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Early management of sickle cell anemia in central Africa: is it possible?

Tshilolo L[1], Wembonyama S[2]

[1] *Centre Hospitalier Monkole/CEFA. Kinshasa, DR Congo*
[2] *Hospital Général Jackson Sendwe, Université de Lubumbashi, DR Congo*

Abstract

Sickle cell disease(SCD) is a worldwide hemoglobinopathy that concerns about 250000 affected children every year. The majority of them are living in tropical regions, particularly in sub-Saharan Africa, India and Middle East. Life expectancy and quality of life of SCD patients have improved since the newborn screening and early management have been introduced in USA and Jamaica. Experts of hemoglobinopathies strongly encouraged WHO to develop in the endemic areas networks based on the Thalassaemia International Federation (TIF) model in order to conduct activities for developing medical services for care and prevention of hemoglobin disorders. Despite the inherent practical, political and economic difficulties, early diagnosis and a comprehensive health care program for SCD could be implemented in most of the African countries where the prevalence is high; but many challenges have to be first resolved. Based on pilot studies conducted in some central African countries, this article proposed some strategies and discusses the different ways of implementing initiatives that are indispensable for decreasing the mortality and morbidity rate of SCD in Central Africa.

Keywords: sickle cell anemia; networks; newborn screening; central Africa

INTRODUCTION

Sickle cell disease (SCD) and other hemoglobin disorders contribute significantly to the global toll of birth defects. Hemoglobinopathies occur most frequently in tropical countries in which malaria was or still is a major cause of death. Approximately 7 percent of the world's population is carriers for hemoglobin disorders, and 200-300000 infants are born with sickle cell anemia(SCA) in Africa each year and approximately 100000 are born with this condition in the Middle East and India. 50-80 percent of children with sickle cell anemia die each year in low and middle income countries, and most of them are living in sub-Saharan Africa[1]. Recently, a group of WHO experts (WHO-TIF meeting, Nicosia, Cyprus, 16-18 November 2007) agreed that SCA is a major public health problem in sub-Saharan countries where only few services exist for the control of hemoglobin disorders. They strongly encouraged WHO to develop in this regional area networks based on the Thalassaemia International Federation (TIF) model in order to conduct activities for developing medical services for care and prevention of hemoglobin disorders.

This objective seems to be a real challenge in most of the sub-Saharan African countries where there is often socio-political instability coupled with economic and organizational difficulties. Is it possible, in this context, to organize a Comprehensive Health Care Program for Sickle Cell Disease? Tentative of answers is proposed in this paper based mainly on the issues regarding the newborn screening from pilot studies in Burkina Faso and DR Congo and the experience of a platform recently organized in Kinshasa.

MATERIALS AND METHODS

Background and objectives

Correspondence to: Léon Tshilolo, MD, Centre Hospitalier Monkole/CEFA. Kinshasa, DR Congo. leon.tshilolo@gb-solution.cd

Frequencies of sickle trait in sub-Saharan countries varies between 5-40% depending of local regions, but only few data are available on health care program for SCA in this region. A Comprehensive Health Care Program for Sickle Cell Disease is effective in Ghana[2] and Benin[3], two west African countries where universal and selective newborn screening of SCD has been implanted respectively. No similar experiences are reported in central African countries. While the main abnormal hemoglobins present in west Africa are HbS and HbC, in many of the central African countries there is only the HbS hemoglobin with sickle cell trait frequencies around 20-25% (Figure 1)[4].

Since the first newborn screenings have been applied in USA and Jamaica, it was evident that the expectancy and quality of life in SCD patients have been increased by the systematic use of oral penicillin, vaccine schedules against streptococcus pneumonia and *Haemophilus influenzae* germs, parent education and a regular follow-up[5,6].

Congolese experience

By January 2006, a pilot study was conducted in Kinshasa (6 millions inhabitants), DR Congo, in order to implant a network for sustaining early care of SCA patients and to promote educational and preventive programs . A 3 years-program provided to screen 28000 newborns, to train 50 medical doctors, 100 nurses and 50 laboratory technicians, to sensitive 15000 scholars and general population, to diffuse 40000 educational leaflets and to sustain sickle cell associations.

The financial support (US. $320000) obtained from UE and France Cooperation permitted the creation of a platform named "PAFOVED" (abbreviation of the French name "Plateforme d'Appui, de Formation et de Veille sur la Drépanocytose") (www.pafoved.org) . The staff of this platform is composed by a director, a medical coordinator, a nurse, a psychologist responsible for the IEC program (Information and Education program), a financial manager and a driver. Offices were installed nearby the "Centre Hospitalier Monkole", a second level referee hospital in a sub-urban area in Kinshasa. Two vehicles and communication facilities (mobile phone, internet access, *etc*) were provided.

The program started with training of the medical and nurse's personnel and with a sustained campaign of mass education. Themes of medical courses on sickle cell disease were focused on epidemiology, diagnostic steps, clinical manifestations and complications, outpatients and inpatients management and the organization of a regular follow-up program.

Systematic newborn screening was conducted in 10 maternal units where nurses were previously trained and pregnant women informed. Cord blood or heel samples were collected on a filter paper stapled on a baby identity card (Figure 2). Samples and the baby identity cards were regularly collected by the pafoved's driver from the maternity units and spent to the Sickle Cell Diagnostic Unit in Monkole Hospital.

Analyses were done by isoelectric focusing (IEF) method on thin layer home made agar gel, prepared in the local laboratory.

As the delay in maternity units, generally doesn't exceed 3 days, parents of suspected patients were visited by the pafoved's team, the community relays members or a local nurse to explain the results and to arrange confirmatory testing. The latter would be done in course of a vaccination schedule program. The new patients were then referred to their primary health care center and included in a comprehensive care program of SCD.

RESULTS

In a 16 month-period, sensitization and mass education program was purchased during 25 public meetings, 7 radio-TV emissions and distribution of 20000 educational leaflets. One of the educational pamphlets related to the newborn screening was entitled baby test in analogy of the HIV test(Figure 3). 150 medical, laboratory and nurses´ personnel were trained on SCD. A total of 16993 newborns were screened and 326 of them were suspected to be homozygous SS (incidence of 1: 50) while 2725 (16%) were suspected to have a sickle cell trait. The only common type of SCD found was SCA (SS). According to the ethno-linguistic origin, 11076 belonged to the Kikongo group, 2350 to the Lingala group, 1096 to the Swahili group and 2471 to the Tshiluba group. The prevalence of HbS trait and HbSS homozygous was almost the same in these ethnic groups. No statistical differences were revealed (Pearson Chi Square test: 0.514).

Screening results were very rarely given directly to the mother before discharge from the maternity

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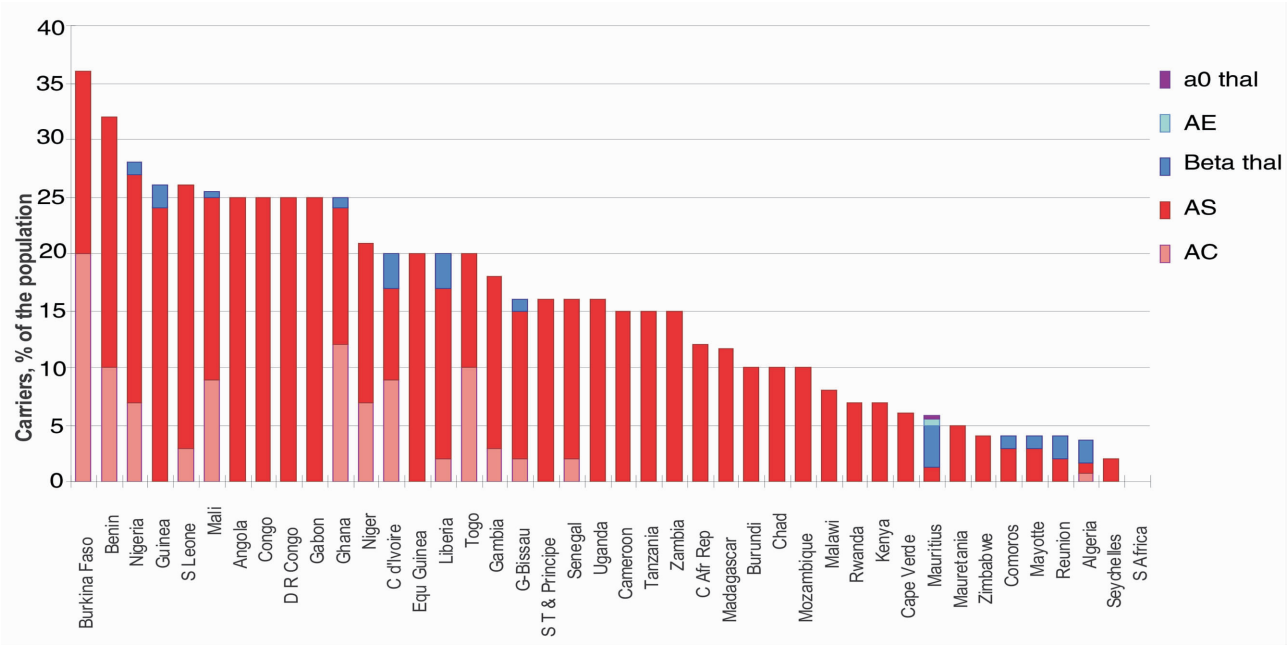

Figure 1 Carriers % of population with hemoglobinopathies in African countries(From WHO-African region, [4])

Figure 2 A baby identity card with fictive names and a dry blood sample

CEFA CENTRE HOSPITALIER MONKOLE

DOCTA SS

Feuillet d'information sur la drépanocytose, Année 7, septembre 2006, N° 34

"Bébé test": Dépistage Néonatal

Mwa Mbuyi vient de rentrer à la maison après un séjour de 3 jours à la maternité. C'est un jour de grande joie : le petit frère de Fifi est là ! Les amis et les membres de la famille sont au rendez-vous.

Fifi : Maman, comme il est beau. Il a les yeux de Grand-Père et le front de Papa.
Mwa Mbuyi : Oui, il a tout pris de son papa…
Papa Matondo : Oui, mais j'espère qu'il n'a pas pris cette fois-ci mon hémoglobine S.
Maman Brigitte : Mais, pour cela, il faudra attendre après 6 mois pour faire l'examen de l'électrophorèse.
Mwa Mbuyi : Ah non ! Les choses ont changé… A la maternité, on a pris un peu de sang pour faire l'examen de l'anémie SS. L'infirmière m'a dit que nous aurons la réponse déjà la semaine prochaine.

Figure 3 A pamphlet entitled baby test used for the newborn screening campaign

unit because of the delay time of obtaining all the results from the laboratory. Only about 20% of suspected SS babies were found in the first month of birth; and about 30% were identified in the successive three months. Penicillin prophylaxis and a follow-up program were established only in 30% of the new detected patients. Vaccination schedules including 23-valent polysaccharide pneumococcal vaccine and conjugate vaccine for *Haemophilus influenzae* type B were available. The usual national schedule of vaccination includes diphtheria, tetanus, pertussis, BCG, measles and polio vaccins. All the new sickle cell patients identified were oriented to the local health center for the follow-up. Annual attended of newborns affected of SCD in DR Congo is about 52000 cases, almost the 1/4 of the total cases attended in Africa.

DISCUSSION

Experiences in Ghana[2], Benin[3] and the recent pilot studies in Burkina Faso and DR Congo allowed to say it's really possible to organize a comprehensive health care sickle cell program in most of the central African countries. It will require supplementary economic resources, new health policy and a vast educational program. A large Information and Educational program is essential to fight against stigmatization of SCA patients; it will be coupled with a specific program of training for medical workers at the primary health level and the referee centers. Information and educational plans will be focus to touch people in the families, at school, in the religious communities, at the market, at the football stadium, *etc*. Regular programs have to be planned in the private and national radio and TV stations. At the local level, themes of SCD will be developed during meetings, theatres, sketch, songs, *etc*. Efforts are needed to increase the effective number of hours dedicated to SCD in the medical courses at university and nurses schools.

Implementation of reference laboratories which will acquire the expertise in SCD newborn screening, with a minimal capacity of 30000 tests per year. Techniques with a high sensitivity and specificity required are isoelectric focusing (IEF) and high performance liquid chromatography (HPLC)[6]. IEF seems to be more adapted to the central African countries since it's less dependent on a regular maintenance of the instrument and on delivery of kits. IEF agarose gels can be home made allowing a reducing of the cost test. Confirmation tests will be coupled with complementary tests as the sickle solubility test (Itano test) and the alkaline electrophoresis.

In central African countries where the incidence of SCD is around 2% in newborns[7], the screening will be universal even though in Benin[3] a target screening is applied in babies who have a mother with a sickle trait or HbC trait. A such approach supposed that all the pregnant women have been previously tested. In Ghana, universal screening has been successfully applied in 177283 newborns leading to identification of 3346 affected children. More than 80 of them were enrolled in a comprehensive health care program[2]. Similar experiences are clearly needed in other African countries where the prevalence of SCA is high. Samples will be collected at birth or before leaving the maternity; but a possibility of rescue the loss children at the BCG vaccination (first week of life) will be planned.

One of the most challenges in the screening program in sub-Saharan Africa is finding families of babies with suspected SCD in order to give them the results and to refer the affected babies to a health center for the follow-up. Mobile phone is one of the ways that would be useful to contact the families; local community relay members and the sickle cell associations would be involved in tracking the families. To convince the families of the importance to get the test results, the antenatal period (prenatal consultations) would be one of the best occasions; and the first visits for vaccination offer another good opportunity and the possibility to confirm the first results.

Another challenge in central Africa will be the implementation of early management of SCA program to all the countries of this region, especially in the rural areas. In the latter, there are less medical workers and no possibilities of accessing to correct diagnosis. Samples collected on filter paper would be easily sent to urban reference laboratories for the IEF analysis and results spent back to the health local center by Email or postal way. Between the WHO main priorities for care and prevention of birth defects and hemoglobin disorders in low and middle-income countries, there are supports for development of capacity in human resources and technology transfer and the development of community-based services

for patients with SCD[8].

Although with limited resources, it's possible to organize in central Africa a comprehensive care for SCD patients based on emergency treatment, hospital inpatient care and outpatient and community care as recommended by European Hematologists[10] and to pursuit the same objectives. The aim of such program is to allow patients more control over their disease, to spend more time at home rather than in hospital, to get a better quality of life, to get a job, *etc*. Emergency treatment is possible in hospitals where there is a nurse's and medical team trained in SCD emergency and the possibility of access to intensive care and surgery. The SCD management will be integrated in the primary health care system according to the PCIME policy (Prise en Charge Intégrée des Maladies de l'Enfance in french), a new strategy for early management of child disease. In the absence of national guidelines in many of the African countries, priority will be the red action of consensual guidelines for managing SCD problems at the different places: home, primary heath care center, hospital and specialized units. Essential medicines are now available in more African countries; and the cost is cheap for analgesic drugs (paracetamol, codeine, aspirin), anti-inflammatory drugs, antibiotics and vitamins. Oral or parental hydration is also available in almost all the medical center in sub-Saharan countries. Efforts are needed for access to some specialties like morphine and hydroxyurea; and to safe blood.

In these last years there is an increase in medical and academic interest in SCD with a consequent progress in the understanding of physiopathology, genetic and biological basis for the enormous variability in phenotypic expression of the disease. This is mainly due to the description of the natural history of SCD in different parts in the world and the formation of research networks within and between countries[9] WHO encouraged the continued North/South partenerships and the development of South/South networks. No effective networks exist in central Africa region; but only some limited experiences are reported in some countries. Regional WHO offices could play a major role in monitoring the progress of the networks and reporting back to individual governments. This support could also include the drafting of regional guidelines on care and prevention of SCD and the advocating of research[8].

One of the main challenges for introducing a comprehensive health care system for SCD in central African countries is obviously the limited financial resources and the lack of a strong willing to introduce SCD in the health priorities. In most of these countries and in DR Congo specifically, financial supports for the main heath priorities are obtained from International Community and different NGO (Non Governmental Organizations)[10]. In these last years efforts in information campaigns and fund raising have been made by the Sickle Cell Disease International Organization (SCDIO/OILD in French), a non profit organization created and launched in the year 2000. Concrete actions have been achieved in organizing three international congresses on SCD (www. drepanetworld. org) and lobbying actions targeting governmental and sanitary authorities in several countries. Actions of mobilization of very important personalities belonging to political arena (The first ladies of African countries, African Union members), international organizations (UNESCO, WHO) and football clubs (Lilian Thuram, the French world soccer champion 1998) have produced encouraging results in recognizing SCD as a public health priority by the international community. According to the success of the Thalassaemia International Federation (TIF), efforts are needed to increase the number of financial donors in order to finance, organize and implement effective initiatives that are indispensable for significantly decreasing the mortality and morbidity rates of SCD.

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