

Evaluation of genetic counseling offered to Brazilian carriers of the beta-thalassemia trait and to their relatives

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ABSTRACT

We evaluated the genetic counseling provided to 200 Brazilian adults with the beta-thalassemia trait. Good participation of the family in the process of genetic counseling was observed, with examination of the spouse and children in 74% and 89% of cases, respectively. Each propositus brought on average two relatives for examination. Long-term evaluation, one to 13 years after genetic counseling, was possible for 50% of this group. In this subsample, 65% of the thalassemia patients who married after genetic counseling brought their spouses for examination. In 82% of the cases, this examination was performed only after marriage and did not influence the choice of a spouse. Similarly, 75% of the thalassemic patients who had children after genetic counseling brought their children for examination. Cognitive evaluation was satisfactory for more than 2/3 of the patient groups regarding information of a practical order, with no significant variation based on sex, educational level, time after genetic counseling or type of professional that provided the counseling. Information of an academic nature was assimilated satisfactorily by approximately 50% of the individuals.

INTRODUCTION

Heterozygotes for the beta-thalassemia gene, who manifest the beta-thalassemia trait, are frequent in the states of the Brazilian South and Southeast, due to the massive immigration of people of Italian extraction and of other Mediterranean peoples. Studies on the Caucasoid population of these states have detected a one to 6.5% prevalence for this alteration (Ramalho, 1976, 1979; Zago *et al.*, 1981; Freita and Rocha, 1983; Naoum *et al.*, 1984, among others). The number of carriers of the beta-thalassemia trait in Brazil

is estimated at more than 1,500,000 (Naoum *et al.*, 1989).

The investigation of the molecular basis of beta-thalassemia in Brazilian patients has revealed a preponderance of mutations associated with more intense clinical manifestations (Costa *et al.*, 1990; Martins *et al.*, 1993). To illustrate, approximately 90% of beta-thalassemia heterozygotes in the region of Campinas, SP, have the β^0 39, β^0 IVS1-1 and β^+ IVS1-110 mutations, which suppress or severely depress the synthesis of β chains of hemoglobin A (Martins *et al.*, 1993). This fact emphasizes the importance of recognizing these individuals in a population, for genetic counseling purposes.

The creation of population programs for hemoglobin diseases in Latin America has been

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recommended by several international organs, such as the World Health Organization (WHO, 1983), the Third World Academy of Sciences (Twas, 1986) and the Panamerican Health Organization (OPS, 1987). Recently, the Committee for the Prevention and Control of Hemoglobinopathies of the World Health Organization has again recommended the creation of community programs for hemoglobinopathies in Latin America, with special emphasis on Brazil (Penchaszadeh, 1993).

In an extensive study carried out on a Brazilian population, Teixeira and Ramalho (1994) detected a good response by the community to a program concerning hereditary hemoglobinopathies offered on an optional basis, with no coercion, as established by ethical conduct (CREMESP, 1988). The indicators of viability and efficiency detected in this study were quite satisfactory and similar to those observed by Rowley et al. (1991) in Rochester, USA. Thus, the rate of acceptance to genetic counseling offered to adult heterozygotes (60%) was considered to be satisfactory and was significantly higher among women (65%) than men (51%).

However, a satisfactory rate of acceptance to genetic counseling obviously does not mean that heterozygotes will properly assimilate and follow the guidelines offered to them in this process. On this basis, the objective of the present study was to evaluate to what extent a carrier of the beta-thalassemia trait who received specialized genetic counseling in Brazil assimilates the information provided (cognitive evaluation) and actually uses this information in his life (pragmatic evaluation).

CASES AND METHODS

The study was programmed so that genetic counseling could be evaluated on a short-term basis, while the process was still underway, and on a long-term basis, i.e., at least one year after its conclusion.

For the short-term evaluation, 200 file cards of beta-thalassemia heterozygotes who had received genetic counseling at the Hemoglobinopathy Service of University of Campinas from 1980 to 1992 were selected at random and the data for evaluation were obtained from their medical records. These individuals resided in the city of Campinas, SP or in the surrounding region and had been identified in population screening programs, in family studies or had been referred to the Hemoglobinopathy Service by physicians. They had

received free and individualized genetic counseling after evaluation by an interdisciplinary team consisting of hematologists and geneticists, biomedical personnel, a psychologist, and a social worker. Genetic counseling had been completed with an identification card and an explanatory booklet about thalassemia supplied to each subject.

The interest of the patients and their families in genetic counseling was evaluated objectively on the basis of the percentage of thalassemia patients who brought their spouses, children or other relatives for a laboratory test while the process was underway. Of the 200 individuals with beta-thalassemia trait, 68% were females ($\chi^2 = 25.9$; $P < 0.001$). Age ranged from 15 to 64 years (mean 32.11 years \pm SD = 11.52 years). Sixty-six percent were married or cohabiting, 33% were single, and 1% were widowed. Genetic counseling had been provided by a physician in 111 cases and by a biologist in 89 cases. The information provided, however, was the same in all cases.

For long-term evaluation, we used the same group of 200 beta-thalassemia heterozygotes and made an attempt to locate them one to 13 years after genetic counseling, and to invite them for an interview at the Hemoglobinopathy Service, or, if they preferred, at home or at work. In addition to satisfying an ethical requirement, this precaution reduced the possibility that only the more receptive individuals or individuals in a better economic situation would be evaluated, a fact that might represent a bias in the study.

Semistructured interviews with free (non-stimulated) replies were held, adopting the clinical method (Trinca, 1984). These responses were used to fill out a form with information of a cognitive and pragmatic nature, as specified below.

The data obtained were related to a few variables such as sex, educational level at the time of counseling, educational level at the time of evaluation, time between counseling and evaluation, and type of professional that had provided genetic counseling. The cognitive data were classified into 5 grades according to the following criterion: 5 - excellent = extensive knowledge of the topic in question, exceeding the minimum indispensable for proper care of one's own health and of the health of one's children, or for calculating the risks of occurrence of patients with thalassemia *minor* and *major* in several situations proposed; 4 - good = knowledge of all the indispensable aspects mentioned above; 3 - regular = knowledge about most of the indispensable aspects; 2 - poor = knowledge of only some of the indispensable aspects; 1 - null = no knowledge about the indispensable aspects. For statistical analysis purposes, grades 3 + 4

+ 5 were considered "satisfactory" and grades 1 + 2, "unsatisfactory".

Statistical analysis was performed using the Microstat software (Ecosoft Inc., 1984) for comparison of proportions by the χ^2 test, with the level of significance set at 5%.

RESULTS

Among the 200 patients evaluated on a short-term basis 68.5% were married, cohabited or were engaged to be married at the time of genetic counseling. Among them, 74% brought their partners for laboratory hemoglobinopathy investigation. The proportion of male heterozygotes who brought their partners for examination (91%) was significantly higher than the proportion of females (69%) ($\chi^2 = 6.67$; $P < 0.01$).

Among the thalassemic patients evaluated, 64.5% had children. Among these, 89% brought their children for examination. The proportion of male patients who brought their children for examination (94%) did not differ significantly from that of female patients (88%) ($\chi^2 = 0.96$; $0.30 < P < 0.50$).

The 200 thalassemic patients brought a total of 421 relatives for examination, corresponding to a "screening index" of $421/200 = 2.105$. Among these relatives, 188 new cases of the beta thalassemic trait were diagnosed, corresponding to a "positivity index" of 45%.

Starting from the initial list of 200 beta-thalassemia trait patients it was possible to interview 50%. Among the patients who could not be evaluated, 98 were not located due to a change in address, one had died and only one refused evaluation.

The time between genetic counseling and our evaluation ranged from one year to 13 years (mean =

5.09 years). Of the 100 patients evaluated on a long-term basis, 73% were females ($\chi^2 = 21.16$; $P < 0.001$). The proportion of female patients did not differ significantly between evaluated (54%) and non-evaluated (46%) thalassemic patients, demonstrating that there was no preferential evaluation of this sex ($\chi^2 = 2.3$; $0.10 < P < 0.20$). The age of these patients ranged from 15 to 59 years ($\bar{x} = 30.34$ and $s(\bar{x}) = 11.8$ years at the time of counseling and from 17 to 64 years ($\bar{x} = 35.79$ and $s(\bar{x}) = 11.8$ years) at the time of evaluation.

Of the 100 thalassemic patients evaluated on a long-term basis, 54% had been counseled by a physician and 46% by a biologist.

Among the 17 patients who married after genetic counseling, 11 brought their spouses for examination, nine of these only after marriage. Similarly, among the 20 relatives who had children after genetic counseling, 15 had their children tested for hemoglobinopathy.

Table I specifies the grades of knowledge of the patients regarding some aspects of the beta-thalassemia trait. Table II shows the proportions of patients with satisfactory knowledge about these aspects related to some variables such as sex, educational level at the time of counseling, educational level at the time of evaluation, professional who provided counseling, and time after genetic counseling.

DISCUSSION

Evaluation of the effects of genetic counseling provided to carriers of the beta-thalassemia trait is a common procedure in countries such as Italy (Barrai and Vullo, 1980) Greece (Stamatoyannopoulos, 1974) and the U.S.A. (Rowley *et al.*, 1984; Loader *et al.*, 1991). In Brazil, genetic counseling is still infrequent due to

Table I - Grade assigned to patient knowledge about some aspects of the beta-thalassemia trait (in percentage for each category).

Grade of knowledge \ Aspect	Name of the alteration	Meaning of beta-thalassemia trait	Health precautions	Reproductive precautions
5 - Excellent	16	23	47	28
4 - Good	30	16	12	14
3 - Regular	10	18	12	26
2 - Poor	14	18	7	23
1 - None	30	25	22	9

Table II - Proportion of patients with satisfactory knowledge about some aspects of the beta-thalassemia trait, grouped according to sex, educational level at the time of counseling, educational level at the time evaluation, type of professional who provided counseling, and time after genetic counseling.

Variable	Aspect	Name of the alteration	Meaning of beta-thalassemia trait	Health precautions	Reproductive precautions
Sex	Male	12/27	13/27	18/27	16/27
	Female	44/73	44/73	53/73	52/73
Educational level (at counseling)	Elementary school	29/59	29/59	41/59	36/59
	High school	12/25	15/25	16/25	18/25
	College	13/16	13/16	14/16	14/16
Educational level (at evaluation)	Elementary school	21/46	22/46	31/46	28/46
	High school	15/28	14/28	18/28	19/28
	College	20/26	21/26	22/26	21/26
Professional	Physician	34/54	34/54	41/54	36/54
	Biologist	22/46	23/46	30/46	32/46
Time	> 5 years	30/47	30/47	37/47	32/47
	< 5 years	26/53	27/53	34/53	36/53

the scarcity of systematic population screening programs for the detection of these carriers and of genetical-clinical orientation.

We found considerable involvement of the families in the process of genetic counseling, with satisfactory percentages of examination of partners and children.

The present data also demonstrate that the genetic counseling process offers a good opportunity for the identification of new beta-thalassemia trait cases. Indeed, each thalassemic patient brought an average of two other persons for examination, with the rate of positivity for beta-thalassemia trait being 45% among these individuals. This screening index was higher than that reported for the Rochester program in the U.S. (Rowley *et al.*, 1991).

The results obtained for the long-term evaluation of the genetic counseling deserve careful analysis. For example, even though 65% of the thalassemic patients who married after genetic counseling brought their spouses for examination, in most cases (82%) this examination was performed after

marriage. This demonstrates that genetic counseling did not have a significant effect on the choice of a spouse, a result also observed in Italy, Greece, and Cyprus (Barrai and Vullo, 1980; Angastiniotis *et al.*, 1986; Modell, 1990).

Although in some cases the spouse was examined before marriage, it is unlikely that a positive result would have affected the couple's decision. In Italy, Greece and Cyprus, in a study of marriage desistance rates, less than 5% were observed in this situation (Modell, 1990). On the other hand, 75% of the thalassemic patients who had children after genetic counseling submitted their children to laboratory investigation of thalassemia, without a significant difference between sexes. This demonstrates the usefulness of genetic counseling for the diagnosis and treatment of children.

The significant excess of women in the series may be attributed to their increased interest in genetic counseling and also to the greater manifestation of anemia in females, resulting in a higher participation rate at the Hemoglobinopathy Service at University of

Campinas (Ramalho *et al.*, 1985). It should be pointed out, however, that there was no preferential evaluation of women since the sex ratio did not differ significantly between evaluated and non-evaluated patients.

Cognitive evaluation analyzed as a whole revealed that carriers of the beta-thalassemia trait better assimilate information of a practical nature (health precautions and reproductive precautions) than information of an academic nature (name of the disorder, meaning of beta-thalassemia trait). Curiously, all patients knew they had a blood disorder and practically all had kept the identification card they had received during genetic counseling. This fact compensates, at least in part, for their lack of academic knowledge about thalassemia. Thus, supplying explanatory documentation proved to be an extremely useful procedure in the process of genetic counseling.

No significant effects regarding patient sex, educational level, time after genetic counseling, or type of professional (physician or biologist) who provided counseling were observed in this cognitive evaluation.

Despite the methodological differences, the results of the present cognitive evaluation agree with those reported by Barrai and Vullo (1980) in Italy and by Rowley *et al.* (1984) in U.S. Indeed, Kessler (1989), in a review of the literature after 1979 based on a large number of genetic counseling programs, observed that, despite methodological differences, all of these programs fulfilled their educational objectives, although they were less effective in terms of their eugenic objectives.

ACKNOWLEDGMENTS

The authors wish to thank Drs. Rosa Chelminsky Teixeira and Cristina Martins, as well as the Social Service of the Blood Center of UNICAMP for their collaboration.

Publication supported by FAPESP.

RESUMO

Avaliou-se no presente trabalho o aconselhamento genético fornecido a 200 brasileiros adultos com o traço talassêmico beta. Observou-se uma boa participação da família dos talassêmicos no processo de aconselhamento genético, com exame do cônjuge e dos filhos em 74% e 89% dos casos, respectivamente. Cada propósito trouxe em média dois parentes para exame.

A avaliação a longo prazo, um a 13 anos após o fornecimento do aconselhamento genético, pôde ser realizada em

50% da casuística. Observou-se nessa subamostra que 65% dos talassêmicos que se casaram após o aconselhamento genético trouxeram o parceiro para exame. Em 82% dos casos, esse exame foi realizado somente após o casamento, sem influir na escolha do cônjuge. Da mesma forma, 75% dos talassêmicos que tiveram filhos após o aconselhamento genético trouxeram a criança para exame.

A avaliação cognitiva foi satisfatória em mais de 2/3 da casuística no que se refere às informações de ordem prática, sem variação significativa com o sexo, escolaridade, tempo após o aconselhamento genético e profissional médico ou biomédico que forneceu o aconselhamento. Já as informações de ordem acadêmica foram assimiladas satisfatoriamente por cerca de 50% da casuística.

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(Received May 2, 1994)