Blood group genotype in determination of feto-maternal red blood cells incompatibility status: Experience of the French National Center for Perinatal Hemobiology (CNRHP)


(1) Centre National de Référence en Hémobiologie Périnatale (CNRHP), AP-HP St Antoine, PARIS, FRANCE ; (2) Laboratoire Central CHI Poissy-Saint Germain en Laye, POISSY, FRANCE ; (3) Institut Jacques Boy, REIMS, FRANCE ; (4) Institut National de la Transfusion Sanguine, PARIS, FRANCE

Background: Hemolytic disease of the fetus and newborn (HDFN) is a significant cause of fetal and neonatal death. The French “Centre National de Référence en Hémobiologie Périnatale” (CNRHP) is dedicated to biological and clinical diagnosis and treatment of feto-maternal red blood cells incompatibilities.

Aim: Review of the molecular biology tools used in determining of the feto-maternal incompatibility status over one year in our reference center.

Methods: To identify fetuses at risk for HDFN, our laboratory uses 3 types of analysis:
- Non invasive fetal RHD genotyping from maternal blood sample of allo-immunized and non immunized woman to guide the prophylaxy and follow-up (Rouillac-Le Sciellour et al., TCB, 2007, 14 : 572-7).

Fetal genotype results were compared with the phenotype of the red blood cells of the babies at birth.

Results:
1) For genetic counseling for future pregnancies of allo-immunized woman with anti-D, 18 determination of the paternal zygosity at the RHD locus were done. 14 fathers were found homozygous RHD/RHD and 4 fathers were found heterozygous rhd/RHD.
2) To determine fetal RHD status,
   1378 non invasive fetal RHD genotype from maternal blood were done: 192 from allo-immunized anti-D woman (142 positive fetuses, 48 negative and 2 undetermined) and 1378 from non allo-immunized woman (847 positive fetuses, 323 negative and 16 undetermined).
   286 invasive fetal RHD genotype from chorionic villus or amniotic cells were done: 9 from allo-immunized anti-D women (7 positive fetuses and 2 negative) and 277 from non allo-immunized women (182 positive fetuses, 94 negative and 1 undetermined).
3) To determine fetal RHE status, 2 invasive fetal RHE genotype from amniotic cells of allo-immunized anti-E woman were done (1 positive and 1 negative fetuses).
4) To determine fetal RHC status, 1 invasive fetal RHC genotype from amniotic cells of allo-immunized anti-C woman was done (positive fetus).
5) To determine fetal RHC status, 2 invasive fetal RHc genotype from amniotic cells of allo-immunized anti-C woman were done (1 positive and 1 negative fetuses).
6) To determine fetal Kell status, 16 invasive fetal Kell genotype from amniotic cells were done (7 positive fetuses and 9 negative).

Conclusion: Molecular biology is a powerful tool to diagnose a feto-maternal red blood cells incompatibility and allows to legitimize a costly and heavy specific antenatal monitoring. In non immunized RHD-negative pregnant woman, it allows to rationalize prophylaxis indicated only for women expecting a RHD-positive baby.