Outros

(21555) - THE IMPACT OF COMPREHENSIVE GENOMIC APPROACHES IN REPRODUCTIVE MEDICINE: PRECONCEPTIONAL CARRIER SCREENING AND PRENATAL DIAGNOSIS

João Parente Freixo[1,2]; Ana Filipa Brandão[1,2]; Fátima Lopes[1,2]; Ana Grangeia[3]; Renata D'oliveira[3]; Inês Carvalho[4,5]; Jorge Oliveira[1,2]

1 - CGPP-IBMC – Centro de Genética Preditiva e Preventiva, Instituto de Biologia Molecular e Celular, Universidade do Porto, Portugal; 2 - i3S – Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal; 3 - Serviço de Genética Médica, Centro Hospitalar Universitário de São João, Porto, Portugal; 4 - Serviço de Genética Médica, Hospital Dona Estefânia, Centro Hospitalar de Lisboa Central, Lisboa, Portugal; 5 - Centro de Diagnóstico Pré-Natal, Maternidade Alfredo da Costa, Centro Hospitalar Lisboa Central, Lisboa, Portugal

Introdução

Genomics entered the stage of reproductive medicine through the application of comprehensive approaches.

First, preconception carrier screening (PCS) improves the couples' reproductive options and reduces the burden of recessive diseases.

Second, for ongoing pregnancies with fetuses depicting ultrasonographic abnormalities, genetic prenatal diagnosis (PND) supports prenatal/perinatal decision-making.

Clinical indications and diagnostic yields (DY) were determined for karyotype and microarrays, but not for whole-exome sequencing (WES).

Objectivos

Present CGPP experience with PCS and PND using WES-based approaches.

Metodologia

A retrospective review of results obtained from multigene panels in different contexts: i) PCS tests requested by clinical geneticists; ii) PND of structurally abnormal fetus requested by clinicians from PND Centers.

Resultados e Conclusões

Fourteen PCS studies have been performed (>2021): 6 couples (2 consanguineous) and 2 females. Study indications were: i) previous history of affected offspring (n=4); ii) gestational losses or TOP due to fetuses' abnormalities (n=3); iii) consanguinity without previous history of disease (n=1). Twenty five variants were reported in the context of carriers and 4 were likely cause of disease in the offspring.

Data from 130 WES from structurally abnormal fetus have been sequenced (>2015) and analyzed resorting to 20 different multigene panels, and WES performed in trio (fetus sample and couple). The most requested panels were skeletal dysplasia (n=40) and clinical exome (n=35). Overall DY was ~35%, ranging from 47% to 10% depending on the selected gene panel.

WES-based approaches are extremely useful tools for reproductive medicine.

PCS was useful to assess the couples' potential risk of having affected offspring, especially with previous family history of disease. Upon the identification of structural fetal abnormalities, WES-based tests increase the success rate of genetic PND.

Considering the possibility of combined application of PND and PCS at different stages, trio analysis would provide the highest diagnostic yield, being also the fastest and most cost-effective approach.

Palavras-chave : Genomics, Genetics, Exome, Preconceptional, Carrier, Screening