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INTRODUCTION

As bacterial resistance has become an increasing problem encountered in patient care, clinicians have been forced to reach deeper into the armamentarium of available antibiotics. One antibiotic family, the polymyxins, fell out of use in the 1970s due to concerns of renal and neurotoxicity, however, the therapy has remained efficacious from an antimicrobial standpoint. Two antibiotics from the polymyxin family are typically used for severe, invasive infections: polymyxin B and polymyxin E (i.e. Colisitin). CUMC preferentially uses polymyxin B. The mechanism of action of the two drugs is similar. The amphiphatic portion of molecule preferentially attaches to endotoxin, while the hydrophobic tail appears to interfere with the outer membrane of gram negative bacteria, similar to a detergent.

There are numerous case reports in the older literature about toxicity associated with the polymyxins. The largest published study examined 288 cases, and found a rate of renal toxicity of 20% (complications found in 64/317 total courses of antibiotic given) (2). However, in patients with pre-existing renal disease, the rate of complications was much higher at 36% (6). Two caveats to be noted are that these prior studies examined the use of colistimethate sodium (thought to be less nephrotoxic than colistin) and that the doses used are higher than doses typically used (1). Since the reintroduction of the antibiotics in the late 1990s, reports of renal toxicity have been considerably less than previously documented. Two studies published in the early 2000s showed incidence of renal toxicity between 14 and 18% (1,5). At our institution, a study was published in 2004 that examined the use of polymyxin in inpatients treated from 2000-2003 (5). The study found the incidence of renal toxicity (defined to be a doubling of serum creatinine) to be 10% (3/29).

This study plans to examine the incidence of renal toxicity, again as defined as a doubling of serum creatinine in patients who have received polymyxin since 2003. Studies undertaken since the re-introduction of the antibiotic have dealt with modest numbers of patients who have received the antibiotic. This study would examine all patients who have received the antibiotic over the last seven years, greatly increasing the chances of finding a statistical difference between the historical rate of renal toxicity and those observed currently. As use of polymyxin has increased, more and more patients have required treatment with polymyxin. I propose that the incidence of renal toxicity is in fact closer to the 10% as seen before rather than the lower limit of 20% as described prior to polymyxin’s disuse.

STUDY DESIGN

This study will be a retrospective chart review of adult (age > 18 years) inpatients who have received polymyxin B from July 2003 to present. All adult inpatients who received polymyxin will be included in the analysis, with the exception of patients who were receiving renal replacement therapy at the time of antibiotic initiation. Patient data will be accessed with the assistance of the electronic medical record.

The primary outcome will be development of a doubling of serum creatinine among patients who received polymyxin. The proportion of these patients will be compared to the patients from the study by Koch-Weser, et al. Statistical analysis for the primary outcome will be undertaken using the chi square model. Other patient characteristics, such as length of hospital stay, necessity for care in the ICU, and comorbid conditions will also be assessed.

Power Analysis:
Assuming a difference of 10% between the recent group of patients to receive treatment and the historical cohort observed by Koch-Weser, et al, we would need a sample size of 110 patients if we wish to achieve 80% power and an alpha of 5%.

STUDY PROCEDURE:

Patients' data will be accessed by utilizing the "data warehouse" feature of WebCIS to obtain the medical record numbers of patients who received polymyxin during their hospitalization. Patient charts will be reviewed. Baseline creatinine levels will be recorded (prior to receiving polymyxin). The creatinine will then be followed both through the duration of their course of antibiotic therapy as well as the intervening week after treatment is completed. Patients who double their creatinine from baseline or require renal replacement therapy will be counted as having renal complications.

STUDY DRUG:

Polymyxin B

MEDICAL DEVICE: N/A

STUDY QUESTIONNAIRES: N/A

STUDY SUBJECTS:

All adult inpatients at CUMC who have received polymyxin during the study period (mid 2003-present) will be eligible for study.

Patients who are already receiving dialysis at the time of antibiotic initiation will be excluded.

RECRUITMENT: N/A

CONFIDENTIALITY:

Unique identifiers will be assigned to each patient. Personal information will be available only to the investigators.

CONFLICTS OF INTEREST:

No conflicts of interest are apparent.

LOCATION:

The study will take place at CUMC.

RISKS/BENEFITS TO SUBJECT: N/A

COSTS/COMPENSATION TO SUBJECT: N/A

References:
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