

Evaluation of Aminoglycoside Monitoring and Dose Titration in the Neonatal Intensive Care Unit

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Introduction

- ❖ Aminoglycosides
 - Frequently used in neonatology for suspected or presumed sepsis
 - Bactericidal against gram negative organisms
 - Relatively low resistance rate
 - Low cost
- ❖ Limitations
 - Narrow therapeutic window
 - Close monitoring required
 - Potential nephrotoxicity and ototoxicity

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Background

- ❖ Extended- interval aminoglycoside administration (EIAA)
 - 24 to 48 hour dosing interval
 - Increased weight-based dosing with prolonged interval

RATIONALE

- | | |
|---------------------------|--------------------------------|
| Improve efficacy | Decrease organ toxicity |
| • post antibiotic effect | • nephrotoxicity |
| • concentration dependent | • ototoxicity |
| • adaptive resistance | |

Neonates → beneficial due to ↑ Vd and ↓ GFR

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Background

Adult vs. Neonatal EIAA

Adults (Hartford Protocol)	Neonates
• Higher peaks	• Higher peaks
• Undetectable troughs	• Detectable troughs

****SIGNIFICANT DELAY IN DRUG MONITORING****

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Background

- ❖ Children's National Medical Center
 - ❖ Level III referral center with 55-bed NICU
 - Currently no standardized EIAA monitoring protocol
 - 24 hour level
 - Around 3rd dose
 - Random levels
- ❖ Variation may lead to out of range levels

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Study Objectives

- ❖ Evaluate EIAA, monitoring, and subsequent dose titration in Children's National NICU
- ❖ Identify serum level monitoring delay due to EIAA

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Research Design

- ❖ Retrospective chart review of NICU patients
- ❖ Non-randomized
- ❖ Inclusion criteria
 - Gentamicin or amikacin use
 - Between May 1 and October 31, 2009
 - Normal renal function
 - At least 2 doses administered

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Data Elements

- Demographics
- Peaks and troughs
- Dosage regimens
- Concomitant nephrotoxic meds
- Urine output
- Duration of therapy
- Number of doses
- Treatment indication

Outcome Measures

- ❖ Primary
 - Incidence of appropriate monitoring of peak and trough levels in NICU patients treated with aminoglycosides
- ❖ Secondary
 - Incidence of aminoglycoside levels outside therapeutic ranges
 - Number of patients on empiric treatment vs. treatment of culture-confirmed infections
 - Concomitant use of other nephrotoxic meds

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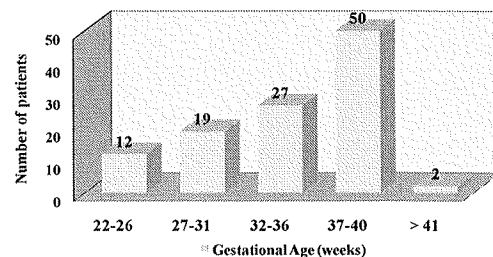
Results

- ❖ 118 patient charts reviewed
 - 110 patients met inclusion criteria
 - Out of 110 patients, 135 instances were reviewed
 - # of instances = subsequent dose changes or different courses of therapy
 - Gentamicin use - 92 %
 - Amikacin use - 8 %

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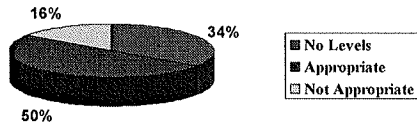
Results

Figure 1: Gestational Age



Results

Figure 2: Appropriate timing of peak and trough levels

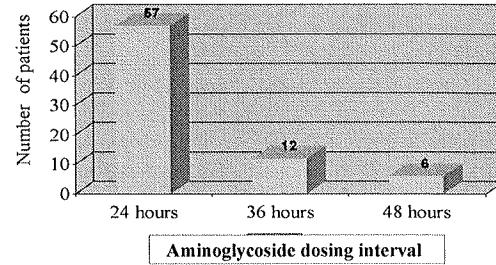


Appropriateness: Trough level → 30 minutes before 3rd dose

Peak level → 1 hour after completion of 3rd dose infusion

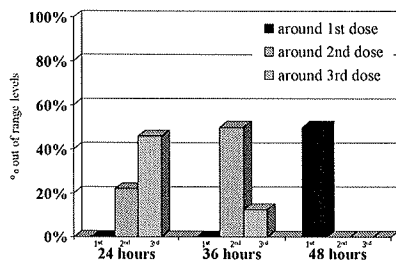
Results

Figure 3: Specific dosing intervals



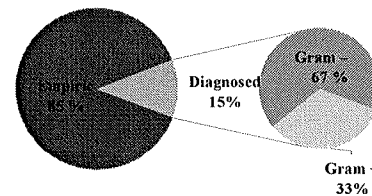
Results

Figure 4: Out of range levels



Results

Figure 5: Empiric vs. Culture-Confirmed Treatment
Gram Negative vs. Gram Positive Infections



Concomitant Nephrotoxins

- ❖ 33 % (n = 35) on other nephrotoxic agents
 - Vancomycin - 69 % (n = 24)
 - Acyclovir - 27 % (n = 9)
 - Indomethacin - 5 % (n = 2)
- ❖ Indication for more frequent monitoring due to increase risk of nephrotoxicity

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Discussion

- ❖ Appropriateness of monitoring
 - Many patients were appropriately monitored
 - Exceptions
 - Discontinuation of therapy before reaching steady- state
 - Noncompliance to dose monitoring
 - Both factors may be directly caused by EIAA
- Out of range levels
 - In all dosing intervals regardless of which dose the level was drawn
 - Levels around 1st or 2nd dose ← controversial
 - Delay in drug monitoring ← controversial

Discussion

- ❖ Earlier sampling may predict steady-state serum levels
 - Further analysis of data needed to determine if earlier sampling in extended intervals will correlate to steady state
 - Assist in early detection of out of range levels
 - Direct subsequent dose changes for better patient outcomes

Conclusion

- ❖ More frequent and standardized monitoring of EIAA is important in NICU population
 - Many patients on other nephrotoxic medications
 - Proper empiric treatment may prevent potentially fatal infections

Question:

What is the difference between routine monitoring and dose titration of extended interval aminoglycoside dosing in adults and neonates?

In adults, the Hartford nomogram is used to determine initial dosing interval based on level drawn at a specific time after the start of the infusion.

In neonates, there is no standardization of practice.

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References

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Peaks and troughs in correlation with intervals

