



Repeat administration of Rh immunoglobulin if undelivered at 40 weeks gestation

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Meeting of Atlantic Society of Obstetricians & Gynecologists
September 18, 2009



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IWK Category A Grant
Reproductive Care Program of Nova Scotia
Rh Program of Nova Scotia

Introduction

- The use of anti-D immune globulin in pregnancy has helped reduce the perinatal morbidity and mortality associated with Rh-alloimmunisation
 - In Canada, postpartum prophylaxis offered since 1968
 - Routine antepartum prophylaxis initiated in 1976
- Guidelines outline recommended use of anti-D immune globulin
 - SOGC Clinical Practice Guidelines (2003)

Introduction, cont'd

- Maternal alloimmunisation continues to occur
 - 6/1000 (USA) vs. 0.4/1000 live births (Canada, UK)
 - 1-2% D-negative women
 - Failure to administer RhlgG to eligible women
 - Inadequate dosing schedules
- Standard in Canada is to administer antepartum prophylaxis at 28 weeks GA
 - Sensitization can occur at any time during pregnancy
 - It is most common in 3rd trimester and during delivery
 - Optimal dosing schedule remains unclear

Introduction, cont'd

- Pharmacokinetics
 - Maximal RhIgG concentration 2-5 days after injection (IM)
 - 12-weeks post-injection (~ 40 weeks GA) residual levels of anti-D are very low or undetectable
 - 0.6-1.0 ng/mL = 5-8 μ g anti-D \rightarrow FMH < 1mL
- \rightarrow ? Significant proportion of women with seemingly inadequate protection at vulnerable time in their gestation

SOGC Guidelines (2003)

- There is insufficient evidence at this time to make a recommendation for or against administering another dose of anti-D to an unsensitized D-negative woman who remains undelivered at 40 weeks
- **A repeat antepartum dose of Rh immune globulin is generally not required at 40 weeks, provided that the antepartum injection was given no earlier than 28 weeks' gestation**

Research Objective

- To evaluate the need for repeat administration of Rh immunoglobulin at 40 weeks if a woman at risk for Rh alloimmunisation remains undelivered

Methods

- Data from Nova Scotia Atlee Perinatal Database (NSAPD) and Rh Database
 - Rh-negative women in Halifax County
 - Infant > 500g & > 20 weeks GA
 - Delivery @ IWK Health Centre (1998-2007)
 - Received both antenatal & postpartum anti-D prophylaxis
 - Categorized according to duration of time between antepartum/postpartum doses
 - **≤ 12 weeks vs. > 12 weeks**

Methods, cont'd

- Outcome variables
 - Need for additional Rh immune globulin
 - Dose
 - Kleihauer-Betke result
 - Postpartum length of stay
 - Neonatal length of stay



Methods, cont'd

- Data access and REB approval obtained from the Nova Scotia Atlee Perinatal Database and IWK Health Centre
- Summary characteristics described using chi-square and Student's t-test
- Calculation of univariate odds ratios
- $P < .05$ significant
- Analyses using SAS 8.2 and EpiInfo

Results

- 4319 Rh-negative women identified
 - Received both antepartum and postpartum doses
 - 3427 women delivered ≤ 12 weeks from ~28 week antepartum dose
 - 892 women delivered > 12 weeks from ~28 week antepartum dose

Table One. Characteristics of Study Population

Characteristic	≤ 12 weeks	> 12 weeks	P value
Maternal age ≥ 35 years (%)	497 (14.5)	115 (12.9)	.22
Multiparous (%)	1 561 (53.1)	292 (40.7)	<.001
Singleton pregnancy (%)	2 829 (96.2)	718 (100)	-
Mean pre-pregnancy weight, kg (SD)	69.3 (16.1)	68.9 (16.3)	1.0
Smoker (%)	462 (16.9)	115 (16.9)	1.0
Mean duration from 28 week injection to PP injection (25 th , 75 th)	80 (73, 85)	95 (92, 97)	<.001

Table Two. Characteristics of Study Population

Characteristic	≤ 12 weeks	> 12 weeks	P value
Method of delivery (%)			
Spontaneous vaginal	1 889 (64.2)	458 (63.8)	<.001
Operative vaginal	265 (9.0)	81 (11.3)	.06
Caesarean	782 (26.6)	178 (27.8)	.27
Delivery > 40 weeks GA (%)	15 (0.4)	520 (58.3)	<.001
Mean birthweight in grams (SD)	3412 (571)	3728 (465)	<.001
Perinatal mortality (%)	7 (0.2)	1 (0.1)	1.0

Table Three. Fetomaternal hemorrhage and RhlgG dosing

	≤ 12 weeks	> 12 weeks	Odds ratio (95% CI)
Kleihauer-Betke > 0.2 (%)	68 (1.0)	14 (1.6)	0.79 (0.42-1.45)
Kleihauer-Betke > 0.5 (%)	33 (1.0)	8 (0.9)	0.93 (0.40-2.11)
RhlgG dose > 120μg (%)	153 (4.5)	29 (3.3)	0.72 (0.47-1.09)
RhlgG dose > 300 μg (%)	48 (1.4)	9 (1.0)	0.72 (0.33-1.52)
Maximum RhlgG dose	2 280	3 300	-

Table Four. Maternal and neonatal length of stay

	≤ 12 weeks	> 12 weeks	P value
Median maternal postpartum length of stay, days (SD)	2.7 (1.7, 3.3)	2.3 (1.7, 3.1)	.41
Median neonatal length of stay, days (SD)	2.4 (1.7, 3.3)	2.5 (1.7, 3.1)	.63

Cost analysis (Step 1!)

- Cost of winRho provided by Canadian Blood Services
 - 120 μg \rightarrow \$30.02
 - 300 μg \rightarrow \$75.04
- Average cost of postpartum dose
 - \leq 12 weeks \$33.22
 - $>$ 12 weeks \$ 32.86

Conclusion

- Delivery at > 40 weeks gestational age does not appear to increase the risk of fetomaternal hemorrhage requiring additional IgG
- No difference in length of hospital stay (maternal or neonatal) identified between groups

Limitations

- Time period of study limited by incomplete linkage between Atlee and Rh databases
- Limited by variables present in databases
- Small numbers may have affected significance of comparisons

Future Work

- Characterize risks for increased RhIgG injections in the third trimester
 - Bleeding, ECV, amnio (FLM), etc.
 - Kleihauer information < 0.2 for whole study group following linkage to Meditech (underway)
 - Clarify intrapartum bleeding
 - Additional outcomes:
 - Rates of isoimmunization
 - Neonatal hyperbilirubinemia/need for phototherapy
 - Maximum bilirubin/minimum hemoglobin
 - Costs per Rh-negative woman
- Further clarify effect of long duration from antepartum prophylaxis

