Med Clin (Barc). 2018;151(4):161.e1–161.e12

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Consensus statement

Recommendations regarding the genetic and immunological study of reproductive dysfunction☆

María Concepción Alonso-Cerezo[a,b,*], Mercedes Calero Ruiz[c,d], Venancio Chantada-Abal[f,g], Luis Alfonso de la Fuente-Hernández[h,i], Inmaculada García-Cobaleda[j,k], Carlos García-Ochoa[l], José Miguel García-Sagredo[m,n], Rocío Nuñez[ñ], Rafael Oliva[o,p], María Orera-Clemente[q,r], David Pintado-Vera[s,t], Silvia Sanchez-Ramon[u,v]

[a] *Asociación Española de Biopatología Médica-Medicina de Laboratorio, Madrid, Spain*
[b] *Genética Clínica, Hospital Universitario de la Princesa, Instituto de Investigación Sanitaria, Madrid, Spain*
[c] *Asociación Española del Laboratorio Clínico, Madrid, Spain*
[d] *UGC Intercentros Laboratorio Clínicos, Hospital Universitario Puerta del Mar, Cádiz, Spain*
[f] *Asociación Española de Urología, Madrid, Spain*
[g] *Complejo Hospitalario Universitario A Coruña, A Coruña, Spain*
[h] *Sociedad Española de Fertilidad, Madrid, Spain*
[i] *Instituto Europeo de Fertilidad, Madrid, Spain*
[j] *Sociedad Española de Medicina de Laboratorio, Barcelona, Spain*
[k] *Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain*
[l] *Centro de Fertilización in Vitro de Asturias, Oviedo, Spain*
[m] *Hospital Universitario Ramón y Cajal, Madrid, Spain*
[n] *Universidad de Alcalá de Henares, Madrid, Spain*
[ñ] *Unidad de Reproducción, Clínica Tambre, Madrid, Spain*
[o] *Asociación Española de Andrología, Córdoba, Spain*
[p] *Unidad de Genética, Departamento de Biomedicina, Facultad de Medicina y Ciencias de la Salud, Universidad de Barcelona, Servicio de Genética y Biología Molecular, Hospital Clínico de Barcelona, Instituto de Investigación Biomédica August Pi i Sunyer (IDIBAPS), Barcelona, Spain*
[q] *Asociación Española de Genética Humana, Madrid, Spain*
[r] *Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[s] *Sociedad Española de Ginecología y Obstetricia, Madrid, Spain*
[t] *Sección de Esterilidad e Infertilidad, Hospital Quirón, Pamplona, Spain*
[u] *Sociedad Española de Inmunología, Barcelona, Spain*
[v] *Servicio de Inmunología, Hospital Clínico Universitario San Carlos, Madrid, Spain*

ARTICLE INFO

Article history:
Received 30 May 2017
Accepted 12 February 2018
Available online 20 July 2018

Keywords:
Cytogenetic
Genetic or immunological studies
Gamete donation

ABSTRACT

In this paper, several members of diverse scientific associations and reproduction experts from Spain have updated different genetic and immunological procedure recommendations in couples affected by reproductive dysfunction with the goal of providing a set of useful guidelines for the clinic. The laboratory test has been considered as highly recommendable for making clinical decisions when the result of the diagnostic test is relevant, moderately recommendable when the results are of limited evidence because they are inconsistent, and low when the benefit of the test is uncertain. It is expected that these recommendations will provide some useful guidelines for the diagnosis, prognosis, and treatment of couples presenting reproductive dysfunction.

☆ Please cite this article as: Alonso-Cerezo MC, Calero Ruiz M, Chantada-Abal V, de la Fuente-Hernández LA, García-Cobaleda I, García-Ochoa C, et al. Recomendaciones para el estudio genético e inmunológico en la disfunción reproductiva. Med Clin (Barc). 2018;151:161.e1–161.e12.

* Corresponding author.
E-mail address: calonsoc@salud.madrid.org (M.C. Alonso-Cerezo).

Recomendaciones para el estudio genético e inmunológico en la disfunción reproductiva

Palabras clave:
Citogenética
Estudios genéticos o inmunológicos
Donación de gametos

R E S U M E N

Varios miembros de diferentes asociaciones científicas y expertos de la reproducción han actualizado las recomendaciones de estudio genético e inmunológico en las parejas con disfunción en la reproducción con el fin de mejorar la asistencia sanitaria. El estudio se ha considerado altamente recomendable cuando la prueba diagnóstica es relevante para la toma de decisiones, moderada cuando estas han mostrado un resultado poco consistente y baja, cuando el beneficio de la prueba es incierto. Con la indicación de estas recomendaciones obtendremos una información relevante para el diagnóstico, pronóstico y tratamiento de la pareja con disfunción en la reproducción.

Introduction

The advance in the knowledge of the human genome and immunopathology as causes of alterations in reproductive function together with the great development of new molecular biology techniques allow us to analyse a large number of diseases obtaining relevant information for diagnosis, prognosis, and treatment of couples with reproductive dysfunctions.[1] This knowledge is being applied to symptomatic individuals/subjects with the idea of confirming a diagnosis, as well as to detect pregnancies with a high genetic risk of developing a hereditary disease or asymptomatic individuals with a family history that entails a high risk of developing a genetic disease in the future.

On the other hand, reproductive immunology studies the changes in the immune response during the different stages of the reproductive process: gamete fertilization, implantation of the embryos in the uterus, endometrial invasion, and placental development in the early and late stages of pregnancy and delivery. However, many questions remain unanswered about how the foetal–placental unit avoids rejection by the maternal immune system, with the foetus being considered a semi-allogenic graft, although knowledge about the active immune mechanisms of the foetal–maternal interface on the part of innate and adaptive immunity mediated by maternal tolerance continues to increase.

Genetic or immunological studies are based on the medical history, clinical characteristics, and family history of the couple. The evaluation of the possible cause in each case should avoid unnecessary examinations and treatments in patients with reproductive dysfunction.

Before incorporating new diagnostic tests at clinical care level, it is essential to consider the health impact of the diseases as well as the prevalence of the genotype, efficacy assurance (analytical validity, clinical validity, and clinical utility), cost-effectiveness, quality of the diagnostic tests, magnitude of the genotype–disease association, interaction with other risk factors, knowledge about the preventive or therapeutic interventions, economic impact of its implementation in the health services, and finally, related ethical, legal, and social implications.[2]

Several members of different scientific associations and human reproduction experts (Table 1) have updated the recommendations[3] published in 2009 in order to improve healthcare in these couples.

The recommendations made in this document refer to men and women with reproductive dysfunction, whether due to primary or secondary sterility or infertility.

The objective of this document is to offer an updated review of the recommendations for the genetic and immunological study in the evaluation of couples with reproductive dysfunction who wish to conceive. The aim is to provide the indications of genetic and immunological studies necessary to determine the aetiology. It excludes the study of mitochondrial and systemic diseases that are associated with reproductive dysfunction.

Table 1
Participating scientific societies.

Spanish Association of Medical Biopathology-Laboratory Medicine
Spanish Association of Clinical Laboratories
Spanish Fertility Society
Spanish Andrology Association
Spanish Society of Laboratory Medicine
Spanish Association of Human Genetics
Spanish Society of Immunology
Spanish Association of Urology
Spanish Society of Gynaecology and Obstetrics, sterility and infertility section
Experts in Clinical Sterility Genetics

The recommendations are aimed at health specialists who assist couples with reproductive dysfunction in their clinical practice such as gynaecologists, urologists, clinical geneticists, andrologists, and laboratory medicine specialists in order to help with and standardize the different genetic or immunological cause studies.

Ethical considerations in genetics and reproduction

The ethical issues raised by the new genetic technologies are diverse and multiple, although all of them have a common characteristic—which needs to be highlighted—that of requiring a double approach: reflection on the concepts involved and the values at stake, and the justification of prudent decision making in specific fields of application.[4,5]

From the point of view of basic ethical principles, the benefit that these techniques can offer is the one that generates more hope both in the professionals and in the population, since their aim is to prevent possible damage in the offspring and promote an improved quality of life.[6] However, the principles of justice and autonomy also come into play, since there is a risk of using technologies that are not sufficiently safe, and also the problem of confidentiality protection and unequal access among patients who request it.

The new genetic technologies put at our disposal the obtained data, which can also be shared with other people. In the case of gamete donation, for example, the information may involve several subjects at the same time. Therefore, the confidentiality of these data is one of the most controversial issues, since sometimes it is not clear whether the privacy of the person should prevail over common interest.

On the other hand, there is also the possibility that the person does not want to know their data, especially in the case of detecting the possibility of having a disease that has no cure.[7] It is very important to emphasize that finding a predisposition to suffer from a disease does not mean that the disease will eventually develop with total certainty. The underlying problem, with this and with other issues related to the influence of advances in genetics in