Prevalence of Use of Preimplantation Genetic Diagnosis in Unidade Clínica de Paramiloidose from Centro Hospitalar do Porto

Prevalência do Uso de Diagnóstico Genético Pré-Implantação na Unidade Clínica de Paramiloidose do Centro Hospitalar do Porto

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ABSTRACT

Introduction: The Familial Amyloid Polyneuropathy, with the world's largest focus in Portugal, is recognized by the National Board of Assisted Reproductive Technologies as a serious disease eligible for Preimplantation Genetic Diagnosis. This study aims to determine the prevalence of the use of Preimplantation Genetic Diagnosis in FAP carriers followed in Unidade Clínica de Paramiloidose, Centro Hospitalar do Porto, and to identify the associated factors.

Material and Methods: Between January and May 2013, a representative sample of Portuguese Familial Amyloid Polyneuropathy carriers, aged between 18 and 55 years, was systematically recruited. The analysis is based on 111 carriers with previous familial diagnosis, who reported having ever tried to get pregnant after 2001. Data on sociodemographic characteristics and use of Preimplantation Genetic Diagnosis were collected through a self-administered questionnaire. Proportions were compared using the chi-square test. Crude and adjusted odds ratios (OR) and the respective confidence intervals of 95% (95% CI) were estimated using multivariate logistic regression.

Results: The prevalence of use of Preimplantation Genetic Diagnosis was 20.7% (95% CI: 13.6-29.5). After adjustment, a household income above 1000 €/month (OR = 11.87; 95% CI 2.87-49.15) was directly associated with the use of Preimplantation Genetic Diagnosis, while carriers with an individual diagnosis (OR = 0.15; 95% CI 0.04-0.57) and children born after 2001 (OR = 0.07; 95% CI 0.02-0.32) revealed a prevalence of use significantly lower than those with a individual diagnosis and children born before 2001.

Discussion: The low prevalence of use of Preimplantation Genetic Diagnosis, as well as the less frequent use of the technique by those with a lower household income, shows the importance of improving access to Preimplantation Genetic Diagnosis in the case of Familial Amyloid Polyneuropathy.

Conclusion: This work contributes to increase the sensitivity of health professionals around the use and accessibility to Preimplantation Genetic Diagnosis among Familial Amyloid Polyneuropathy carriers.

Keywords: Preimplantation Diagnosis; Amyloid Neuropathies, Familial; Genetic Testing; Assisted Reproductive Technologies.

RESUMO

Introdução: A Polineuropatia Amiloidótica Familiar, cujo maior foco mundial é em Portugal, é reconhecida pelo Conselho Nacional de Procriação Medicamente Assistida como uma doença grave elegível para Diagnóstico Genético Pré-Implantação. Pretendemos determinar a prevalência do uso de Diagnóstico Genético Pré-Implantação nos portadores de Polineuropatia Amiloidótica Familiar seguidos na Unidade Clínica de Paramiloidose, Centro Hospitalar do Porto, e identificar os fatores associados.

Material e Métodos: Entre janeiro e maio de 2013, recrutamos sistematicamente uma amostra representativa de portadores entre os 18 e 55 anos. A análise baseia-se em 111 portadores com diagnóstico familiar prévio da doença, que referiram estar envolvidos numa tentativa de gravidez alguma vez depois de 2001. Através de questionário autoadministrado, recolhemos dados sociodemográficos e informações sobre o uso de Diagnóstico Genético Pré-Implantação. Para comparação de proporções, utilizamos o teste de qui-quadrado. *Odds ratios* brutos e ajustados e os respetivos intervalos de confiança de 95% (IC 95%) foram estimados através de regressão logística multivariada.

Resultados: A prevalência de uso de Diagnóstico Genético Pré-Implantação foi de 20,7% (IC 95%: 13,6-29,5). Após ajuste, o rendimento familiar superior a 1000 €/mês (*OR* = 11,87; IC 95% 2,87-49,15) associou-se diretamente ao uso Diagnóstico Genético Pré-Implantação, enquanto portadores com diagnóstico individual (*OR* = 0,15; IC 95% 0,04-0,57) e filhos nascidos após 2001 (*OR* = 0,07; IC 95% 0,02-0,32) revelaram uma prevalência de uso significativamente menor do que aqueles com diagnóstico individual e filhos nascidos antes de 2001.

Discussão: A baixa prevalência de uso de Diagnóstico Genético Pré-Implantação, bem como a utilização menos frequente da técnica por aqueles com um rendimento familiar mais baixo evidenciam a importância de melhorar a acessibilidade ao Diagnóstico Genético Pré-Implantação no caso da Polineuropatia Amiloidótica Familiar.

Conclusão: Este trabalho contribui para o aumento da sensibilidade dos profissionais de saúde em torno do uso e da acessibilidade ao Diagnóstico Genético Pré-Implantação entre os portadores de Polineuropatia Amiloidótica Familiar.

Palavras-chave: Diagnóstico Genético Pré-Implantação; Polineuropatia Amiloidótica Familiar; Testes Genéticos; Procriação Medicamente Assistida.

INTRODUCTION

The world's largest group of Familial Amyloid Polyneuropathy (FAP) occurs in Portugal.[1] This is a chronic autosomal dominant, multisystem and gradually disabling disease (in other words, there is a 50% probability of

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transmission of the gene to the offspring) usually presenting between 25 and 35 years of age. FAP was considered in 1976 as a public health issue in Portugal, due to the number of carriers (431 described until 1976) and to the severity of its disabling manifestations.[2] It is estimated the presence of 1,657 patients with FAP in Portugal, according to the most recent mapping (March 2011 – carried out at the *Unidade Clínica de Paramiloidose* (UCP) from the *Hospital de Santo António (HSA)* in *Centro Hospitalar do Porto (CHP)*. From these, 54% are female, 80% are aged under 55 and 27% are asymptomatic. The disease is mostly prevalent in Póvoa de Varzim/Vila do Conde, Braga and Barcelos' municipalities.

Transmission may be avoided when carriers decide not having biological children, when confirmation is undertaken in Prenatal Diagnosis (PND) resulting in a Voluntary Termination of Pregnancy (VTP) when the foetus is affected or when Pre-implantation Genetic Diagnosis (PGD) – allowing for embryo FAP screening and selection before their transfer to the uterus. Based on the importance assigned to genetic paternity in the construction of human individual and collective identity, mainly in the Portuguese society,[3] as well as to emotional and healthcare costs involved in VTP,[4] PGD is available to be used whenever any FAP carrier wishes to have a child.[5]

PGD is available in Portugal since 1997[6] and the first protocol involving its use in FAP was published in 2001.[7] FAP was considered in December 2012 one of the major diseases eligible for PGD by the National Council for Medically-Assisted Procreation (*Conselho Nacional de Procriação* Medicamente Assistida [CNPMA])[8], meeting all the requirements for such classification: FAP induces a significant suffering and/or premature death; its genetic causality has been established and there is a clear relationship between the presence of a genetic change and the presence (or high risk) of disease in carriers; there is a technical possibility of identification of an embryo or oocyte genetic defect, there is over 90% reliability of the genetic screening test and the risk of transmission to the offspring is significantly higher than the risk in general population.[9]

This may allow Medically-Assisted Procreation (MAP) techniques to be made available to these patients, one of the objectives established by the World Health Organization (WHO) for this millennium.[10-12] This issue was considered by the Portuguese Government since the publication of the first legislation regarding the use of these techniques in 2006, together with the standardization of healthcare costs and quality assessment over the subsequent years.[13,14] The PGD must follow a genetic counselling program carried out by a clinical geneticist and compulsory consent from both partners should be obtained.[9] In addition, PGD application must be oriented by a clinical geneticist together with a multidisciplinary team including reproduction medicine specialists, embryologists, clinical geneticists, cytogeneticists and molecular geneticists.[15]

PDG recommendations were published in Feb 2013 by the CNPMA providing data on the number of treatments and their indication, as well as the results of the confirmatory PND, when obtained, to be included on the annual report of the MAP centres.[9] However, there is still no national data register regarding the use of PDG by FAP carriers. Therefore, our study aimed to determine the prevalence of the use of PDG in FAP carriers at the UCP from the CHP and to identify any associated factors.

MATERIAL AND METHODS

Our study was carried out at the UCP from the CHP. Our study's protocol was approved by the Administration Board of the *Centro Hospitalar do Porto*, upon approval by the Ethics Committee for Health and by the Research Coordination Department, as well as by the Clinical Directory. All participants gave their written informed consent at the time of completing the questionnaire.

The number of FAP Portuguese carriers was established in March 2011 by our Department, based on the information collected from the following healthcare units and professionals: clinical units where FAP carriers were followed in Porto and Lisbon; liver transplantation units in Lisbon, Coimbra and Porto, responsible physicians for outpatient FAP departments in the municipalities of Covilhã, Seia, Figueira da Foz, Barcelos and Esposende; *Associação de Paramiloidose* (FAP Association) and their local groups of patients. According to these data, there is an estimated number of 1,657 FAP carriers in Portugal, 64% (n = 1,055) of which are followed by our unit (non-published report).

All our patients aged between 18 and 55 were considered as eligible for inclusion in our study and, in December 2012, 913 patients met these criteria. Between January and May 2013, 271 FAP carriers were consecutively invited to be included in the study, ensuring a 5% significance level and a 95% statistical significance. A representative sample of 266 carriers was systematically selected, corresponding to a 98.2% participation percentage.

The patients were selected at the time of a routine programmed medical control by several specialties (Neurology, Nephrology, Psychiatry and Ophthalmology, among others). Two health professionals were selected to invite the eligible carriers for inclusion in the study, following the unit's normal operation and availability, in order to obtain a participant's daily, consecutive and systematic selection. A program leaflet was handed to every eligible carrier, asking for cooperation and explaining possible doubts.

Patient's demographic and socio-economic data were obtained, based on a self-administered questionnaire,

including data on the reproductive and obstetric history and on PGD use and awareness (including data sources and the reasons for using/not using this technique). Data included patient's gender, age (classified as < 35 and ≥ 35 years of age), place of residence, marital status (single *vs*. married, living-as-a-couple, divorced or widow), level of schooling (≤ 12th year and > 12th year), professional status (employed vs. unemployed, housework, unpaid work, student or retired), family household's monthly income (≤ 1,000 € and > 1,000 €), subjective social class (lower/middle lower *vs*. higher/middle higher), religion (Catholic, Protestant or other Christian *vs*. without religion), number of natural children born upon the 31st Dec 2001 and the use of PND. PGD use was considered as positive when it was referred at least on one pregnancy attempt. FAP's year of individual and familial diagnosis was obtained at our unit's database.

This analysis is based on 111 patients with a life cycle that included the possibility of facing a decision of using or not using the PGD. These were patients with prior family diagnosis describing having been involved at least once in a pregnancy attempt after the 31st December 2001, the year when the first protocol of application of PGD to the FAP was published.[7] Full information regarding all variables included in the final model was available for 107 of these patients.

The statistical analysis was carried out using the STATA 11.0 (College Station, TX, 2009) software. The prevalence of PGD use is shown with a 95% confidence interval (95% CI). Chi-square test was used for comparison of proportions. Gross and adjusted odds ratio (OR) were estimated with 95% CI by logistic regression, in order to assess PGD use-related factors. Multivariate models were built using the variables showing a statistically significant association with the use of PGD in this sample or those that researchers considered to be potential biases to this association. Those variables that did not show an independent association with the use of PGD and that did not bias the effect of the remaining variables were excluded from the final model.

RESULTS

In our study, 61.3% of the patients were female and half of them were aged 35 or above (Table 1). Approximately 70% lived in the municipalities of Braga or Porto and more than 90% had already lived in cohabitation. In our group of patients, 46% had over 12-years schooling, 76.4% were employed and approximately 42% had a household monthly income above 1,000€, while only 13.8% were considered from higher/middle higher social class. More than 95% of FAP carriers referred as following a religion and Catholic religion was more frequently referred (88.3%). Approximately 60 and 85% of the patients were diagnosed with FAP and had children after 2001, respectively. PND was referred by 20% of the patients.

From the 111 PGD-eligible carriers or, in other words, from those with a FAP diagnosis that referred a pregnancy attempt upon the 31st December 2001, a 20.7% prevalence of PGD use was found (95% CI 13.6-29.5). The patients that underwent PGD had mostly over 12-years schooling (73.9% *vs*. 38.6%; $p = 0.003$), over 1,000 € family monthly income (72.7% *vs*. 33.7%; $p = 0.001$) and were considered more frequently in higher/middle higher social class (27.3% *vs*.10.3%; $p = 0.039$) when compared to those that never underwent PGD. FAP carriers diagnosed (39.1% *vs*. 65.9%, $p = 0.019$) and with children born after 2001 (65.2% *vs*. 90.9%, $p = 0.002$) showed statistically significant less tendency to become PGD-users. We did not find any statistically significant differences between PGD-users and non-users regarding gender, patient's age, place of residence, marital status, professional status, religion and PND use (Table 1).

The main factors associated to the use of PGD by FAP carriers are shown in Table 2. Upon adjustment to patient's age, gender and all the variables significantly associated to the PGD use, only the associations regarding family income, the date of diagnosis and child's birth after 2001 remained statistically significant. Therefore, the described statistic effects regarding the schooling level and subjective social class seem to be explained by the effect of income, which stands out as the most relevant socio-economic factor to the use of PGD. FAP carriers diagnosed after 2001 (*OR* = 0.15; 95% CI 0.04-0.57) and with children born after that year (*OR* = 0.07; 95% CI 0.02-0.32) showed a significantly lower prevalence of PGD use when compared to those diagnosed and with children born before 2001, respectively. Household income was directly associated to PGD use by FAP carriers (*OR* = 11.87; 95% CI 2.87-49.15).

DISCUSSION

Our study assessed for the first time ever, to the best of our knowledge, the prevalence of PGD use by Portuguese FAP carriers. Considering that Portugal is the most affected country with the disease involving severe, disabling clinical manifestations with a major impact on patient's quality of life and survival, the prevalence of PGD use is an important indicator. Our results showed that 20% of FAP carriers used PGD and that a higher family income is directly associated to the use of this technique, while an individual diagnosis and a birth after 2001 showed to be inversely associated to the use of PGD. The only publicly disclosed data regarding this issue was an oral presentation at the European Advanced Postgraduate Course on Transthyretin Amyloidosis, held in May 2013 at the CHP (Filipa Carvalho, unpublished data). We found that, between January 1999 and May 2013, 62 male and 36 female FAP carriers underwent PGD at the *Centro Hospitalar de S. João*, the only public

Table 1 - Characteristics of our group of patients as regards the use of PGD

	Total	Users	Non-users	
	n = 111	*n* = 23	*n* = 88	
	n (%)	*n* (%)	*n* (%)	*p*
Gender				
Male	**43 (38.7)**	9 (39.1)	34 (38.6)	
Female	**68 (61.3)**	14 (60.9)	54 (61.4)	0.965
Age (years)				
< 35	**55 (50.0)**	11 (47.8)	44 (50.6)	
≥ 35	**55 (50.0)**	12 (52.2)	43 (49.4)	0.815
Place of residence				
Braga	**39 (35.4)**	7 (31.8)	32 (36.4)	
Porto	**38 (34.6)**	12 (54.6)	26 (29.5)	
Other municipality	**33 (30.0)**	3 (1.6)	30 (34.1)	0.057
Marital status				
Single	**7 (6.3)**	0 (0.0)	7 (7.9)	
Married/Living as a couple/Divorced/Widow	**104 (93.7)**	23 (100.0)	81 (92.1)	0.162
Level of schooling				
≤ 12th year	**60 (54.0)**	6 (26.1)	54 (61.4)	
> 12th year	**51 (46.0)**	17 (73.9)	34 (38.6)	0.003
Professional status				
Employed	**84 (76.4)**	19 (82.6)	65 (74.7)	
Others	**26 (23.6)**	4(17.4)	22 (25.3)	0.428
Household monthly income (€)				
≤ 1,000	**63 (58.3)**	6 (27.3)	57 (66.3)	
> 1,000	**45 (41.7)**	16 (72.7)	29 (33.7)	0.001
Subjective social class				
Lower/lower middle	**94 (86.2)**	16 (72.7)	78 (89.7)	
Higher/higher middle	**15 (13.8)**	6 (27.3)	9 (10.3)	0.039
Religion				
Catholic/Protestant/Other Christian	**107 (96.4)**	23 (100.0)	84 (95.4)	
No religion	**4 (3.6)**	0 (0.0)	4 (4.6)	0.298
Individual diagnosis (year)				
≤ 2001	**44 (39.6)**	14 (60.9)	30 (34.1)	
> 2001	**67 (60.4)**	9 (39.1)	58 (65.9)	0.019
Children born before 31st Dec 2001				
No	**16 (14.4)**	8 (34.8)	8 (9.1)	
Yes	**95 (85.6)**	15 (65.2)	80 (90.9)	0.002
Prenatal Diagnosis (PND)				
No	**84 (80.0)**	14 (77.8)	70 (80.5)	
Yes	**21 (20.0)**	4 (24.2)	17 (19.5)	0.796

Total may not reach 111 due to missing data. PND variable does not reach 111 as 6 patients were involved on an always unsuccessful pregnancy attempt and therefore were not confronted with this option.

Table 2 - Factors associated to the use of PGD by FAP carriers (n = 107)

	Overall OR (95% CI)	Overall OR* (95% CI)
Individual diagnosis (year)		
≤ 2001	1	1
> 2001	0.36 (0.14-0.94)	0.15 (0.04-0.57)
Children born upon 31st Dec 2001		
No	1	1
Yes	0.18 (0.06-0.56)	0.07 (0.02-0.32)
Household monthly income (€)		
≤ 1000	1	1
> 1000	5.15 (1.82-14.57)	11.87 (2.87-49.15)

CI – confidence interval; OR – Odds ratio. * Adjusted to patient's age, gender and all the variables in the table.

healthcare centre where this test is available. In total, 186 PGD cycles were performed (136 cycles followed and 50 non-followed by embryo transfer), 40 clinical pregnancies were confirmed (28 single, seven multiple, three ongoing and two terminations), from which 43 children were born. Therefore, 98 carriers underwent PGD in our unit, at a time when a total of 1,657 FAP carriers were estimated to exist in Portugal (March 2011), 64% (*n* = 1,055) of which were followed at the UCP from the CHP. Our results regarding the prevalence of PGD use in our unit are in line with these data, considering that our patients underwent PGD both at our public healthcare centre and in other private MAP centres.

Our results should be considered within the social, cultural, political and economic context on which the availability of these techniques (and particularly PGD) is based on. Free access (subject to return) to support clinical equipment and full reimbursement of medication is available to patients with 70% or higher disability.[16,17] However, the current public funding of PGD only includes couples with a female partner aged below 40 and with no more than one child in common at the time of undergoing this technique[18] and these therapies are not covered by private health insurances. A price of 2,613 € for each intracytoplasmic sperm injection (ICSI) therapy was established by the Ordinance (*Portaria n.º 67/2011*),[19] lower than the price charged in a private centre of 4,200 € for a complete ICSI cycle, in addition to 450 € for the PGD through embryo biopsy.[20] These factors may certainly explain the use of PGD by FAP carriers with a higher family income.

This conclusion is supported by the results found by a recent systematic review regarding the factors influencing the couple's decision process as regards the use of PGD[21] which emphasizes the importance of cognitive evaluation of the financial costs involved in PGD. This evaluation should include other factors that were not included in our study, namely the estimated time delay to pregnancy, as well as the complex and uncertain information regarding the relatively low success rates and the awareness of the short and long-term risk involved in medical procedures.[22,23] In addition, the emotional responses associated to pain and suffering and the meaning of happiness have an important role in this decision process,[24] as well as the attitudes and social roles regarding the status of the human embryo and the moral acceptability of the use of techniques oriented towards disease-prevention.[25,26] The decision of PGD users is also influenced by factors as the time needed to organize, to program and to attend to medical appointments, as well as the number and type of education and counselling sessions with health professionals (like for instance with genetic specialists and psychologists).[27] Therefore, the identification of major factors influencing the decision regarding the use of PGD shows the complexity, dynamics and interactivity of information processing in this area, as well as the heterogeneity of the meanings assigned by users to genetic risk associated to their reproductive life.[28] These elements are crucial to explain the reason why FAP diagnosis and children born before 2001 are associated to the use of PGD by FAP carriers. These patients may have identified their risk condition or may have been involved in longer-established paternity active approaches with more chances to know the technique and to consider the different reproductive options as they become more aware about the outcomes of the disease.

We should note that all the patients diagnosed after 2001 had a family diagnosis of the disease when they were involved in a pregnancy attempt, which may show a more or less clearly expressed attempt not to know the results of the individual diagnosis before having a child or the perception of FAP as a family heritage. In addition, the failure to use

PGD may be associated to concerns regarding the status of the human embryo and to the possible relationship of this technique to stigmatization, intolerance and discrimination of FAP carriers.[25,26,29] However, these reasons were very rarely selected by the patients to explain not using the PGD and financial costs, lack of confidence on the technique and time delay to pregnancy were the major reasons for such an option.[30] Therefore, it is important to promote the access to PGD, as well as to support awareness and information campaigns aimed to release correct knowledge regarding this technique, particularly among FAP carriers.

CONCLUSION

The low prevalence of PGD use by FAP carriers shows the need to understand how the information is processed by the carriers and how the risk is assessed by the PGD, in order to promote interventions aimed to increase compliance to the technique. In addition, the less frequent use of PGD by carriers with a lower family income shows the importance of improving the access to PGD in FAP in order to prevent spreading of the disease and to reduce disparities regarding healthcare access and use.

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CONFLICT OF INTERESTS

The authors declare that there was no conflict of interests in writing this manuscript.

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REFERENCES

1. Sousa A. Epidemilogia genética da polineuropatia amiloidótica familiar. Sinapse. 2006;6:74-9.
2. Freitas A. Aspectos clínicos da polineuripatia amiloidótica familiar tipo andrade. Boletim do Hospital. 1976;1:17-25.
3. Silva S, Machado H. The construction of meaning by experts and would-be parents in assisted reproductive technology. Sociol Health Illn. 2011;33:853-68.
4. Canário A. Aspetos éticos e psicológicos do abortamento no casal. Porto: Faculdade de Medicina da Universidade do Porto: Tese de Mestrado; 2009.
5. Associação Portuguesa de Paramiloidose [homepage na Internet]. Ter um filho sem medo que sofra de mal incurável; [consultado 2013 Nov 7]. Disponível em: http://www.paramiloidose.com/sm20.15567/pag4935.html.
6. Projeto de Lei n.º140/X. Diagnóstico Genético Pré-Implantação e Intervenções na Linha Germinativa; 2005; [consultado 2013 Nov 7]. Disponível em: http://app.parlamento.pt/webutils/docs/doc.pdf?path=6148523063446f764c3246795a5868774d546f334e7a67774c325276593342734c576c75615668305a586776346347707347d5451774c5667755a47396a&fich=pjl140-X.doc&Inline=true.
7. Carvalho F, Sousa M, Fernandes S, Silva J, Saraiva MJ, Barros A. Preimplantation genetic diagnosis for familial amyloidotic polyneuropathy. Prenat Diagn. 2001;21:1093-9.
8. Conselho Nacional de Procriação Medicamente Assistida [homepage na Internet]. Lista de situações para as quais o pedido prévio de autorização para DGPI será dispensado; 2012 [consultado 2013 Nov 7]. Disponível em: http://www.cnpma.org.pt/Docs/DGPI_Lista_DEZEMBRO2012.pdf.
9. Conselho Nacional de Procriação Medicamente Assistida [homepage na Internet]. Diagnóstico genético pré-implantação e rastreio de aneuploidias pré-implantação; 2013 [consultado 2013 Nov 7]. Disponível em: http://www.cnpma.org.pt/Docs/Orienta%C3%A7%C3%B5es%20DGPI%20FEV2013.pdf.
10. Vayena E, Rowe P, Griffin D, editors. Current practices and controversies in assisted reproduction. Geneve: World Health Organization; 2002.
11. Pennings G, Wert G, Shenfield F, Cohen J, Tarlatzis B, Devroey P. ESHRE Task Force on Ethics and Law 14: equity of access to assisted reproductive technology. Hum Reprod. 2008;23:772-4.
12. Ombelet W. False perceptions and common misunderstandings surrounding the subject of infertility in developing countries. ESHRE Monographs. 2008;1:8-11.
13. Silva S, Barros H. Perspectives on access to in vitro fertilization in portugal. Rev Saude Publica. 2012;46:344-50.
14. Ministério da Saúde. Despacho nº 14788/2008. Diário da República, 2ª série;102: 23832-3; 2008; [consultado 2013 Nov 7]. Disponível em: http://www.portaldasaude.pt/NR/rdonlyres/71BF02C8-2F2F-40DB-A8F5-66F9EEE478C9/0/2383223833.pdf.
15. Assembleia da República. Lei nº 32/2006. Diário da República, 1ª série;143:5245-50; 2006; [consultado 2013 Nov 7]. Disponível em: http://dre.pt/pdf1s/2006/07/14300/52455250.pdf.
16. Gabinete do Secretário de Estado da Saúde. Despacho nº 4521/2001. Diário da República, 2ª série; 54:4140; 2001; [consultado 2013 Nov 7]. Disponível em: http://www.dre.pt/pdf2s/2001%5C03%5C054000000%5C0414004140.pdf.
17. Assembleia da República. Lei nº 1/89. Diário da República, 1ª série; 26:395-6; 1989; [consultado 2013 Nov 7]. Disponível em: http://dre.pt/pdf1s/1989/01/02600/03950396.pdf.
18. Administração Central do Sistema de Saúde. Circular Normativa nº 18/2011. 2011; [consultado 2013 Nov 7]. Disponível em: http://www.cnpma.org.pt/Docs/Legislacao_CircularACSS_18_2011.pdf.
19. Ministério da Saúde. Portaria nº 67/2011. Diário da República, 1ª série; 25: 681-2; 2011; [consultado 2013 Nov 7]. Disponível em: http://www.sg.min-saude.pt/NR/rdonlyres/F1071041-A28D-4B06-8CB5-D640D1D60D80/25595/Portaria67_2011.pdf.
20. Centro de Genética da Reprodução Prof. Alberto Barros [homepage na Internet]. Tabela geral de preços; [consultado 2013 Nov 7]. Disponível em: http://www.cgrabarros.pt/MOD%20074%20R05.pdf.
21. Hershberger P, Pierce P. Conceptualizing couples' decision making in PGD: emerging cognitive, emotional, and moral dimensions. Patient Educ Couns. 2010;81:53-62.
22. Lavery S, Aurell R, Turner C, Castello C, Veiga A, Barri P, et al. Preimplantation genetic diagnosis: patients' experiences and attitudes. Hum Reprod. 2002;17:2464-7.
23. Pergament E. Preimplantation diagnosis: a patient perspective. Prenat Diagn. 1991;11:493-500.
24. Sanfey A. Decision neuroscience: new directions in studies of judgment and decision making. Curr Dir Psychol Sci. 2007;16:151-5.
25. Snowdon C, Green J. Preimplantation diagnosis and other reproductive

options: attitudes of male and female carriers of recessive disorders. Hum Reprod. 1997;12:341-50.
26. Teles N. Diagnóstico genético pré-implantação: aspetos técnicos e considerações éticas. Acta Med Port. 2011;24:987-96.
27. Zeiler K. Reproductive autonomous choice - a cherished illusion? Reproductive autonomy examined in the context of preimplantation genetic diagnosis. Med Health Care Philos. 2004;7:175-83.
28. Hershberger P, Gallo A, Kavanaugh K, Olshansky E, Schwartz A, Tur-Kaspa I. The decision-making process of genetically at-risk couples considering preimplantation genetic diagnosis: initial findings from a grounded theory study. Soc Sci Med. 2012;74:1536-43.
29. Savulescu J. In defence of procreative beneficence. J Med Ethics. 2007;33:284-8.
30. Valdrez K, Silva S, Coelho T, Alves E. Awareness and motives for use and non-use of preimplantation genetic diagnosis in familial amyloid polyneuropathy mutation carriers. Prenat Diagn. 2014;34:886-92.

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