PReFiNe PROJECT: STRATEGIC PLAN TO IMPROVE KNOWLEDGE & RECOGNITION OF FABRY DISEASE AMONG SPANISH NEPHROLOGISTS

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INTRODUCTION

Fabry disease is a lysosomal storage disease caused by α-galactosidase A deficiency[1].

Patients with Fabry disease (FD) have an increased risk of death from renal, cardiovascular or cerebrovascular disease[2].

Screening of FD has been performed in "high-risk" populations, including renal failure requiring dialysis or kidney transplantation. However, the majority of those studies have been performed within hemodyalisis populations[3].

The observed prevalence of FD in haemodyalisis ranges from 0.11-1.17%.However, in these studies FD diagnosis has been determined by α-galactosidase activity and women might have been missdiagnosed[3].

In a previous spanish study, 3,650 subjects in hemodyalisis were screened, stablishing the FD prevalence in this population as 0.30%[4].

OBJECTIVES

The aim of the PrEFiNE project is to improve the knowledge and diagnosis of FD in the renal disease population.

METHODS

An advisory comnmittee, a scientific committee and 12 regional committees have been created (Fig. 1). Three meetings of these committees were scheduled.

The current knowledge in FD among nephrologists has been evaluated by a survey in the first regional committees. An educational program and a university course have been started to improve the knowledge of the disease.

To stablish the prevalence of FD in renal disease population, three studies have been assessed: dialsysis (peritoneal and hemodialysis), kidney transplant (KTx), and a pilot study in chronic kidney disease (CKD) (stages 3-5 pre-dialysis) (Fig. 1). All those studies are currently ongoing.

A pedigree study is being conducted in those patients that have been genetic diagnosed as index cases affected of FD.

The FD was screened by DBS kits (Centogene®, Germany) (Fig. 2), following a different algorithm according to the patient's gender.

Figure 1. PrEFiNe Project

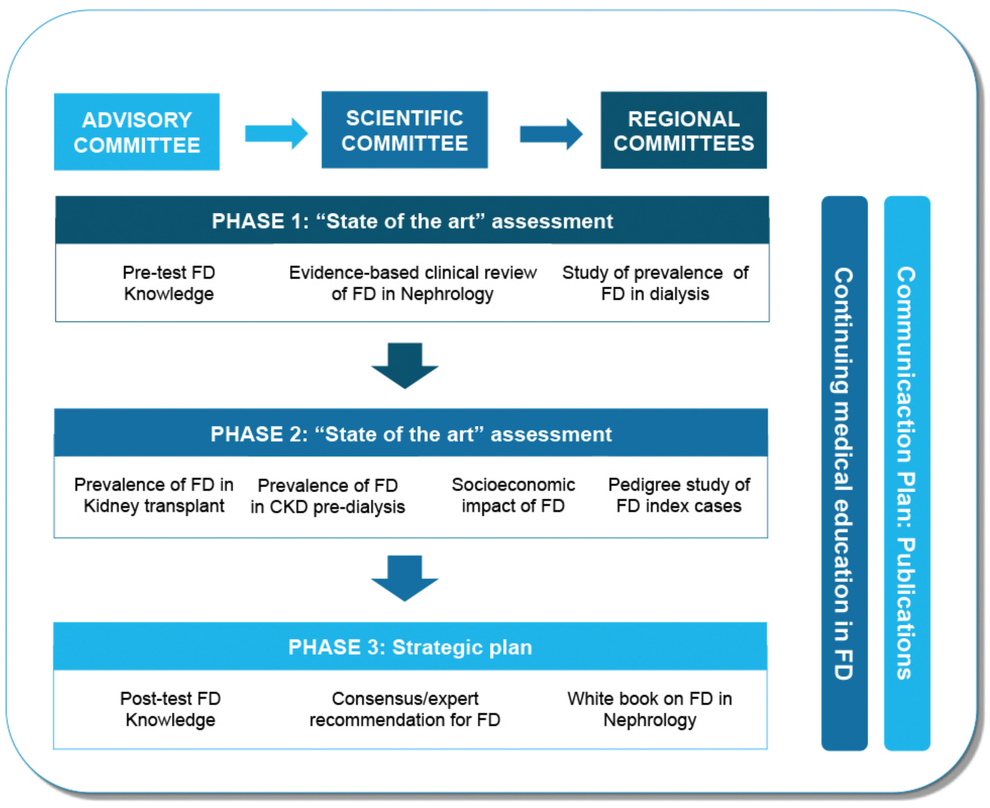


Figure 2. Algorithm testing of FD by using DBS kits

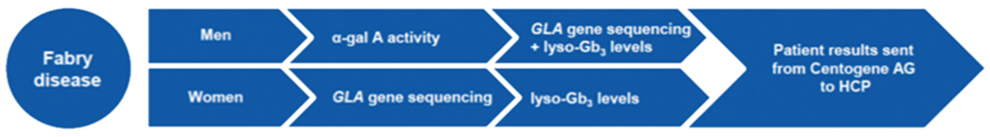
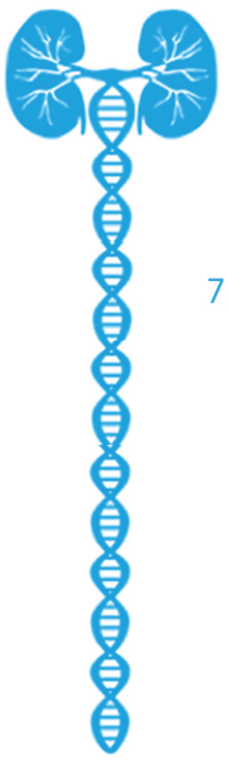


Figure 3. Results obtained up to January 2017 in PrEFiNe dyalisis study



202 centers have been included in PrEFiNe
with 164 nephrologists
~10,000 estimated patients in dyalisis
(hemodyalisis and peritoneal)

Up to January 2017

7,654 patients have been included in ECD
(61.6% males; 67.7 [16-97] years old)

4,061 subjects were sequenced to identify *GLA* variants

70 subjects were identified as hemyzgotes or heterozygotes for FD related variants:
51 subjects with p.D313Y; 7 with p.R118C; 1 with p.R112C, 3 with p.S126G; 2 with p.D83N; 1 with p.D175E, 2 p.A143T; 1 with p.P214A, 1 with p.R220Q and 1 with p.S238N

RESULTS

In the dyalisis study, 202 centers with ~10,000 estimated patients have been included in the study.

7,654 subjects (61.6% males; 67.7 [16-97] years old) have been registered with enzymatic and/or genetic test results for 4,061 patients. *GLA* sequencing was performed in all female and 51% males.

Seventy subjects with variants related to FD have been identified: 51 p.D313Y, 7 p.R118C, 3 p.S126G, 2 p.D83N, 1 p.R112C, 2 p.A143T, 1 p.D175E, 1 p.P214A, 1 p.R220Q, and 1 p.S238N.

The KTx study, with six centers included, and CKD study, with a unique center, are ongoing. It has been estimated that 3,000 subjects will be included in each of these studies. The FD survey was completed by 94 out of 164. Only 3% showed the maximum score. The 32.25% identified the enzyme responsible of this disease, 64% answered that FD shows X-linkage inheritance and 48% answered that women are also affected of FD. A great variability was observed in those questions related to clinical symptoms.

CONCLUSIONS

This project allows customize activities to improve FD knowledge among nephrologist and perform largest studies to assess real prevalence of FD in renal disease population.

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