

PRENATAL DIAGNOSIS OF SICKLE-CELL ANEMIA, PERCEPTIONS OF PROFESSIONALS AND PATIENTS

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ABSTRACT

Although prenatal diagnosis of sickle-cell anemia has been facilitated by DNA analysis techniques, there is an ethical controversy about the validity of this procedure. We surveyed 59 geneticists, 55 hematologists and 52 adult patients in Brazil, on their perception of the disease. These patients regularly received medical and psychosocial guidance at the UNICAMP Hemocenter. Most consider their quality of life to be satisfactory despite the high level of discomfort caused by the disease. Although a majority of the geneticists (66%) and hematologists (67%) considered the probability of a patient with sickle-cell anemia leading a productive and socially adjusted life high when properly treated, most (59% of the geneticists and 51% of the hematologists) considered prenatal diagnosis to be an important resource for prevention of the disease. Nearly all patients would seek prenatal diagnosis for their children. Of these, 3/4 would prepare for early treatment and 1/4 would opt for abortion.

INTRODUCTION

The question concerning how severe an alteration must be to justify its prenatal diagnosis for therapeutic abortion is the source of much concern among geneticists and those who study ethics. As commented by Nora and Fraser (1985), some diseases are so terrible that there would be almost general agreement about the justification of this procedure, whereas other alterations generate doubts and debates. Sickle-cell anemia, which is the hereditary disease of highest prevalence in Brazil (Ramalho, 1986), may be included in the latter category. Indeed, although the technical aspect of prenatal diagnosis

of sickle-cell anemia was resolved at the beginning of the 1980's by direct DNA analysis and by the use of synthetic oligonucleotides (Chang and Kan, 1981; Geever *et al.*, 1981; Orkin *et al.*, 1982; Conner *et al.*, 1983; Goossems *et al.*, 1983), the ethical discussion of the use of these techniques continues. A survey of the recent literature shows that some authors favor prenatal diagnosis of sickle-cell anemia as a form of population control of the disease (Granda *et al.*, 1991; Rowley *et al.*, 1991; Svarch *et al.*, 1991), whereas others question this procedure, either by emphasizing that neonatal diagnosis and early treatment improve the quality of life of the patient (Bowman, 1991), or by pointing out that the patient has a potential for integration into society as long as properly assisted from a medical and a psychosocial viewpoint (Paiva and Silva, 1992). As pointed out by Modell (1990), however, there is general agreement about the right of parents to opt for prenatal diagnosis due to the lack of a directive attitude in genetic counseling.

Another important aspect is the genetic variability of sickle-cell anemia, the severity of which depends on the DNA haplotypes and on interaction with alpha thalassemia. This variability has been greatly emphasized in recent years (Powars *et al.*, 1990; Ballas and Castillo, 1991; Costa *et al.*, 1989; Zago *et al.*, 1991, 1992; Costa *et al.*, 1992).

Since Molecular Genetics techniques for prenatal diagnosis of sickle-cell anemia have already become routine in some Brazilian research centers, this is an opportune time to start a broad discussion of this topic in our country. We took a first step in this direction by determining the perception of the disease by Brazilian geneticists and hematologists and by the patients themselves.

CASES AND METHODS

A total of 160 hematologists and 145 geneticists from different region of Brazil were invited to participate in the study by responding to a questionnaire containing five questions with four alternatives. Among the geneticists registered with the Brazilian Genetics Society, we selected those who devote themselves to medical Genetics or Clinical Genetics, and especially those who engage in genetic counseling. Since the number of Brazilian hematologists exceeds by far the number of medical geneticists, we only consulted the professionals registered with the Brazilian Society of Hematology and Hemotherapy who participated in the Annual Meeting of this Society in 1990.

The questionnaire was personally delivered to some professionals (19 geneticists and nine hematologists) with whom we keep constant contact, and the remaining ones were sent by mail, together with a stamped self-addressed envelope. The hematologists and geneticists were invited to participate on a voluntary and anonymous basis; however, the number of refusals or abstentions was recorded. When a letter was not answered, no second mailing was sent.

The perception of the disease by the patients was evaluated using semistructured interviews involving 52 patients (34 women and 18 men) followed up for at least three years at the UNICAMP Hemocenter. This criterion followed the recommendation of Ballas and Castillo (1992) that the patient with sickle-cell anemia needs to be followed up for at least three years for an appropriate analysis of his/her information. Patient age ranged from 18 to 44 years (mean: 25 years; standard deviation; seven years).

The clinical method was adopted (Trinca, 1984), with the data being obtained during several sessions. An attempt was made to interview the patients both during stable phases of the disease and during a crisis. Data were analyzed statistically using Microstat computer software.

RESULTS

The questionnaire was answered by 59 geneticists and 55 hematologists, with no significant difference in sex, age or time since graduation from Medical School between subsamples. The letters sent by mail were answered by 33% of the geneticists and 31% of the hematologists. Of the 88 questionnaires answered by mail, 53 were from Southeast Brazil, 20 from the South, nine from the Northeast, four from the North, and two from the Center-West. There was a significant predominance of participation from the State of São Paulo, with 58/114 of the questionnaires answered.

The questions asked and the replies given are listed in Table I.

The patients' own perception of their disease did not differ between interviews conducted during a phase of equilibrium or during a crisis, demonstrating that these patients already had a definite and stable opinion about sickle-cell anemia. The questions asked during the interviews and the patient's replies are listed in Table II.

DISCUSSION

We were surprised to note that virtually all patients interviewed consider currently available treatment to permit them to lead a life of acceptable quality and that most of them consider their quality of life to be satisfactory when compared to that of the people with whom they live (Table II). However, this is a selected patient sample which is regularly followed up at the UNICAMP Hemocenter, where they receive free medical and psychosocial guidance. Furthermore, these are individuals who had the opportunity to overcome the selective barrier of childhood mortality since, according to Hutz (1981), the mean survival of Brazilians with sickle-cell anemia is 16.4 ± 12.1 years. However, even though these data may not reflect the reality lived by most patients with sickle-cell anemia in Brazil, they demonstrate that these individuals have a potential for adaptation to society which can be developed by medical and psychosocial guidance.

Table I - Questionnaire for hematologists (H) and geneticists (G).

	Percent response	
	H	G
1. Your knowledge comes from:		
a) routine patient care	65	8
b) sporadic patient care	11	24
c) the literature	15	39
d) medical school and/or medical residency	9	29
2. Therapy permits:		
a) patients to lead a satisfactory life	24	14
b) most patients to lead a satisfactory life	45	46
c) a minority of patients to lead a satisfactory life	29	20
d) no opinion	2	20
3. Degree of suffering:		
a) severe	33	34
b) variable	67	54
c) small	-	7
d) no opinion	-	5
4. Probability treated patient leading productive and socially adjusted life		
a) null	6	-
b) low	27	22
c) high	67	66
d) no opinion	-	12
5. Prenatal diagnosis:		
a) an important technical tool for disease prevention	51	59
b) dispensable	9	7
c) questionable	27	19
d) no definite opinion about this topic	13	15

Paiva e Silva (1992), in a study of 80 adult patients with sickle cell anemia (49 women and 31 men) seen at the UNICAMP Hemocenter, observed that 43% of them worked regularly despite the absence of a program of support and professional guidance.

Table II - Questionnaire for patients with sickle-cell anemia.

	Percent response	
	Men	Women
1. Therapy permits adequate life?		
a) yes	89	100
b) no	11	-
2. Do you lead a satisfactory life?		
a) yes	78	91
b) no	22	9
3. If at risk would you submit to prenatal diagnosis?		
a) yes	100	88
b) no	-	12
4. Purpose of early diagnosis?		
a) to be ready for early treatment if the child should be affected	72	80
b) to perform a therapeutic abortion	28	20
5. Why not prenatal diagnosis?		
Not relevant	-	(n - 3)
Knowing in advance is worse	-	(n - 1)

The information provided by the patients interviewed in the present study may also reflect a process of adaptation to chronic disease. Leavell and Ford (1983) noted a wide gamut of personal adjustment to the disease among their adult North American patients. Damlouji *et al.* (1982) noted that the degree of discomfort caused by sickle-cell anemia and by diabetes is not always associated with the extent of psychosocial impairment of the affected individuals.

The fact that the perception of their disease by the patients did not differ significantly when the data obtained during a stable period were compared to those obtained during crises of sickle-cell anemia reinforces this hypothesis of acceptance of, or resignation to an incurable disease. The patients were aware of the fact that their pain crises and periods of hospitalization are part of their clinical condition. According to

Powars *et al.* (1990), sickle-cell anemia is never a benign clinical entity even though it may have a milder course in some patients. Clinical studies by Hutz (1981) and by Zago *et al.* (1983) on Brazilian victims of sickle-cell anemia have shown a high frequency of severe clinical alterations, and DNA studies by Zago *et al.* (1991, 1992) and by Costa *et al.* (1992) have revealed that the Bantu or CAR haplotype, of worst prognosis, predominates among patients with sickle-cell anemia in Southeast Brazil. Among patients evaluated by Paiva and Silva (1992) at the UNICAMP Hemocenter 44/80 considered the level of discomfort caused by sickle-cell anemia to be high, significantly more than reported in the opinion of the hematologists and geneticists surveyed in our study, (38/114) ($\chi^2 = 9.04$; $P < 1\%$).

Prenatal diagnosis was perceived by most patients as a means of preparing for the possibility of the child having sickle-cell anemia, with the institution of early treatment. These patients rejected the hypothesis of a possible clinical abortion, reflecting the opinion of most of the persons interviewed (Table II). However, this was a hypothetical situation discussed in the absence of a true risk of generating a child with sickle-cell anemia.

Though most geneticists and hematologists were of the opinion that currently available treatment permits the patient to lead a satisfactory life, more than half of them considered prenatal diagnosis to be an important tool in the prevention of the disease (Table I). However few were familiar with sickle-cell anemia on the basis of routine patient care.

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RESUMO

Embora o diagnóstico pré-natal da anemia falciforme tenha sido facilitado pelas técnicas de análise do DNA, existe uma controvérsia ética a respeito da validade desse procedimento. No presente trabalho avaliou-se a percepção de 59 geneticistas e 55 hematologistas brasileiros, bem como de 52 pacientes adultos, a respeito da doença. Constatou-se que a maioria (87%) desses pacientes, seguidos regularmente no Hemocentro da UNICAMP, onde recebem orientação médica e psicossocial, considera a sua qualidade de vida satisfatória, apesar de o nível de incômodo causado pela doença ser alto. Embora a maioria dos geneticistas (66%) e dos hematologistas (67%) tenha considerado alta a probabilidade de um paciente com a anemia falciforme, tratado adequadamente, levar uma vida produtiva e socialmente ajustada, a maioria deles (59% dos geneticistas e 51%

dos hematologistas) considerou o diagnóstico pré-natal como um recurso importante na prevenção da doença. Tal procedimento foi considerado questionável por 27% dos hematologistas e por 19% dos geneticistas e dispensável por 9% dos hematologistas e 7% dos geneticistas, sendo que 15% dos geneticistas e 13% dos hematologistas não tinham opinião formada sobre o assunto.

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