Rh Program of Nova Scotia

The presenter does not have any involvement with industry that may be perceived as potentially influencing the presentation of the educational material contained within

Blood Matters
Oct 29, 1010
M.C. Van den Hof
Rh Program of Nova Scotia

- Provide overview of Nova Scotia’s Rh program
- Review guidelines for perinatal antibody screening
- Review guidelines for Rh immunoglobulin administration
Rh Program of Nova Scotia

History:

Early 1960’s: !% of all births were Rh(D) alloimmunized in Nova Scotia

NS infant mortality among highest in Canada

1964: Rh Committee established, modelled on Winnipeg Rh Program

2nd Fetal Transfusion in Canada --Halifax, 1964
Program Goals

- Reduce Rh(D) alloimmunization to lowest possible (0.4 per 1000 total pregnancies)
- Achieve 0% mortality & morbidity due to red cell and platelet antibodies
Rh Program of Nova Scotia

Effectiveness

• New Rh(D) alloimmunized women in NS: reduced from 1 per 100 in 1964 to 1.5 per 1000 in 1982 to <0.4 (.27) per 1000 total births in 2009

• Excellent Provincial compliance with guidelines

• Early detection and management of women with antibodies
Rh Program of Nova Scotia

Program Structure:

Provincial program: NS Department of Health
IWK Health Centre-----Dept Obs & Paeds

Medical Director
Nurse coordinator
Nurse part time

Rh Committee
RCP - administrative support/ database
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Links

IWK Health Centre: FATC; transfusion services; nursing units; Perinatal Centre Provincial hospital transfusion services; obstetrics departments Obstetrics clinics, physicians offices Laboratories and clinicians throughout the Maritime provinces Fetal antigen testing: Wisconsin
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Nursing Role

Promote guidelines for antibody screening & WinRho SDF administration

Review/record data: antibody screens; RhIG (WinRho SDF) administration; cord typing; Kleihauer-Betke for FMH; procedures/events; pregnancy outcomes

Maintaining/updating:
- Guidelines for Perinatal Antibody Screening and RhIG administration
- Patient pamphlet
- Consent for WinRho SDF

Resource for:
women who are Rh negative or have antibodies; family care providers; obstetricians; nursing staff

Education: medical students, nursing staff; nursing students; Telehealth

Database and Research

Website: www.rcp.nshealth.ca/rh
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Managing red blood cell & platelet antibodies

Contacting physician: letters, calls, faxes

Maternal antibody testing
Paternal antigen testing

Arranging/assisting with special procedures:
ultrasounds
amniocentesis
fetal transfusions
delivery alerts & followup
Stimulus

- Fetal red blood cells (feto-maternal hemorrhage)
- Blood transfusion
- Drug abuse - sharing needles
- Naturally occurring

- Primary response (IgM); may take 2wks to 6 months to become IgG antibody
What antibodies do

- permanent IgG antibodies fit through placental barrier
- attach to antigen on fetal red blood cells
- hemolysis causes fetal anemia antenatally
- hemolysis causes neonatal anemia and hyperbilirubinemia
Antibody types

- Rh antibodies: (D*, C, c, E, e)
  * preventable (17% of pop. Rh neg, missing Rh antigen on RBC’s)

- Other examples (non-preventable):
  - Kell
  - Duffy (Fya, Fyb)
  - Kidd (Jka, Jkb)
Scheme of Placental Circulations
White arrows depict separate routes of fetal and maternal circulations within the placenta. Dotted lines represent oxygen, nutrient and waste exchange through the placental barrier.
Separation of Placenta Following Delivery

Diagram portrays the rupture of placental vessels (villi) and connective tissue allowing escape of fetal blood cells. Prior to complete constriction of open-end maternal vessels, some fetal blood may enter maternal circulation.
Mother’s Spleen After Delivery of Incompatible Infant

Antigen on fetal red blood cells triggers immune response causing production of antibody

Incompatible fetal cells enter maternal spleen

Permanent antibody enters maternal circulation

Kernicterus risk

After delivery

**Subsequent Incompatible Pregnancy**

Residual antibodies produced as a response to red cells of a previous incompatible fetus or donor are transported through the placental barrier. They attach to the specific red cell antigen sites of the incompatible fetus of the current pregnancy. Sensitized cells do not have a normal life span; the baby suffers from anemia and its consequences.
Genotyping

- MOM is Rh neg = missing D antigen
- DAD is Rh neg = also missing D antigen
- BABY will be Rh (D) neg (cannot inherit D)
Genotyping (continued)

MOM is Rh neg (d/d = missing D antigen)
DAD is Rh pos (carries D antigen)

Dad can be D / d
50% chance baby will be D-pos
OR Dad can be D / D
100% chance baby will be D-pos
Laboratory Testing

Initial --- ABO; Rh; screen

Positive antibody for HDN

Repeat titres q monthly or as directed by Rh Program
May require further investigations depending on titre
May require antenatal Rx depending on investigations

Neonatal bloods --- ABO; Rh; DAT; Hgb; Bili
Laboratory Testing

Initial --- ABO; Rh; screen

No antibody associated with HDN

Rh neg (check father) --- repeat screen at 28 weeks; repeat at delivery

Rh pos --- repeat screen at 24-28 weeks

Neonatal bloods --- ABO; Rh; DAT
Antibody screening
“group & screen”

- 1st prenatal visit (all women)
- 28 weeks (all women)
- delivery (Rh- or HDN antibodies)
- pre- Rho(D) immune globulin (Rh-)
- **MONTHLY or q 2 wks (if antibodies causing HDN are detected)**
Risk of Rh (D) immunization

- <28 weeks: 0.1%
- 28 weeks to delivery: 1.7%
- Postpartum: 2 to 8%
- Spontaneous abortion: 2-3%
- Therapeutic abortion: 4-5%
- Antenatal bleeding: ?
Prevention:
Rh Immune Globulin (WinRho SDF™)

- 28 weeks (Rh- Dad?)
- postpartum (Rh+ baby)
- abortion/ectopic
- antepartum bleeding
- special procedures (amniocentesis, cordocentesis, CVS)
- external version
- platelet transfusion
- abdominal trauma
- partial molar pregnancy
- blighted ovum
- inadvertent transfusion Rh+ blood
**Prevention of Primary Immune Response to Rh, (D) at Delivery of an Incompatible Fetus**

RhoGAM Rh, (D) Immune Globulin (Human) is injected into the mother within 72 hours of delivery and the immune globulin enters the spleen and lymph nodes. Incompatible Rh, (D) positive fetal cells are not capable of initiating a primary response in the presence of adequate antibody of the same specificity.

Fetal Rh positive red cells plus passively administered antibody (RhoGAM)

No permanent maternal antibody is produced

From: Ortho Diagnostics Inc. (1968). *Blood group antigens and antibodies as applied to hemolytic disease of the newborn.* Raritan, NJ; Author
Rho(D) Immune Globulin
“WinRho SDF™”  “RhoGAM™”

- WinRho SDF™ used in Canada
- blood product
- deep I.M.  \textit{Or}  I.V. route
- ALWAYS draw antibody screen \textit{first}
- 120 \( \mu g \) \textit{or} 300 \( \mu g \) dose
- Kleihauer when indicated
- obtain informed consent (may refuse)
Informed Consent

- blood product (from plasma)
- donors screened for Hep B, C, HIV
- viral inactivation step
- no reports of disease transmission
- risk of Rh disease from 1:10 to 1:1000
- mandated by Krever Inquiry
Kleihauer-Betke Test
% fetal red blood cells in maternal circulation

- Amniocentesis
- antenatal bleeding (2nd & 3rd trimester)
- postpartum (Rh- mom/Rh+ baby)
- Formula for Kleihauer > 0.2%
- Massive feto-maternal hemorrhage (abruptio, stillbirth) Rh - or Rh+
Figure 4. Cord blood of baby with severe Rh erythroblastosis fetalis who required multiple fetal transfusions and exchange transfusions. Smear treated by Kleihauer technique and Wright’s stain. Note adult donor ghost red cells, dark fetal red cells, and early fetal erythroid series from erythroblasts through to normoblasts.
Fetus at Risk

- Fetal anemia diagnosed by:
  - amniocentesis
  - cordocentesis
  - ultrasound

- Hydrops
- Middle cerebral artery Doppler

- Treatment:
  - Intravascular fetal transfusion
  - Preterm birth
Infant at Risk

**Diagnosis:**
- history of HDN antibodies?
- early jaundice < 24 hours
- cord DAT ("Coombs’s") **positive** (due to HDN or ABO antibodies)

**Treatment:**
- Phototherapy
- Exchange or Direct blood transfusion
CORD blood testing

- Direct Antiglobulin Test (DAT) or “Direct Coomb’s”
- POSITIVE test = antibodies on baby’s red blood cells
Cord DAT test

- Most COMMON reason for POSITIVE DAT:
  1. ABO incompatibility
     eg. Mom group O, baby group A or B
  2. Winrho (anti-D) from Mom’s recent injection coats some of baby’s red blood cells
Cord DAT positive

- Other reasons, less common:

  Hemolytic disease causing antibodies crossed over from mother
  (anti-D, c, Kell, Duffy, etc)
Case Study

- 27 y o G1 P0 is Rh neg; partner is Rh pos

  Has antibody screen and WinRho at 28 weeks
  Antibody screen is positive

  What has happened?
Case Study

- 27 y o G1 P0 is Rh neg; partner is Rh pos

  Has antibody screen and WinRho at 28 weeks
  Antibody screen is positive

  What has happened?

  1) Isoimmunization or
  2) Antibody screen taken after injection instead of before
Case Study

- 29 y o G3 P1 A1 at 28 weeks
- A neg ; Positive screen for Fya  1/64
- What are the next two steps?
Case Study

- 29 y o G3 P1 A1 at 28 weeks
- A neg ; Positive screen for Fya 1/64
- What are the next two steps?
  - Assess for fetal anemia; paternal genotype
  - WinRho
Case Study

- 29 y o G2 P1 presents @ 29 weeks with antenatal bleeding, U/S shows small marginal abruption, fetus well, uterus non-tender

- Other important Mx issues?
Case Study

- 29 y o G2 P1 presents @ 29 weeks with antenatal bleeding, U/S shows small marginal abruption, fetus well, uterus non-tender
- Other important Mx issues?
- Check Rh; pt is neg and had just received her WinRho 300ug 5 days earlier; Is this adequate?
Case Study

- 29 y o G2 P1 presents @ 29 weeks with antenatal bleeding, U/S shows small marginal abruption, fetus well, uterus non-tender
- Other important Mx issues?
  - Check Rh; pt is neg and had just received her WinRho 300ug 5 days earlier; Is this adequate?
  - No---needs Kleihauer
A healthy baby after six in-utero transfusions
**BILIRUBIN**

- **In UTERO** = unconjugated changed to conjugated; excreted by mother

- **After Birth** = baby cannot do this well
  Unconjugated bilirubin causes JAUNDICE and risk of KERNICTERUS (staining of brain cells) if not treated
Feto-maternal hemorrhage

- Baby’s and mother’s blood systems are separate in placenta
- Break in barrier can let come baby’s red blood cells enter mother’s circulation
WinRho Dosing

300 ug  28 weeks
antenatal bleed*
amniocentesis, etc*
abd trauma*
>12 wk preg loss

120 ug  postpartum*
<12 wk preg loss
external version
platelet transfusion

* Kleihauer--- 120 ug for <0.2%; 300ug for <0.5%
Antibody types

- Rh antibodies: (D*, C, c, E, e)
  * preventable (17% of pop. Rh neg, missing Rh antigen on RBC’s)

- Other examples (non-preventable):
  - Kell
  - Duffy (Fya, Fyb)
  - Kidd (J ka, J kb)
## Cause of anti-D sensitization [NS residents]

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Failed 28 week injection</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Failed postpartum injection</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>Sensitized before 28 weeks</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>28 week not given</td>
<td>5</td>
<td></td>
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<tr>
<td>Postpartum not given</td>
<td>2</td>
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<tr>
<td>Antenatal bleeding – not given</td>
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<tr>
<td>Spontaneous abortion – not given</td>
<td>6</td>
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<tr>
<td>Mismatched blood – not given (plasma)</td>
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<tr>
<td>Therapeutic abortion – not given</td>
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<tr>
<td>Patient refusal</td>
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<tr>
<td>Unknown sensitization time</td>
<td>4</td>
<td>16</td>
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<tr>
<td>Not given before protocol established</td>
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<tr>
<td><strong>TOTALS (% based on # Rh-/yr reported to Rh Program)</strong></td>
<td>73 (0.32%)</td>
<td>45 (0.27%)</td>
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