

Retrospective analysis of prenatal samples with unbalanced structural rearrangements using BAC array-CGH

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The introduction of array-CGH into prenatal diagnosis (PD) presents controversy to the clinical cytogenetic community. The advantages of aCGH are multiple: enhanced detection of fetal chromosome aberrations, shorter reporting times and need for relatively small amounts of fetal DNA. However, there is a principal challenge with its application to PD that is related to the detection of Copy Number Variations (CNVs) with questionable clinical significance. CNVs number increases with the enhancement of the platform resolution and this aspect has obvious implications for genetic counselling. On this basis many authors agree on its application limited to specific prenatal indications: i.e. fetuses with multiple structural malformations but normal karyotypes; characterization of minute structural rearrangements not definable using conventional cytogenetic and molecular cytogenetic techniques.

Herein we present a retrospective analysis of prenatal samples (chorionic villi and amniocytes) with unbalanced structural rearrangements using two whole genome BAC platforms (1Mb and 0.6Mb resolution). The aim of this study is to verify the sensitivity in revealing CNVs related and unrelated to the cytogenetic unbalances and to draw limits and advantages coming from the application of the aCGH in these prenatal cases. All deletions/duplications were detected and the CNVs unrelated to the cytogenetic unbalances, telomeric in the majority of cases, were present in a mean number of 3 a case. Whole genome amplification products seems to be a reliable copy of the original DNA since evident bias are not present after their analysis. In conclusion, the application of the aCGH combined with conventional cytogenetic might be a useful tool for a fast and comprehensive understanding of minute cytogenetic unbalances permitting a more accurate genetic counselling.