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A Comparison of the Effect of Intermittent and Continuous Infusion of Meropenem on the Prevalence of Nausea in Pediatric Cystic Fibrosis Patients

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STATEMENT OF THE PROBLEM

- **Background**
  - Cystic Fibrosis and Treatment
    - Cystic Fibrosis (CF) is a genetic disease, leading to changes of membrane secretions causing obstruction of smaller airways
    - CF patients often develop pulmonary infections and require antibiotic treatment
      - Loss of lung function increases the risk of death in CF patients
      - Standard treatment involves beta-lactam antibiotics ex. meropenem
  - Pharmacokinetics and Pharmacodynamics of Meropenem
    - Meropenem is a broad spectrum beta lactam that acts by lysing microbes through interfering with bacterial cell wall synthesis.
      - Safe and effective treatment, however data on pediatric patients is limited
    - Effectiveness of meropenem determined by time sensitive dosing and is effective only when the minimum inhibitory concentration (MIC) is reached
    - Meropenem can be administered as a continuous infusion or intermittent bolus
- **Significance of the Problem**
  - There is a lack of information regarding the use of meropenem in pediatric CF patients
  - There is a lack of supporting information for the use of one treatment regimen over the other
  - Quality of Life – CF patients struggle with malnutrition and treatment with meropenem compounds the problem due to significant nausea
  - Would a different dosing regimen reduce side effects of meropenem treatment?

OBJECTIVES

To test establish clinical protocols for meropenem administration in pediatric CF patients admitted to Dayton Children's with the goal of reducing nausea as a side effect.

To assess reported nausea and its relationship to serum concentration of meropenem in pediatric CF patients after administration of meropenem in either a continuous or intermittent IV infusion.

HYPOTHESES

Null Hypotheses:

•Continuous IV administration of meropenem will have no effect on the side effects of nausea when compared to intermittent administration.

•The differences in serum concentrations between intermittent and continuous IV administration of meropenem do not change the number of dosages of anti-nausea medications ordered in pediatric CF patients

Alternative hypotheses:

•Continuous IV administration of meropenem will reduce the side effects of nausea when compared to intermittent administration

•The differences in serum concentration between intermittent and continuous IV administration of meropenem do change the number of dosages of anti-nausea medications ordered in pediatric CF patients

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PROPOSED METHODS

Study Design

Crossover study designed to compare blood levels of meropenem and effect on nausea in pediatric cystic fibrosis patients

Sample

This pilot study will comprise approximately 10 subjects from ages seven to twenty-one

Data Collection and Measurement

Cross over study

- Patients randomly divided into two treatment groups
  - One initially receives intermittent dosing of meropenem
  - One receives continuous infusion of meropenem
  - Then groups will switch after four days
- Continuous dose 120 mg/kg/day
- Intermittent dose 40 mg/kg/dose infused over 30 minutes every 8 hours

Serum Meropenem

- Determined through blood draw
  - Intermittent dose: After the third dose
  - Continuous dose: After day three

Nausea Scale

- Levels of nausea will be determined by recording frequency of Kytril doses requested

PICC line

- Sub-study to be conducted to determine reliability of serum levels taken from PICC line
  - Serum levels of meropenem in both groups compared between PICC line blood draws and peripheral blood draws.

HPLC Assay

- Meropenem concentrations will be measured utilizing a High Pressure Liquid Chromatography (HPLC) instrument

PROPOSED ANALAYSES

Nausea levels: average the doses of Kytril requested by each patient, number of episodes of emesis

Two tailed t test (α =0.05, and β = 0.2)

Comparison of the means of two treatment arms.

Concentration of meropenem in blood

Arithmetic mean will be calculated for each sample (95% confidence interval)

Comparison of Treatment Arms

Two-tailed t-test will be used to compare means of the two treatment arms

Two-tailed t-test will be used to compare the two types of blood draw methods

LIMITATIONS

- Small sample size will limit the generalizability of the results.
- Additional medication regimens may contribute to nausea.

FUTURE DIRECTION

The goal of this study is to provide a framework for further multi-site studies of the same nature.

TIMELINE

- **September 2013:** Obtain IRB approval
- **September 2013-2014:** Enrollment and sample collection
- **September 2013-March 2015**: Sample and Data analysis

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