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Fetal DNA in maternal blood in prenatal screening of aneuploidies: Preliminary study for the adoption of the test

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Objective

The study of fetal DNA in maternal blood (DNAf) is the most important recent advance as a non-invasive prenatal aneuploidy screening since it improves the diagnostic accuracy compared to the biochemical and ultrasound screening of the current public health programs. For this reason, the most convenient strategy for its application was studied. To plan and compare several strategies for the application of DNAf techniques. A cost- benefit analysis was performed, taking into account the number of DNAf to be performed, the invasive tests (IT) and the detection rate (DR) in comparison to the current biochemical and ultrasound screening.

Methods

Retrospective multicentre study (6 laboratories) including pregnant women examined in 2016 (n=23. 513 screenings in first trimester) classified by risk index intervals. Detection rates were calculated with a series we had from the 2010-2015 period (n=578, trisomy 21). 10 scenarios were planned for the application of DNAf (for all pregnant women or as a contingent screening technique) and for each one, the number of DNAf, IT and DR were evaluated. In order to compare strategies, sensitivity values and false positives of DNAf weree set (100% and 0. 2%, respectively). Strategies studied: 1. DNA of all pregnant women 2. DNA Risk index >1: 800 3. DNA Risk index >1: 1000 4. DNA Risk index >1: 1500 5. DNA Intermediate risk index 1: 10 to 1: 1000 6. DNA Intermediate risk index 1: 50 to 1: 1000 7. DNA Intermediate risk index 1: 100 to 1: 1000 8. DNA Intermediate risk index 1: 10 to 1: 1500 9. DNA Intermediate risk index 1: 50 to 1: 1500 10. DNA Intermediate risk index 1: 100 to 1: 1500.

Results

Current situation: 3. 52% invasive tests, 91. 07% detection rate Strategy 1: 100% DNAf, 0. 44% invasive tests, 100% detection rate, -87. 50% reduction IT, +9. 81% increase DR Strategy 2: 7. 60% DNAf, 0. 24% invasive tests, 94. 29% detection rate, -93. 19% reduction IT, +3. 54% increase DR Strategy 3: 8. 94% DNAf, 0. 24% invasive tests, 94. 81% detection rate, -93. 08% reduction IT, +4. 11% increase DR Strategy 4: 12. 65% DNAf, 0. 25% invasive tests, 95. 67% detection rate, -92. 81% reduction IT, +5. 06% increase DR Strategy 5: 8. 39% DNAf, 0. 68% invasive tests, 94. 81% detection rate, -80. 76% reduction IT, +4. 11% increase DR Strategy 6: 7. 93% DNAf, 1. 08% invasive tests, 94. 81% detection rate, -69. 26% reduction IT, +4. 11% increase DR Strategy 7: 7. 40% DNAf, 1. 59% invasive tests, 94. 81% detection rate, -54. 71% reduction IT, +4. 11% increase DR Strategy 8: 12. 1% DNAf, 0. 69% invasive tests, 95. 67% detection rate, -80. 49% reduction IT, +5. 06% increase DR Strategy 9: 11. 64% DNAf, 1. 09% invasive tests, 95. 67% detection rate, -68. 99% reduction IT, +5. 06% increase DR Strategy 10: 11. 11% DNAf, 1. 60% invasive tests, 95. 67% detection rate, -54. 47% reduction IT, +5. 06% increase DR.

Conclusion

All of the strategies reduce the IT and increase the DR. Therefore, as far as these factors are concerned, their application is desirable. However, to select the optimum strategy it is necessary to establish the order of priorities of the three different aims - to reduce the IT, to increase the DR and to perform a manageable number of DNAf – given that the results for the three objectives are divergent. Prioritising the reduction in IT, the best strategy studied is to establish a cut-off point of 1: 800. Furthermore, it is one of the techniques that requires fewer DNAf determinations, although the DR is lower. The greatest DR is achieved performing DNAf in all pregnant women and a further four strategies (a cut-off point of 1: 15000 or two points between 1: 10-1500, 1: 50-1: 1500 and 1: 100-1: 1500). Prioritising the performance of a minimum number of DNAf, the best options are a risk index of 1: 100-1: 1000 or 1: 800 (this latter option generates less IT). The complete

substitution of screening by DNAf represents a significant reduction in invasive tests while permitting the maximum detection rate to be achieved.