Couples at risk for spinocerebellar ataxia type 2: the Cuban prenatal diagnosis experience

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Abstract Cuba reports the highest worldwide prevalence of spinocerebellar ataxia type 2 (SCA2) and the greatest number of descendants at risk. A protocol for genetic counseling, presymptomatic testing, and prenatal diagnosis of hereditary ataxias has been under development since 2001. Considering that the revision of the experience with prenatal diagnosis for SCA2 in Cuba would enable comparison of ours with international findings, we designed a descriptive study, based on the retrospective revision of the medical records belonging to the 58 couples that requested their inclusion in the program, during an 11-year period (2001–2011). Most of the participants in the prenatal diagnosis program were known presymptomatic carriers, diagnosed through the presymptomatic testing in the

same period of study, for an uptake among them of 22.87 % (51 out of 223). In 28 cases, the fetuses were carriers, 20 of these couples (71.43 %) decided to terminate the pregnancy; the rest continued the pregnancy to term, this resulting in a predictive test for their unborn children. A predominance of females as the at-risk progenitor was observed. Except for a slightly lower average age, the results attained in the Cuban SCA2 prenatal diagnosis program resulted similar to the ones reported for Huntington disease in other countries. It is necessary to have easy access to the Cuban program through its expansion to other genetic centers along the island. Future research is needed to evaluate the long-term impact of both the predictive testing in unborn children and the selection of other reproductive options by the at-risk couples.

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Introduction

In Cuba, the National Network of Medical Genetics serves the entire country; it includes more than 100 clinical geneticists and at least two health professionals (medical doctors, nurses, special educators, biologists, and psychologists) with the degree of master in genetic counseling per municipality (Lantigua et al. 2007). Among other roles, genetic counselors develop a continuous research work in their communities, identifying individuals or families with increased genetic risk, especially women at reproductive age, who receive a multidisciplinary attention in order to treat the modifiable risk factors.

When a Cuban woman gets pregnant, she is immediately assessed by a team of health professionals that includes a family doctor, a gynecologist, a clinician, an estomatologist, a social worker, a psychologist, and, more recently, a genetic

counselor. This strategy allows the early diagnosis and/or prevention of genetic disorders and birth defects. Furthermore, once the baby is born and discharged from the hospital, he/she is followed by the family doctor and the pediatrician at the community. The genetic counselor examines him/her at 1 month of age looking for any possible defect, in which case the child is referred to the clinical geneticist office.

Cuba reports the highest worldwide prevalence of spinocerebellar ataxia type 2 (SCA2; 6.57 cases per 10^5 inhabitants) and the greatest number of descendants at risk (7,173). It is an adult-onset neurodegenerative condition mainly characterized by a progressive cerebellar syndrome (ataxic gait, cerebellar dysarthria, dysmetria, and dysidiadochokinesia) associated with saccadic slowing, peripheral neuropathy, and cognitive disorders (Velázquez et al. 2009, 2011; Magaña et al. 2013).

In order to provide with a specialized attention to the SCA2 Cuban families, the National Center for the Research and Rehabilitation of Hereditary Ataxias (CIRAH) was created in 2000. It is located in Holguín province, where the greatest number of affected individuals comes from, due to a founder effect (Velázquez et al. 2009). In 2001, a multidisciplinary team at the CIRAH designed a protocol for genetic counseling, presymptomatic testing (PST) and prenatal diagnosis (PND) of hereditary ataxias (Paneque et al. 2007a). The predictive testing protocol was written in accordance with the international guidelines for predictive testing in Huntington disease (HD), Machado–Joseph disease and other hereditary ataxias (European Community Huntington Disease Collaborative Study Group 1993; Sequeiros 1996).

The CIRAH functions as a tertiary level center, at-risk consultands are usually first counseled by family doctors and genetic counselors at their communities, then they are referred to the municipal or provincial centers of genetics along the country, where genetic counseling is also provided, and finally individuals interested in predictive testing come to our center to request it. Nevertheless, some patients assist directly to the center without previous contact with the aforementioned services, these cases present with a lower level of knowledge about the predictive testing program, being therefore tributaries of more wide pretest counseling sessions.

HD is the first adult-onset, autosomal-dominant disorder for which predictive testing was an option, subsequently the developed protocols were extended to reach other adult-onset disorders (Creighton et al. 2003). Given this fact, the revision of the 11-year experience with PND for SCA2 in Cuba would enable comparison of ours with international findings.

Materials and methods

A descriptive study was designed, based on the retrospective revision of the medical records belonging to the 58 couples

that requested their inclusion in the SCA2 PND, during an 11-year period (2001–2011). The sociodemographic data, uptake, and outcome of tests were gathered from the genetic database.

The protocol for the Cuban predictive testing program has been published elsewhere (Paneque et al. 2007b). Access to PND was given to couples with at least one member carrying the *ATXN2* expanded gene (either clinically affected or in a presymptomatic stage), both members attending in agreement and expressing their intention to terminate the pregnancy were the fetus diagnosed as a carrier of the SCA2 mutation.

The protocol for PND that was used during the period of study included at least two genetic counseling sessions, as well as psychological screening/diagnostic evaluations prior to genetic testing (in order to estimate whether consultands were able to handle results, and to accurately estimate the real willingness the couple had regarding termination of pregnancy). Apart from the psychological test batteries, an anamnesis guide was used to obtain sociodemographic data, psychological antecedents, and personal history of both members of the couple.

The amniocentesis to obtain the amniotic liquid sample was performed between weeks 16 and 20 of gestation at the Provincial Centre of Genetics of Holguín in all the cases. Chorionic villus sampling is not available in Cuba; this impeding an earlier diagnosis, together with the fact that many of the at-risk subjects requested their inclusion in the PST in the context of an ongoing pregnancy. At disclosure, the participants were informed of both fetal alleles' sizes.

Psychological follow-up evaluations were offered at 1 week, 4 weeks, 6 months, and 1 year after disclosure of the genetic testing results. All participants were informed about the PND procedures and protocol, as well as the possibility of using information from the clinical records in clinical research; they gave their separate written consent for both. The study was approved by the Institutional Ethics Committee. Data analyses were performed using the software STATISTICA 6.1 (USA, 2003) and included descriptive statistics and proportion comparisons through χ^2 test. Significance was defined for $p < 0.05$.

Results

Prenatal diagnosis uptake and outcome

Among the 58 couples that requested their inclusion in the PND, there was a member clinically affected by SCA2 in seven (12.07 %) and one presymptomatic member in 51 (87.93 %). Considering the 223 SCA2 presymptomatic carriers diagnosed in this population in the same period of study (Cruz et al. 2013), we estimated an uptake among known carriers of around 22.87 % (51 out of 223).

If we take into account that 103 presymptomatic carriers did not have children when they were diagnosed and that 46 of them took the PND, an uptake for PND among known carriers without children of around 46.19 % can be estimated.

Some couples took the test more than one time, increasing the number of inscriptions in the program to 72 (Fig. 1); 2 cases had three studies (3.45 %), 10 cases had two studies (17.24 %), while 46 cases had only one study (79.31 %).

Three positive results were obtained in one of the couples that took three PNDs and they decided termination of all pregnancies. In the second couple, the first time they were tested, the result was positive and the couple decided to terminate the pregnancy. The second time, the test was also positive and the last one resulted non-informative. In both last cases, they continued to term.

Four couples lost the product of their conception to a miscarriage at 10, 11, 16, and 17 weeks of pregnancy. Risk factors for these events could not be identified. In three cases, the carrier parent had alleles sized 39 or more CAG repeats (39, 40, and 43 CAG repeats). In another couple, the pregnant woman was at risk for miscarriage, so they decided to avoid the amniocentesis and withdrew.

In this way, 67 amniocentesis were performed between the weeks 16 and 20 of pregnancy (mean, 17.4 weeks). Two couples withdrew with 19 weeks of pregnancy previous to the communication of results session—in one of them, the female was 25 years old, already affected, and without children; in the other, the female was a presymptomatic patient, 37 years old, and with one previous child.

The results of 65 tests were informed. In 28 cases (43.08 %), the fetuses were carriers. Twenty of these couples (71.43 %) decided to terminate the pregnancy, while the

eight left (28.57 %) continued to term. In one of the cases, the female carrier took the final decision of continuing, in disagreement with her husband; while in other, the male carrier pressured his wife into terminating when her desire was to continue.

Due to maternal blood contamination of the samples during amniocentesis, 11 studies were non-informative. Among them, nine continued to term (81.82 %) and two decided to terminate the pregnancy (18.18 %). A second amniocentesis was offered to the nine couples whose first test results were delivered before 22 weeks of pregnancy, among them two couples decided to take a second test, the shallow aspect of the amniotic liquid due to the previous maternal blood contamination avoided the establishment of a definitive diagnosis. The two cases who decided to terminate the pregnancy were among the ones who received a second amniocentesis offer, but they did not agree to it.

In 26 cases, the fetuses were diagnosed as noncarriers. They all continued to term. The 61.11 % of the PNDs have been performed in the last 4 years (Fig. 2).

Test-positive fetus carried to term

The couples that decided to carry the pregnancy of a test-positive fetus to term had some characteristics in common: in all the cases, the gender of the carrier progenitor was female, they were married or in a common-law relationship, their educational level was secondary school or higher, and the majority (seven out of eight) were presymptomatic carriers (the left case was clinically affected). Six out of eight were nonreligious (Table 1). Their average age was 27.12 years (SD, 7.6 years; range, 16–37 years).

Seven cases did not have children before testing. The other subject had had two children before the PST and PND were available; she was the only among seven at-risk individuals who requested the PST out of the context of an ongoing pregnancy, and she was diagnosed as a presymptomatic carrier with an intermediate allele of 32 CAG repeats (genotype 22/32). Later, she decided to take the PND for her third

Fig. 1 Outcome of the Cuban program for the prenatal diagnosis of SCA2 in an 11-year period (2001–2011)

Fig. 2 Participants in the prenatal diagnosis program according to the uptake year

Table 1 Social and demographic characteristics of participants in the prenatal diagnosis program

Prenatal diagnosis program					
Carrier/affected progenitors			Progenitors of test positive fetus carried to term (<i>n</i> =8)		
Variable	<i>n</i>	%	Variable	<i>n</i>	%
Age at the test moment (<i>n</i> =72)			Age at the test moment		
<18	3	4.16	<18	1	12.5
18–30	49	68.06	18–30	4	50
31–37	20	27.78	31–37	3	37.5
Gender of the carrier progenitor (<i>n</i> =58)			Gender of the carrier progenitor		
Female	43	74.14	Female	8	100
Male	15	25.86	Male	0	0
Marital status (<i>n</i> =58)			Marital status		
Married	24	41.32	Married	2	25
Common law	34	58.62	Common law	6	75
Children before testing (<i>n</i> =72)			Children before testing		
None	53	73.61	None	7	87.5
One	16	22.22	Two	1	12.5
Two	2	2.78			
Three	0	0			
Four	1	1.39			
Education (<i>n</i> =72)			Education		
Illiterate	0	0	Secondary school	2	25
Primary school	5	6.95	Pre-university school	1	12.5
Secondary school	15	20.83	Technician	3	37.5
Pre-university school	33	45.83	University	2	25
Technician	6	8.33			
University	13	18.06			
Religion (<i>n</i> =58)			Religion		
Religious	4	6.9	Religious	2	25
Nonreligious	54	93.1	Nonreligious	6	75

pregnancy and the fetus was shown to be also a carrier of the 32 CAG repeats intermediate allele (genotype 22/32). The couple decided to carry the pregnancy to term; their decision was mainly based in the late age at onset of the disease they had observed in her affected grandfather with 32 CAG repeats (after his 60s; Cruz et al., under review).

The clinically affected case had been diagnosed as homozygous (genotype 32/36), when the fetal positive test result was disclosed (genotype 23/32) the couple decided to carry the pregnancy to term because although expanded, the 32 CAG repeats allele was the shortest allele the fetus could most probably inherit, since intergenerational contractions of the CAG repeats are infrequent (Velázquez et al. 2009).

Two cases had taken the PST in the context of an ongoing previous pregnancy and had terminated those pregnancies. The first one, aged 13 decided to terminate her first pregnancy, without taking the PND, once she knew she was a mutation carrier; now at the age of 16 years, she requested the PND for her second pregnancy, the fetus was test positive and she

continued the pregnancy to term against her husband's will. The second case took her first PND at the age of 26 years, opting for the termination of pregnancy once known the fetal positive test result; this time at 28 years of age, she decided to carry to term her second test-positive fetus. The other four cases made a simultaneous request for PST and PND.

An interdisciplinary follow-up (psychologist, neurologist, clinical geneticist, and social worker) was offered at CIRAH to the eight families. Only one of them is currently attending the programmed consultations.

Sociodemographic characteristics

A total of 44 couples were from Holguín province (75.86 %), 5 from Santiago de Cuba (8.62 %), 3 from Granma, 3 from Camaguey (5.17 % each), 1 from Tunas, 1 from Guantanamo, and 1 from Ciudad Habana (1.72 % each; Fig. 3). Except for Ciudad Habana, the rest are provinces close to Holguín.

Fig. 3 Participants in the prenatal diagnosis program according to the province of origin

The average age was 26.67 years (SD, 5.4 years; range, 16–37 years). Three teenagers were included (4.16 %), 49 women between 18 and 30 years (68.06 %), and 20 between 31 and 37 years (27.78 %; Table 1).

Two teenagers had participated in the presymptomatic testing program; after their inclusion in the PND, one had a miscarriage and the other decided to continue the pregnancy of a carrier fetus to term. The third teenager was a clinically affected patient whose fetus resulted to be noncarrier, thus she continued to term.

In 43 cases (74.14 %), the carrier progenitor was the women and only in 15 cases (25.86 %) was the men (χ^2 : 27.03; $p=0.0001$). All participants were married (41.32 %) or in a common-law relationship (58.62 %). Most of the participants did not have children yet at the moment of the PND (73.61 %): 46 carriers and the 7 affected individuals. The pre-university school level predominated (45.83 %) and only four women (6.9 %) referred to have religious beliefs.

Discussion

Prenatal diagnosis for SCA2: what have we learned?

Most of the participants in the PND come from the PST program, while the minorities are childless-affected patients. If we consider that mean age for the onset of the disease is 33 years (Velázquez et al. 2011), it is possible that many affected patients had gotten descendants before the PND was available. Though, it could also be the result of the reduction in their fitness once the cerebellar syndrome begun.

A similar predominance of carriers or at-risk individuals has been observed for the PND of HD: in 14 years, only six PND were performed in Greece, all the parents were aware carriers (Panas et al. 2011). In Australia, five carriers had a total of six prenatal tests (Richards and Rea 2005). In Leiden, the Netherlands, 72 prenatal tests were performed during 10 years in 43 couples, 26 were proven carriers and 17 at-risk persons (Maat-Kievit et al. 1999). In Britain, 146 prenatal tests were reported in 4 years, 45 % in carriers and 54 % in at-risk parents (Simpson et al. 2001). A European

collaborative study reported an amount of 305 prenatal tests for the period 1993–1998 in six countries—in 51 % of the cases, the prospective parent was an asymptomatic carrier; in 42 %, the parent remained at risk; and in only 6 %, the parent showed clinical features of HD, 1 % of the parents having an intermediate allele (Simpson et al. 2002).

Estimated uptake for SCA2 PND among carriers duplicates when we analyze the uptake among childless carriers, being the latter the main candidates for PND. Anyway, these are very low figures in comparison with the expected uptake among carriers for this population: in 2001, previous to the beginning of the program, our group developed a research aimed at determining the level of acceptance of PND in couples at risk. A total of 186 at-risk individuals were studied, as well as 40 of their couples, the 31.72 % of at-risk subjects did not want to have children and 68.28 % wanted. Among them, only one (0.79 %) would not request PND, the rest accepted it (99.1 %; Paneque et al. 2001).

In other programs for HD predictive testing, PND is neither a frequent request, the uptake being also low. (Yapjakis et al. 2002; Simpson et al. 2002; Creighton et al. 2003; Richards and Rea 2005; Panas et al. 2011). In general, the proportion of carriers using PND has been less than 20 % (Maat-Kievit et al. 1999; Harper et al. 2000; Simpson et al. 2001; Evers-Kiebooms et al. 2002; Creighton et al. 2003; Decruyenaere et al. 2007). Similarly, the uptake has remained lower than predicted by surveys of at-risk persons' intentions with regard to such testing (Evers-Kieboom et al. 1987; Kessler et al. 1987; Hayden 2000; Simpson et al. 2001).

In Portugal, 61 % of at-risk individuals for Machado–Joseph disease (MJD) living in the Azores Islands would not have children if they carried the mutation. Acceptance of PND and termination of pregnancy in the presence of the mutation in the fetus was low for this population (Lima et al. 2001; Rolim et al. 2006).

Around 30 % of the participants in the SCA2 PST program had religious beliefs, some of them contraries to PND and termination of pregnancy (this explaining the low percentage of religious persons in the PND), and the 53.81 % of the identified carries already had children (Cruz et al. 2013). At the same time, during genetic counseling sessions, the

potential risks that the amniocentesis and abortion procedures bring to the fetus and to the mother are discussed with the couple. As pointed by Tibben (2007), after in-depth discussion about the couple's intentions regarding pregnancy termination and the possible consequences of prenatal testing, many couples may decide not to proceed with such testing. These are factors probably related to the low uptake in the Cuban SCA2 PND program.

A European collaborative study found that identified HD carriers had significantly fewer postresult pregnancies than noncarriers (Decruyenaere et al. 1995; Evers-Kiebooms et al. 2002). This would also explain the low uptake of PND among carriers. Other reported reasons in deciding against HD PND have been: the hope for an effective future therapy in the child's lifetime, the reluctance to pregnancy termination for an adult-onset condition, the fear of social stigma, the complete denial of child bearing, and the possible psychological defense mechanisms of mutation carriers and partners (Adam et al. 1993; Maat-Kievit et al. 1999; Simpson et al. 2002; Evers-Kiebooms et al. 2002; Creighton et al. 2003; Decruyenaere et al. 2007; Panas et al. 2011).

The fact that some of the couples took more than one PND evidences their strong desire to not passing the mutated gene into the next generation, as well as their confidence in the program. We believe that this could also be a self-selected population with better knowledge about the diagnosis process, the disease, and the reproductive options.

The couple with three PNDs and adverse results in all of them requested a tube ligation after the last PND. Reproductive technologies like in vitro fertilization with pre-implantation genetic diagnosis (PGD) are available for SCA2 since 2008 (Moutou et al. 2008). This could be a good option for such couples, but PGD is not currently available on the island, for their costs are prohibitive for developing countries.

It is known that two thirds of all pregnancies are lost mainly due to chromosomal aberrations (Boué et al. 1975). Regarding the specific finding of four miscarriages in couples that had requested the PND, we speculate that some of these fetuses could have carried massive expansions that avoided fetal survival through different mechanisms. The reasons for this idea come from the lack of risk factors in the couples and the presence of large expansions in three of the at-risk parents, similar to what was described for children carrying massive expansions, whose affected parents had alleles with 40 CAG repeats or larger (Paciorkowski et al. 2011). Furthermore, miscarriages have taken place with a higher frequency than expected in other conditions due to dynamic mutations such as: fragile X syndrome (Loesch and Hay 1988; Terracciano et al. 2004), myotonic dystrophy (Rudnik-Schoneborn et al. 2006), and Friedreich ataxia (Cruz et al. 2010).

Taking into account the informative studies, carrier and noncarrier fetuses were almost equally frequent (28

carrier/26 noncarrier). This result significantly differs from the one that we obtained in the SCA2 PST, where non-carriers were 2.44 times more frequent than carriers (Cruz et al. 2013).

In many of the international PST programs for HD, individuals with a negative test result were more frequent than individuals with a positive one (Harper et al. 2000; Tassicker et al. 2006; Alonso et al. 2009; Futter et al. 2009; Dufrasne et al. 2011). Brazil, on the contrary, reports rates of heterozygotes in SCA3 PST very similar to those observed in Mendelian segregation (51 %), which could be in accordance with the hypothesis of a preferential transmission of expanded alleles over the normal ones (Rodrigues et al. 2012).

SCA2 usually starts during adulthood, with a mean onset age of 33 years (Velázquez et al. 2011). In the case of SCA2 PST, the mean age at the time of testing was 37.24 years (Cruz et al. 2013); therefore it is probable that carriers at this age are in denial about their genetic condition, despite the presence of slight symptoms, this psychological mechanism keeping them away from taking the test. Noncarrier subjects, on the contrary, lack symptoms and are more prone to self-select themselves to request the test because their risk perception diminishes at the time their age increases. This processes (psychological denial and self-selection) are both absent in the fetuses, this explaining the almost 50 % frequency observed.

Similarly to other predictive testing programs (Dufrasne et al. 2011), in ours, pregnant women are encouraged to postpone SCA2 presymptomatic testing, but all the couples that went to PND had expressed their intention to terminate the pregnancy being the fetus a carrier. Nevertheless, once the result was received, some couples decided to continue to term. One possibility for this is that couples feel pressure because in some way their inclusion in the PND is conditioned to the desire of terminating the pregnancy should the fetus be a carrier, which is sustained in the aim to protect the autonomy of the unborn child. Then either being in doubt or sure that they will not terminate, they could lie about their true intentions to get included in the program (Erez et al. 2010).

The nondirective genetic counseling process during the pretesting phase of the PND protocol conceives the voluntariness of the consultands along the whole process a crucial aspect, beginning with the test request. Trained professionals in charge of the program discuss in deep with the consultands the information about the test implications. Reinforcement of this information takes place with the discussion of the informed consent during the second genetic counseling session. Other reproductive options are discussed as well. Along the programmed consultations, they receive professional support from the psychologist and psychiatrist and discuss their decisions with them, particularly the one related with termination of pregnancy and the risks associated to the amniocentesis

procedure. The couple's decision making is supported all the time by the genetic counselor and all their choices are equally respected.

Quite often, at-risk subjects request their inclusion in the SCA2 PST in the context of an ongoing pregnancy, having a very short period for psychological adjustment to the carrier diagnosis; it was the case of half of the pregnancies with gene-positive fetus carried to term in our program. In Portugal, 7 % of the consultands who requested PST for late-onset neurological disorders (like HD, familial amyloid neuropathy type I, MJD, etc.) attended with an ongoing pregnancy and made also a simultaneous request for PST and PND (Sequeiros et al. 2006). In France, 5 % of the requests for HD and spinocerebellar ataxias PST occurred also in the context of pregnancy (Lesca et al. 2002). It is necessary to reinforce our educational actions and to develop genetic counseling activities at the community level focused in those individuals interested in preventing the transmission of SCA2, and aiming at avoiding the simultaneous request of PST and PND.

It is possible that at the moment, when our consultands request the inclusion in PND, they are honestly considering termination, but the amniocentesis is performed between 16 and 20 weeks of pregnancy and the molecular diagnosis will yet take another 2–3 weeks; consequently, they will receive the result in an advanced gestational age. By then, the woman may have experienced the fetal movements; the family, neighbors, and colleagues are aware of the pregnancy because of the abdomen size; and the fetus has probably a known sex and a name—so what was at first a clear decision, gets blurred as time passes by and may convert itself in the opposite by the time when the result is received.

The nontermination of an affected pregnancy has been also a reality in countries where the HD PND has been offered; in Europe, 123 out of 131 unfavorable results were terminated (Simpson et al. 2002); in Britain, 61 out of 66 (Simpson et al. 2001); and in Canada, 11 out of 12 (Creighton et al. 2003). Nevertheless, in the Netherlands and Australia, all pregnancies with an unfavorable result were terminated (Maat-Kievit et al. 1999; Richards and Rea 2005).

The nontermination of pregnancy results in a predictive test for the unborn child, thus denying the child's autonomy to make his or her own decision about testing as an adult and bringing about ethical, legal, and psychosocial implications (Clarke et al. 1994; Simpson et al. 2002; Creighton et al. 2003; Richards and Rea 2005). A long-term clinical and psychosocial follow up must be offered to these cases and a research project must be conducted aiming at investigating the potentially harmful effects of this scenario over time (Creighton et al. 2003).

The decision to continue the pregnancy to term in the majority of the cases where a non-informative result was

obtained underlies the strong motivation of having children in these individuals where the risk of passing the mutated gene to their descendants could not be ruled out.

In Cuba, therapeutic abortion is allowed when it is performed previous to the 26 weeks of pregnancy. The communication of a positive test result to a couple after this gestation time would not lead to the termination of pregnancy if the fetus was a carrier, this is why only couples who received their first test result previous to the 22 weeks of pregnancy were offered a second amniocentesis.

At the same time, the two aborted fetuses had a 50 % probability of being healthy. The trauma associated with termination of any pregnancy is considerable (Tolmie et al. 1995; Simpson et al. 2002); therefore making the decision of terminating or continuing the pregnancy in cases with a non-informative result is a new challenge for the at-risk couples.

The increase in the PND uptake by presymptomatic subjects in the last 4 years may be related to its general acceptance in the at-risk population, as well as the favorable impact of the test in other family members. Also, the attained experience in the collaborative work with the genetic center where amniocentesis is performed allows better articulation in the procedures.

Sociodemographic profile of participants in PND

Most participants in the PND come from Holguín province (Fig. 3), which is related with the high prevalence of the disease in this province due to a founder effect (Velázquez et al. 2009). Except for Camaguey and Ciudad Habana, there have not been PND requests from the rest of the provinces of the central and western regions in the country. An explanation for this could be found on the lower prevalence of the disease in these regions together with the lack of previous participants, whose shared experiences could have brought a positive impact in other at-risk couples. Another possibility is the fact that the SCA2 PND is only offered at the CIRAH in Holguín province; this way, couples coming from distant places could rethink the decision of requesting the PND due to the necessity of attending several in-person consultation sessions at the center.

The National Network of Medical Genetics constitutes a strength of the Cuban health system, since genetic counselors reach every community in the country; this is why the spread of the SCA2 PND program to some other genetic centers located along the island is currently being considered.

Average age resulted slightly lower in our PND program than in other programs for HD (Simpson et al. 2002; Creighton et al. 2003); nevertheless, it was similar to the average maternal age in Cuba (26 years; Anuario Estadístico de Cuba 2009).

The offering of predictive testing to minors for adult-onset conditions is a controversial subject (Borry et al.

2009; Parker 2010; Sequeiros et al. 2010); the inclusion of three minors in the PND program was based on their intention to terminate the pregnancy if the fetuses were a carrier.

There was a clear predominance of women as the SCA2 carrier progenitors in the couples requesting the PND. This result is in agreement with the finding of a female predominance in the PST as well (Cruz et al. 2013), emphasizing their greater capability to face difficult decisions and their consequences, as well as their interest in preventing the transmission of the disease to their descendants, together with the females' assertive role in the Cuban society (Paneque et al. 2007b).

Something similar has been reported for HD, suggesting reluctance by male carriers to burden their partners with the invasive procedures of prenatal testing and pregnancy termination, or men choosing reproductive options other than prenatal testing since they differ in response to information about risks to their own health, preferring to cope with denial rather than confronting the issues of being at risk. On the other hand, these findings could be explained by women having a greater willingness to deal with the emotional consequences of risk alteration and more intimate involvement with reproductive and child care decisions (Bloch et al. 1989; Maat-Kievit et al. 1999; Simpson et al. 2002; Creighton et al. 2003; Richards and Rea 2005). These results are in contrast with the study by Decruyenaere et al. (2007), which reported that male carriers were more likely to choose for PND whereas females were more likely to refrain from having children.

The finding that all participants were involved in a relationship and attended together the PND, highlights the importance that family support has for individuals interested in such predictive studies. Nevertheless, the disagreement regarding termination of pregnancy observed in two couples after the communication of results session, indicates one more time that it is a difficult decision to make, sometimes resulting quite different what individuals thought they would do when they requested the test, and what they finally decided to do once the results were known.

The educational level of the Cuban population is above secondary school (Torres 2011). Furthermore, most of the couples attending the PND presented an educational level above the average, which may have influenced the comprehension of provided genetic counseling.

Conclusions

Except for a slightly lower average age, the results attained in the Cuban SCA2 prenatal diagnosis program resulted similar to the ones reported for HD in other countries. The prenatal diagnosis seems to be a valuable tool to prevent the transmission of the disease into the next generation for those individuals who choose to do that, especially in developing

countries with no access to pre-implantation genetic diagnosis, as it is the case of Cuba.

Despite the fact that Cuba counts with a National Network of Medical Genetics and that genetic counseling education is provided at the community level, the SCA2 prenatal diagnosis uptake is low, particularly in the central and western provinces. This highlights the complexity of the decision making process, at the time that suggest the necessity of easing the access to the program through its expansion to other genetic centers along the island.

Educational actions and genetic counseling activities at the community level aiming at avoiding the simultaneous request of PST and PND must be reinforced. Future research is needed to evaluate the long-term impact of both, the predictive testing in unborn children (which resulted from the nontermination of an affected pregnancy), and the selection of other reproductive options by the at-risk couples.

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Compliance with ethical guidelines The prenatal diagnosis procedures are in compliance with the laws existing in Cuba.

Conflict of interest statement Authors declare no conflicts of interest.

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