickle cell disease - the first ten years. Semin. Hematol. 1975;12:267-85.
2. Gaston MH, Verter J, Woods G *et al*. prophylaxis with oral penicillin in children with sickle cell anemia. N Engl J Med. 1986;314:1593-9.
3. Accioly J. Anemia falciforme. Arq Univ Bahia. 1947;1:16
4. Machado L. Da incidência da drepanocitemia em grupos de indivíduos da cidade de Salvador. Med Cir Farm. 1958;270:471-5.
5. Salzano FM, Tondo CV: Hemoglobin types in brazilian populations. Hemoglobin. 1982;6(1):85-97.
6. Ministério da Saúde. Secretaria de Assistência à Saúde. Coordenação-Geral de Atenção Especializada. Manual de Normas Técnicas e Rotinas Operacionais do Programa Nacional de Triagem Neonatal/ Ministério da Saúde, Secretaria de Assistência à Saúde, Coordenação-Geral de Atenção Especializada. Brasília: Ministério da Saúde, Portaria GM/MS n.º 822/GM. Junho, 2001.
7. Ministério da Saúde (MS). Portaria n. 1.391/ GM em 16 de agosto de 2005. Institui no âmbito do Sistema Único de Saúde, as diretrizes para a Política Nacional de atenção Integral às Pessoas com Doença Falciforme e outras Hemoglobinopatias. - Brasília, MS/ ago. 2005.
8. Portaria SAS/MS Nº 872, de 06 de novembro de 2002, publicada no Diário Oficial da União, de 8 de novembro de 2002, seção 1, página 169 - Aprova o protocolo clínico e diretrizes terapêuticas /Doença Falciforme/ Hidroxiuréia.
9. Portaria Nº 55, de 29 de janeiro de 2010, publicada no Diário Oficial da União - Aprova o protocolo clínico e diretrizes terapêuticas - Doença Falciforme
10. Cançado RD, Lobo C, Ângulo IL, Araújo PIC, Jesus JA. Protocolo clínico e diretrizes terapêuticas para uso de hidroxiureia na Doença Falciforme. Rev. Bras. Hematol. Hemoter. 2009;31(5):361-6.
11. Adams R, Mckie VC, Hsu L, *et al.* Prevention of first stroke by transfusion in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. N Engl J Med. 1998; 339(1):5-11.
12. Powars D, Schroeder WA, White L. Rapid diagnosis of sickle cell disease at birth by micro column chromatography. Pediatrics. 1975; 55(5):630-5.
13. Mendonça JM. Meniscocitemia, sua freqüência no Brasil. Arq Inst Biol Exército. 1944;5(5):83-8.
14. Naoum PC, Alvarez F, Domingos CRB, *et al*. Hemoglobinas anormais no Brasil. Prevalência e distribuição geográfica. Rev Bras Pat Clin. 1987;23(3):68-79b.
15. Bezerra TM, Andrade SR. Investigação sobre a prevalência de hemoglobinas anormais entre doadores de sangue. Rev Bras Anal Clin 1991;23(4):117-8.
16. Castilho S, Silva ME, Lopes M, Souza R, Amorim L, Pecego MM, *et al.* Pesquisa de Hemoglobina S em doadores de sangue do Hemorio. Bol Soc Bras Hematol Hemoter. 1996;18:1
17. Lobo CLC, Bueno LM, Moura P, *et al*. Triagem neonatal para hemoglobinas no Rio de Janeiro, Brasil. Panam. J. Public Health. 2003;3(2/3):154-9.
18. Bookchin RM, Nagel RL. Molecular interaction of sickling hemoglobin. In: Abramson, H.; Bertles, J. F.; Wethers, DL. (eds.). Sickle Cell Disease: diagnosis, management, education and research. St. Louis: Mosby, 1973. p. 140-54.
19. Cooper, MR; Toole, JF. Sickle-cell trait: benign or malignant? Ann. Intern. Med. 1972;77(6):997-8.
20. Marra VL, Rugani MA, Lobo CL. Consenso brasileiro sobre atividades esportivas e militares e herança falciforme no Brasil - 2007 Cl. Rev. Bras. Hematol. Hemoter. 2008;30(6):488-95.
21. Herrick, JB. Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia. Arch Int Med. 1910;20:586-98.

Submitted: 8/2/2010
Accepted: 8/4/2010

Hematology Hemotherapy – Instituto Estadual de Hematologia – Arthur de Siqueira Cavalcanti – Hemorio, Rio de Janeiro (RJ), Brazil

***Correspondence:** Clarisse Lobo*
Rua Frei Caneca, 08 – Centro
20211-030 – Rio de Janeiro (RJ), Brazil
E-mail: diretoria@hemorio.rj.gov.br