Use of non invasive prenatal fetal blood group genotyping in the monitoring of allo-immunised pregnant women: experience of the French National Center For Perinatal Hemobiology (CNRHP)

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Background

The French "Centre National de Référence en Hémobiologie Péridérale" (CNRHP) is dedicated to biological and clinical diagnosis and treatment of feto-maternal red blood cells incompatibilities. This disease is common and may result in hemolytic disease of the fetus and newborn (HDFN), characterised by anemia and hyperbilirubinemia which may lead to fetal hydrops, kernicterus or death. Three antibodies are associated with severe fetal disease: anti-RH1 (D), anti-RH4 (c) and anti-KEL1 (Kell). High concentration of anti-RH3 (E) can too lead to HDFN during the third pregnancy trimester. Since the discovery of free fetal DNA into peripheral maternal blood, non-invasive prenatal determination of fetal RHD genotype on maternal blood is used in the management of pregnancies of RH-1 (D negative) women. CNRHP provide non invasive fetal genotyping as a routine service to help the practitioners to improve the accuracy follow-up in pregnant woman anti-RH1, anti-KEL1, anti-RH4 and anti-RH3 allo-immunised.

The aim of this presentation is the review of non-invasive fetal genotypes used in the CNRHP in determining of feto-maternal RH1, KEL1, RH4 or RH3 incompatibility status in order to spare a specific antenatal monitoring.

Methods

Monitoring of allo-immunised anti-RH1 or anti-KEL1 or anti-RH4 or anti-RH3 pregnant women in France

Non invasive fetal RHD or KEL1 or Rhc or RHE genotyping

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Non invasive fetal RHD or KEL1 or Rhc or RHE genotyping

Blood collected on EDTA and received before 72h/48h/72h/48h

<table>
<thead>
<tr>
<th>Variant</th>
<th>Rhd</th>
<th>Rhd</th>
<th>Rhd</th>
<th>Other</th>
<th>Total</th>
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<tbody>
<tr>
<td>Fetus +</td>
<td>957</td>
<td>65</td>
<td>29</td>
<td>0</td>
<td>1047</td>
</tr>
<tr>
<td>Fetus - confirmed +</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fetus - not confirmed</td>
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<td>4</td>
<td>0</td>
<td>0</td>
<td>32</td>
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<tr>
<td>Blood collected on EDTA and received before 72h/48h/72h/48h</td>
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</tbody>
</table>

Sensibility : 96.4%
Specificity : 95.3%
VPN : 100%
20% of pregnancies are compatible for anti-RH1 allo-immunised women

Conclusion

Non invasive fetal genotyping is a powerful tool to diagnose a feto-maternal red blood cells incompatibility and allows to legitimize a costly and heavy specific antenatal monitoring only to pregnant women carrying incompatible fetus.

VPN : 100 %
-42% of patients have a dosage ≥ 5IU/ml
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-24% of patients have a dosage ≥ 500UCHP or a titration ≥ 20 IU/mI
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-20% of pregnancies are compatible for anti-RH1 allo-immunised women
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-15% of patients have a dosage ≥ 700UCHP or a titration ≥ 80 IU/mI
-15% of patients have a dosage ≥ 700UCHP or a titration ≥ 80 IU/mI
-42% of pregnancies are compatible for anti-RH3 allo-immunised women
-42% of pregnancies are compatible for anti-RH3 allo-immunised women