Central apnea of prematurity in neonatal patients: Evaluation of caffeine citrate monitoring in a pediatric institution

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1

Acknowledgements

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2

Introduction

- Apnea of Prematurity (AOP)
  - Cessation of respiratory airflow
  - Pathologic condition
    - Pause in respiration ≥ 20 seconds ***OR***
    - Cyanosis, pallor, or bradycardia
  - Occurs in 25% of all premature infants
    - ≤ 28 weeks: almost 100 %
    - 30 – 31 weeks: 50 %
    - 32 – 33 weeks: 14 %
    - 34 – 35 weeks: 7 %

3

Background

- Caffeine Citrate
  - CNS stimulant
  - Increases central respiratory drive
  - Improves diaphragmatic contractility
  - Preferred agent over theophylline for AOP
  - Adverse Effects
    - Tachycardia
    - Restlessness
    - Hyperactivity

4

Background

- Caffeine Monitoring
  - Utility of measuring caffeine concentrations remains debatable
  - Serum caffeine concentrations are inconsistently drawn in the NICU at Children's National
    - Every 1 – 2 weeks
    - Increased symptoms
    - Increased toxicity indicators

5

Objective & Primary Outcome

Objective

- Determine the correlation between the number of symptomatic episodes or toxicities to caffeine levels in the neonatal population at Children's National

Primary Outcome

- Frequency of routine caffeine level monitoring

6

Secondary Outcomes

- Number of dose adjustments made without caffeine levels
- Incidence of tachycardia with therapeutic caffeine levels
- Absence of dose changes made with monitoring
- Number of caffeine levels drawn
  - Once daily dosing
  - Twice daily dosing
- Incidence of apneic episodes
  - Once daily dosing
  - Twice daily dosing
- Baseline demographics
  - Birth weight
  - Gestational age
  - Hepatic and renal function

7

Research Design

- Retrospective review
  - January 1, 2009 to September 30, 2009
  - Non – randomized
- Institutional Review Board (IRB) approval prior to data collection

8

Research Design

Inclusion Criteria

- Admission to NICU
- ≥ 1 dose of caffeine citrate
- Documented diagnosis of AOP
- Birth weight ≤ 1500 gm
- Post Menstrual Age (PMA) ≤ 28 weeks

Exclusion Criteria

- Any major congenital abnormality
- Any neurological condition
- Previous treatment with methylxanthines
  - Aminophylline
  - Theophylline

9

Research Design

Data Elements

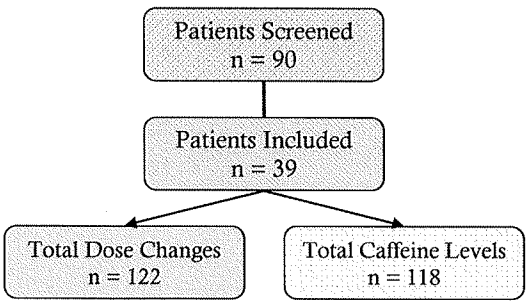
- Gestational age
- Date of birth
- Birth Weight
- Dosing regimen
  - mg/kg
  - Interval
- Indication for dose change
- Indication for caffeine level monitoring
- Incidence of apnea
- Incidence of tachycardia
- Baseline heart rate
- Baseline renal and hepatic function

Statistical Analysis

- Pearson's Correlation Coefficient (X^2)

10

Results



11

Results

Table 1. BASELINE DEMOGRAPHICS

VARIABLE (n = 39)	VALUE *
Gestational Age (wks)	27 ± 2 (23 – 32)
Birth Weight (gm)	959.2 ± 276.2 (510 – 1450)
Hepatic Function	
AST	37 ± 28 (12 – 141)
ALT	19 ± 6 (7 – 35)
Renal Function	
BUN	22 ± 12 (7 – 61)
SCr	0.9 ± 0.7 (0.2 – 4.2)

* Mean ± SD (range)

12

Results

Table 2. PRIMARY OUTCOME MEASURE

VARIABLE	n (%)
Routine serum monitoring present	16 (41 %)
Non – routine monitoring	23 (59 %)

13

Results

Table 3. SECONDARY OUTCOME MEASURES

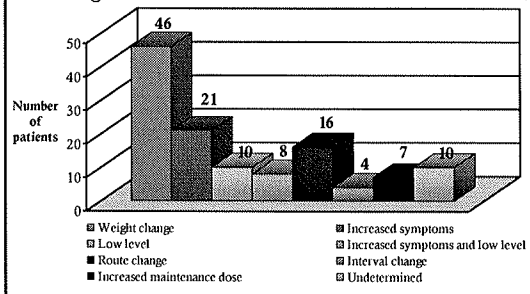
VARIABLE	n (%)	p - value
Dose adjustments without caffeine levels (n = 122)	104 (85 %)	0.06
Incidence of tachycardia with therapeutic caffeine levels (n = 39)	11 (28 %)	0.54
Number of caffeine levels drawn (n = 118)		
Once daily dosing	76 (63.8 %)	0.03†
BID dosing	43 (36.1 %)	0.04†
Incidence of apneic episodes		
Once daily dosing (n = 26)	18 (69.2 %)	0.80
BID dosing (n = 18)	11 (61.1 %)	0.58
Absence of dose changes with caffeine levels (n = 39)	2 (5 %)	0.29

† = p – value ≤ 0.05

14

Results

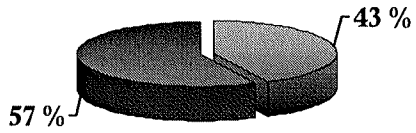
Figure 1. RATIONALE FOR DOSE CHANGES



15

Results

Figure 2.
HEART RATE ASSOCIATED WITH DOSE CHANGES



Tachycardia

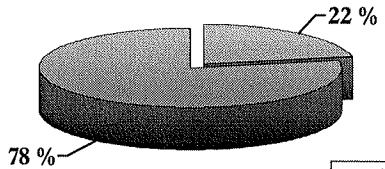
Normal Heart Rate

p ≤ 0.05

16

Results

Figure 3.
CAFFEINE LEVELS USED TO GUIDE DOSE CHANGES



p > 0.05

Changes based on levels

Monitoring with no dose changes

17

Limitations

- Limitations
  - Small patient sample size
  - Study not powered to detect significant results
  - Non – randomized

18

Discussion

- Majority of patients
  - Absence of routine caffeine monitoring
  - Apneic episodes with both dosing regimens
  - Did not have a dose adjustment made which correlated to a caffeine serum concentration
  - Had dose changes based on increasing weight
  - Seemed to maintain normal heart rates with increased dosing regimens

19

Conclusion

- Clinical application of routine caffeine monitoring may be questionable
  - Inconsistent monitoring
  - No major toxicities seen with caffeine regimens
  - No significant differences with apneic episodes with dosing regimens

20

Future Directions

- Possible implementation of a caffeine monitoring protocol
- Higher PMA inclusions
  - Include patients > 28 weeks
- Perform subgroup analysis
  - Pulmonary hypertension
  - Reflux

21

Question

Why is caffeine citrate preferred for use in neonates over caffeine sodium benzoate?

✓Caffeine sodium benzoate is associated with "gasping syndrome" in neonates; which consists of gasping respirations, metabolic acidosis, respiratory distress, CNS dysfunction (convulsions and intracranial hemorrhage), hypotension and cardiovascular collapse.

22

Questions ?

23

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24

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