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DOES EXPANDED CARRIER SCREENING REDUCE THE RISK OF CONCEIVING AN AFFECTED CHILD THROUGH ASSISTED REPRODUCTION?

Mataró D (ES) [1], Guillén J (ES) [2], Palahí M (ES) [3], Alsina E (ES) [4], Vassena R (ES) [5], Rodriguez A (ES) [6]

Context:
The fast and affordable detection of a large number of mutations causative of recessive or X-linked diseases has recently become feasible due to the advances of genomic technology. These expanded carrier screenings (ECS) can detect couples at an increased risk of generating a child affected by a severe disease, and could offer a preventive medicine approach to assisted reproduction. Nevertheless, it is not clear yet what the risk reduction afforded by ECS is.
Objective
The objective of this retrospective multicentric study is to evaluate if expanded carrier screening (ECS) reduces the risk of conceiving an affected child through assisted reproduction.
Methods:
Patients were tested with ECS CarrierMap (Recombine) test covering 2647 mutation causative of 311 diseases. DNA samples were purified following the QIAamp DNA Purification Protocol via QIAcube (QIAGEN), and assayed using the Infinium iSelect HD Custom Genotyping BeadChip platform (Illumina).
Patient(s)
Prospective cohort study including 2380 women (both patients and donors) and 986 men attending 4 fertility clinic in Spain and Italy.
Intervention(s)
A total of 3366 ECS tests were performed; 894 matches to identify the reproductive risk were performed (747 between donor and patient, 114 between two donors and 33 between patients).
Main Outcome Measure(s)
Of the 3366 individuals tested, 1458 (43.3%) were carriers for at least one mutation; of those, 1091 (32.4%) carried one, 306 (9.1%) two and 54 (1.6%) three mutations; 7 individuals carried four or more of the mutations analyzed.
Results:
The most frequently carried diseases were Nonsyndromic Hearing Loss and Deafness (GJB2 Related): 152 (10.4%); carrier frequency 1:22. Pseudocholinesterase Deficiency: 98 (6.7%); 1:34. Fragile X syndrome: 97 (6.6%); 1:34. Cystic Fibrosis: 89 (6.1%), 1:38. Familial Mediterranean fever (FMF): 82 (5.6%), 1:41. Out of 894 matches, 26 (2.9%) returned a high reproductive risk, as both members carried

[1] CIRH, [2] EUGIN, [3] Reprogenetics, [4] Reprogenetics, [5] EUGIN, [6] EUGIN

mutations causative of the same disease, with a 1 in 4 chance to generate an effected child. Increased risk matches involving donor were solved by selecting different donors; 2 couples of patients with high reproductive risk received genetic counseling and PGD was recommended.

Conclusions:

ECS returned a high risk match rate of 2.9%. This value should be higher in unselected patients, as most attempted matchings were made with donors preselected for lower carrier status by screen out with an initial genetic test.