Vancomycin for Intrapartum Antimicrobial Prophylaxis for Group B Streptococcus: Is a Dose Change Necessary?

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Background

- Group B streptococcus (GBS) is the leading cause of neonatal sepsis.
- In 1996, the first guideline on intrapartum antimicrobial prophylaxis (IAP) for women colonized with GBS was published. Since then, the incidence of GBS early onset disease (EOD) has declined to 0.23 newborns per 1000 live births in 2015.
- In 2019, the American College of Obstetricians and Gynecologists (ACOG) issued an updated version of this guideline that recommended increasing the dose of vancomycin for IAP from 1 gm every 12 hours to 20 mg/kg every 8 hours (maximum 2 gm/dose).
- This newly recommended dosing of vancomycin for IAP stems from two small pharmacokinetic studies that targeted maternal serum and cord blood vancomycin levels of 10-40 mcg/ml despite the minimum inhibitory concentration (MIC) breakpoint being 1 mcg/ml.
- Vancomycin has been shown to rapidly decrease GBS colony counts in women receiving IAP, with median colony counts decreasing to 6.7 % of their initial value within 2 hours of the infusion and to approximately 0% within 6 hours.

Hypothesis

- The current dose of vancomycin for IAP is resulting in higher-than-anticipated rates of GBS EOD.

Methods

- Study site: 448-bed community hospital
- Study population: All patients who received vancomycin for IAP between January 1, 2018 and June 27, 2019.
- Maternal charts were reviewed retrospectively for weight, body mass index (BMI), gestational age at delivery, prior infant with GBS disease, duration of rupture of membranes (ROM), intrapartum fever, additional antibiotics, mode of delivery, and vancomycin dosing.
- Neonatal charts were reviewed retrospectively for mortality, infection, and level of care.

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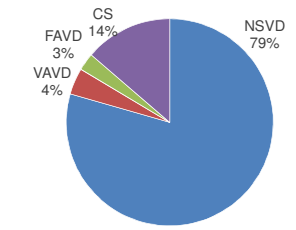
Results

- A total of 73 maternal charts and 74 neonatal charts were reviewed.

Table 1: Maternal Factors (N = 73)			
	No. (%)	**Average ± STD**	**Median (IQR)**
Dose (mg)		1000 ± 36.1	
Maternal weight (kg) at delivery		94 ± 20.5	89.8 (99.6-72.3)
Vancomycin dose (mg/kg/dose)		11.3 ± 2.9	11.0 (9.0-12.6)
Dose < 20 mg/kg/dose	72 (98.6)		
Total dose of vancomycin (mg/kg)		15.8 ± 10.0	12.6 (10.4-17.1)
Number of doses given		1.4 ± 0.6 (range: 1-3)	
Time from first dose to delivery (hr)		10.5 ± 8.4	8.8 (3.7-14.5)
Time from last dose until delivery (hr)		6.0 ± 4.3	5.1 (2.5-9.0)
Time from first dose to delivery < 4 hr	20 (27.4)		
Time from first dose to delivery < 2 hr	12 (16.4)		
Pre-pregnancy BMI (kg/m^2)		29.6 ± 7.0	29.1 (22.8-34.7)
Delivery BMI (kg/m^2)		34.2 ± 6.8	34.3 (28.3-38.8)
Prior infant with GBS disease	1 (1.4)		
Gestational age at delivery (weeks)		38.4 ± 2.9	39 (37.7-39.7)
Gestational age at delivery < 37 weeks	11 (15.1)		
Intrapartum temp >38 °C	4 (5.5)		
ROM (hrs)		8.7 ± 9.3	5.4 (2.5-12.8)
ROM > 18 (hrs) or unknown	12 (16.4)		

Figure 1: Mode of Delivery



CS = cesarean section; NSVD = normal spontaneous vaginal delivery; FAVD = forceps-assisted vaginal delivery; VAVD = vacuum-assisted vaginal delivery

Table 2: Additional Maternal Antibiotic Use (N = 73)	
Reason	**No. (%)**
None	54 (73.9)
Pre-operative	11 (15)
Chorioamnionitis	3 (4.1)
Alternative GBS regimen	2 (2.7)
Urinary Tract Infection	1 (1.4)
Clostridium difficile suppression	1 (1.4)
Sinusitis	1 (1.4)

Table 3: Fetal Outcomes (N = 74)	
	No. (%)
NICU admission, non-sepsis	5 (6.8)
NICU admission, sepsis rule out	6 (8.1)
NICU admission, culture negative sepsis	1 (1.4)
NBN admission, sepsis rule out	4 (5.4)
Death	0 (0)
Standard Care	58 (78.4)

NICU = Neonatal Intensive Care Unit; NBN = Newborn Nursery

Discussion

- Given the rates of GBS EOD in 2015, the current dose of vancomycin for IAP did not result in higher-than-anticipated rates of GBS EOD.
- The new, recommended dose of vancomycin is based on outdated targets derived from studies and guidelines prior to the adoption of the area under the curve to minimum inhibitory concentration (AUC/MIC) concept.
- The new, recommended dose of vancomycin is based on pharmacokinetic goals and not clinical outcomes. It has yet to be determined that maternal serum and cord blood levels are appropriate surrogate endpoints.
- The mechanism of GBS IAP is unknown (decolonization vs. maternal serum and/or cord blood level).
- The risk of maternal adverse events (nephrotoxicity, vancomycin-induced histamine release reaction) increases with higher doses of vancomycin.

Conclusions

- At UnityPoint Health-Meriter, the current dose of vancomycin for IAP (1 gm every 12 hours) did not result in higher-than-anticipated rates of GBS EOD.

Limitations

- Given the rate of GBS EOD in 2015, only 1 neonate out of every 4350 maternal patients who received IAP would develop GBS EOD. Given the rate of vancomycin use for IAP, it would take approximately 90 years to obtain this sample size.

Further Directions

- Continue to review cases of GBS EOD to determine if a dose-adjustment of vancomycin for IAP is indicated.

References

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