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Optimal non-invasive diagnosis of fetal achondroplasia combining ultrasonography and circulating cell-free fetal DNA analysis

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Objective

To assess the performance of non-invasive prenatal testing of achondroplasia using high-resolution melting (HRM) analysis. To propose an optimal diagnosis strategy combining ultrasound scan and cell-free fetal DNA (cffDNA) analysis.

Methods

Prospective multicenter study. CffDNA was extracted from maternal blood from women at risk for fetal achondroplasia (paternal achondroplasia, previous affected child or suspected rhizomelic shortening). The presence of one of the two main FGFR3 mutations was determined by HRM combined with confirmation by SNaPshot minisequencing. Results were compared with phenotypes obtained by 3D computed tomography, post-natal examination and/or molecular diagnosis by an invasive procedure. Fetal biometry was also analyzed (head circumference and femur length) in order to offer cffDNA for achondroplasia in selected cases.

Results

Eighty-six blood samples from women at risk were collected (and sixty-five from control women). The overall sensitivity and specificity of the test were respectively 1. 00 (95% CI 0. 87-1. 00) and 1. 00 (95% CI 0. 96-1. 00). Critical reduction of femur length for affected fetuses can be observed from 26 weeks of gestation.

Conclusion

HRM combined with SNaPshot minisequencing is a reliable method for non-invasive prenatal testing of achondroplasia. Its implementation in routine clinical care combined with ultrasonography is an efficient strategy for non-invasive diagnosis of achondroplasia.