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Original article

QF-PCR-based prenatal detection of common aneuploidies in the Czech population: Five years of experience

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Abstract

We present the results from the largest clinical application of QF-PCR for antenatal rapid aneuploidy detection (RAD) in routine prenatal diagnosis in the Czech Republic. QF-PCR was performed in addition to karyotyping (dual testing) in two settings: the first was a single multiplex reaction testing only trisomy 21 and amelogenin X/Y alleles in the second trimester screened positive cases (T21 test), and the second setting consisted of two multiplexes (2M test) for common aneuploidies (13, 18, 21, X and Y) in cases with other RAD indications such as ultrasound findings, late booking or maternal anxiety.

Dual testing was performed in 6349/12,778 (49.7%) of prenatal samples using either T21 or 2M test between 2002 and 2007. The clinical acceptability of our dual testing policy, methodological efficiency of RAD and residual risks of other chromosomal aberrations (CHAs) were evaluated.

QF-PCR detected 92% (175/190) of significant CHAs. The 2M test identified 93.5% and the T21 test identified 87.5% of the significant CHAs with complete specificity. The residual risk of significant CHA was 1/231 in the 2M test and 1/565 in the T21 test. If RAD for all common aneuploidies is used as the sole prenatal diagnosis method, the odds of missing a CHA of any type are 1:90 and the odds of missing significant CHA with no ultrasound findings are 1:1513. If prenatal karyotyping were used as an additional procedure to RAD in cases only with ultrasound findings, 186/190 (97.8%) of the significant CHAs would be detected when 15.7% cases were karyotyped, according to our data.

We consider RAD directed towards trisomy 21 alone (our T21 test) as an economically and clinically acceptable part of second trimester screening for Down syndrome. Both RAD tests allow fast alleviation of maternal anxiety with low residual risk when the test results are negative, and allow fast decision

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making if the results are positive. However, replacement of dual testing with only the RAD procedure in specific indications accepted in some countries (Great Britain) remains in the Czech Republic a theme for debate.

Keywords: Prenatal diagnosis; QF-PCR; Rapid aneuploidy detection (RAD); Dual testing

1. Introduction

The average turnaround time for prenatal karyotype analysis is 14 days. With the development of DNA technologies, an alternative method called rapid aneuploidy detection (RAD) of common aneuploidies, which uses quantitative fluorescent polymerase chain reaction (QF-PCR) of highly polymorphic short tandem repeats (STR) markers, has been introduced [1,2,10,13,17,18]. Trisomies 13, 18, 21, as well as sex chromosome aneuploidies and triploidies account for more than 80% of significant chromosomal aberrations (CHAs). The QF-PCR technique allows the detection of most of these prevalent aneuploidies within 24 h [15]. Positive RAD allows early decisions on pregnancy management to be made, and in case of negative RAD result the residual risk of other CHA is low. With the use of RAD, the question has been raised as to whether it is necessary to carry out full karyotyping in certain indication groups [11,16].

A positive result from second trimester serum screening for Down syndrome is often significant part of indication for cytogenetic examination of amniotic fluid (AF). With the exception of a higher incidence of trisomy 13, there is no significant risk of CHA other than trisomy 21 in this group [19]. In some prenatal programs, RAD is directed towards trisomy 21 in screen positive cases, and all common aneuploidies are only tested after ultrasonographic indications [20].

The aim of this study was to evaluate the methodological and clinical feasibility of two dual testing policies. The first policy was RAD of trisomy 21 only in cases that had tested positive for Down syndrome after second trimester biochemical screening but were negative with ultrasound scan. The second policy was RAD of common aneuploidies suggested by other indications.

2. Materials and methods

In this study, 6349 samples consisting of 142 chorionic villi (CV) and 6207 AF were referred for dual testing from November 2002 to February 2007. The test for common aneuploidies (2M test) was used instead of short term cultivation of all CV samples that had been indicated to have a risk of trisomy 21 or trisomies 13/18 higher than 1/100 after combined screening in the first trimester. Dual testing of the AF group was offered and accepted by 6207/12,639 (49%) mothers counselled in the second trimester. The 2M test was performed in 2764/6207 (44.5%) samples with the following indication criteria: (1) ultrasound findings, (2) multimarker risk of Edwards syndrome, (3) late booking and (4) maternal anxiety. The T21 test was performed in 3443/6207 (55.5%) of dually tested AF samples. The multimarker risk of trisomy 21 higher than 1/250 revealed by second trimester biochemical screening served as the sole indication for T21 test. The average mother's age in the 2M test group was 32 years, with 27% of