ABO Hemolytic Disease of the Fetus and Newborn: Is a New Paradigm Needed?

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1. The ABO blood group antigens.
2. Spectrum, from the literature, of severity range of ABO hemolytic disease of the fetus/neonate.
3. At Intermountain Healthcare, what is our risk of severe ABO hemolytic disease since adopting the “universal” bilirubin screening/management tool in 2004?

Pair of dimes = 4 nickels = 4 chances at a nickel slot
Not a pair of dimes!
Paradigm = a standard way of doing something.

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ABO Hemolytic Disease of the Fetus/Newborn

Mother is Blood Group O and Fetus is Blood Group A or B

ABO Hemolytic Disease of the Fetus/Newborn

A

A

ABO Hemolytic Disease of the Fetus/Newborn

B

B

A

A

ABO Hemolytic Disease of the Fetus/Newborn

B

B

A
The ABO Blood Group Antigens (A and B) are sugars attached to the red blood cell surface. They attach to a sugar molecule called the H antigen.

The A antigen is a galactosamine sugar attached to H

The B antigen is a galactose sugar attached to H

Group O Mother can have IgG antibodies against Group A or B red cell antigen.

Those antibodies cross the placenta, bind to fetal RBC, and lead to fetal/neonatal hemolysis.

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Textbook description of ABO hemolytic disease. Typically mild/moderate hyperbilirubinemia, but includes the possibility of the severe-end of the hemolytic spectrum, including…

- Hydrops with erythroblastosis fetalis
- Extreme hyperbilirubinemia (TSB >25 mg/dL)
- Hospital readmission for jaundice
- Kernicterus (6% of USA kernicterus registry and 4 of 20 in Canadian report of kernicterus)
Some experts have recommended performing blood type and Coombs, at delivery, on all neonates born to group O women.

**Purpose:** rapid identification of neonates at risk for ABO hemolytic disease, to prevent serious sequella (extreme hyperbilirubinemia, hospital readmission for jaundice, kernicterus).

**Problems:**
1) None of the reports of severe-end ABO hemolytic disease (bili >25 mg/dL, hospital readmission for jaundice, kernicterus) are “post” AAP bili management guidelines (2004).
2) The risk of severe-end hemolysis from ABO hemolytic disease at Intermountain Healthcare, since 2004, is not known.

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**Hypothesis:** We can judge the severity of ABO hemolytic disease at Intermountain by comparing specific outcomes of two groups of neonates born to group O(+) mothers since 2004.

**Control Group**…Babies of blood group O (not at risk)

**Test Group**… Babies of blood groups A and B (at risk)

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**Should Intermountain Healthcare advocate performing blood type and Coombs, at delivery, on all neonates born to group O women?**

What do our own data show over the past 13 years?
O or B

**Control Babies**
At no risk of ABO hemolytic dis

**Study Babies**
At some risk of ABO hemolytic dis

**Outcomes of Interest (Severity):**
1. Hydrops fetalis with erythroblastosis
2. Extreme hyperbilirubinemia (TSB $\geq 25 \text{ mg/dL}$)
3. Hospital readmission for jaundice treatment
4. Acute kernicterus

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**Study:** Compare outcomes of group O (control) vs. group A and B Neonates

<table>
<thead>
<tr>
<th>Neonate's Blood Group</th>
<th>Number of neonates</th>
<th>Number with ≥1 TSB in database</th>
<th>Highest TSB (mg/dL) mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>28,729</td>
<td>28,552</td>
<td>10.3±4.1</td>
</tr>
<tr>
<td>A</td>
<td>10,682</td>
<td>10,641</td>
<td>11.0±4.2</td>
</tr>
<tr>
<td>B</td>
<td>3,109</td>
<td>3,097</td>
<td>11.5±4.3</td>
</tr>
</tbody>
</table>

Highest TSB, P value, A and B vs. O <0.001

Highest TSB, P value, A vs. B <0.001

**Results #1.** Total serum bilirubin (TSB) during the first 10 days after birth

- Group A and B neonates had higher TSB than the group O controls (1 mg/dL).
- Group B neonates had a higher TSB than Group A (0.5 mg/dL).

**Results #2.** Number who had a TSB ≥25 mg/dL.

- Group A and B neonates did not have a higher relative risk of a TSB ≥25 than did the group O controls.
- Group B neonates did not have a higher relative risk of a TSB ≥25 than Group A.
Results #3. Did a positive DAT (Coombs) affect the TSB?

- A positive DAT (Coombs) was associated with a higher TSB (2 mg/dL). This was equally so in neonates of group A, B, and O (controls).

Results #4. Relative risk of being rehospitalized for jaundice treatment within 10 days of birth.

- Group A and B neonates were not more likely than controls to be readmitted for jaundice treatment.

Results #5. Relative risk of developing kernicterus

<table>
<thead>
<tr>
<th>Year</th>
<th>Highest TSB (mg/dL)</th>
<th>DOL highest TSB</th>
<th>Gestat Age (wk/day) at birth</th>
<th>Mother's Blood group</th>
<th>Neonate’s Blood group</th>
<th>D A T</th>
<th>Other Hemolytic Conditions Discovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>38.0</td>
<td>9</td>
<td>38 5/7</td>
<td>A+</td>
<td>O+</td>
<td>-</td>
<td>PK deficiency</td>
</tr>
<tr>
<td>2012</td>
<td>41.7</td>
<td>6</td>
<td>37 2/7</td>
<td>O+</td>
<td>B+</td>
<td>-</td>
<td>Hereditary Spherocytosis, Band 3 mutation E508K</td>
</tr>
<tr>
<td>2013</td>
<td>41.0</td>
<td>5</td>
<td>40 0/7</td>
<td>O+</td>
<td>B+</td>
<td>-</td>
<td>G6PD (Mahidol) 487A</td>
</tr>
<tr>
<td>2014</td>
<td>41.9</td>
<td>6</td>
<td>38 4/7</td>
<td>O+</td>
<td>O+</td>
<td>-</td>
<td>G6PD (African) 202A and 376G plus Gilberts (TA)?</td>
</tr>
<tr>
<td>2016</td>
<td>29.0</td>
<td>3</td>
<td>39 3/7</td>
<td>O+</td>
<td>A+</td>
<td>+</td>
<td>Anti-c (1:256)</td>
</tr>
</tbody>
</table>

- One of 5 with kernicterus was DAT (+) and ABO incompatible. However anti-little-c titers were extremely high. Blood bank eluted anti-little-c from baby’s RBC. Unclear whether anti-B played any role, but certain it was not the major hemolytic antibody.

Results #6. Relative risk of being born with hydrops fetalis and erythroblastosis/anemia

- Group A and B neonates were not more likely than controls to have hydrops, or to have erythroblastosis (congenital anemia with elevated NRBC and retics.)
Carbohydrate Antigens (ABO) tend to generate weak antibody responses, compared with Protein Antigens (RH, Kidd, Duffy).

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**Conclusions:** In a health system where bilirubin is measured from all neonates in the birth-hospital, and reported with recommendations for management and follow-up:

1. We have had no severe jaundice cases in our health system in the past 13 years attributable to ABO hemolytic disease (same incidence as controls).
2. We do not have outcome data for health systems that do not use this, or a comparable bilirubin management system.
3. We doubt that ABO incompatibility ever causes hydrops fetalis/erythroblastosis.
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3. We doubt that ABO incompatibility ever causes hydrops fetalis/erythroblastosis.
4. At Intermountain healthcare, any case of severe hemolytic disease should probably not be ascribed to ABO alone. Look for another coexisting hemolytic condition (hereditary spherocytosis, G6PD, PK).

Over this 13 year period, had we performed a neonatal DAT and blood type at each birth to a group O mother, we would have spent nearly $19,000,000 on reagents and personnel.

DAT and blood typing, including phlebotomy, reagents, medical laboratory scientist time, recording and reporting, about $100 at each delivery of a group O women. 47% X 400,531 live births X $100 = $18,824,957).

Limitations

1. Our population is relatively homogenous.
2. No available data on use of phototherapy usage.
3. May not be as useful if the facility does not have a rigorous bilirubin screening practice?

Now can we use our Pair of dimes? Or maybe we can change our Paradigm?

Thanks for your kind attention
Reference List Session #215c
ABO Hemolytic Disease of the Fetus and Newborn: Is a New Paradigm Needed?
Vickie Baer, BSN

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