Serial Sinus Aspirate Sampling (SSAS): A Novel Technique for Evaluating Antimicrobial Therapy of Acute Maxillary Sinusitis (AMS)

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INTRODUCTION

The relationship between drug exposure and the time course of antimicrobial effect at the primary infection site for acute maxillary sinusitis has not previously been explored. To quantify the time course of sinus sterilization, describe gatifloxacin effect at the infection site, and to pose the hypothesis that the use of continuous and sustained exposure of organisms to gatifloxacin was associated with rapid sinus sterilization and describing drug exposure at the infection site provides more robust information than standard approaches used for evaluating antimicrobial therapies of acute maxillary sinusitis. The collection of pharmacokinetic data from the site of infection may allow for better pharmacokinetic characterization of antimicrobial agents for the treatment of acute maxillary sinusitis. This may result in useful evaluation of the efficacy of antimicrobial agents with these patients.

METHODS

Study Design

- Single-center, open-label study evaluating the pharmacokinetics and pharmacodynamics of gatifloxacin in adult patients with acute maxillary sinusitis.

PATIENTS

- Eligible and aged 18 to 70 with at least 1 of the following: acute maxillary sinusitis, facial pain/tenderness over the maxillary antra, or purulent nasal discharge.
- Randomized to receive gatifloxacin 400 mg orally twice daily for 5 days.

EXCLUSION CRITERIA

- Pregnancy or lactation.
- Allergy to any component of the investigational drug.
- Known drug resistance to gatifloxacin.
- Use of any non-antimicrobial drugs that could affect pharmacokinetics.

METHODS, continued

Pharmacokinetic Analysis

- Individual patient pharmacokinetic parameters were determined using non-compartmental methods using WinNonLin® Version 5.0.1.5

Pharmacokinetic/Pharmacodynamic (PD) Analysis

- A biophase model was developed to describe the concentration of gatifloxacin in the sinus and plasma compartments.

Pharmacodynamic Analysis

- The primary outcome measure was the time to microbiological eradication of pathogenic organisms from the sinus.

Clinical Outcomes

- The primary outcome measure was microbiological sterilization of the sinus.

ADVERSE EVENTS

- Adverse events were noted and graded in nature for various adverse events.

RESULTS

Pharmacokinetic Analysis

- Median predicted steady-state gatifloxacin concentration versus time profile in plasma and sinus aspirate with a representative patient insert is presented in Figure 2.

Pharmacodynamic Analysis

- Of the 10 clinically evaluable patients, 7 had sufficient pharmacokinetic data for analysis.

Clinical Outcomes

- Seven of the 10 patients enrolled had sufficient data for clinical response evaluation.

ADVERSE EVENTS

- Adverse events were noted and graded in nature for various adverse events.

DISCUSSION AND CONCLUSIONS

- The objectives of this study were to quantify the time course of antimicrobial sterilization and to describe gatifloxacin exposure at the infection site in order to determine the efficacy of this antimicrobial agent at the infection site.

- We successfully used time to sterilization as an endpoint and characterized organism eradication rather than clinical success/failure as the primary endpoint, we estimated the power to detect clinically important differences with a Type I error (α) of 0.05 for various sample sizes.

- Given that the FDA is encouraging the development of valid pharmacodynamic models for antimicrobial agents in the development of new antibiotics, this study has potential to inform the design of future studies using comparable patient populations.

- The use of a continuous and sustained exposure of organisms to gatifloxacin was associated with rapid sinus sterilization and describing drug exposure at the infection site provides more robust information than standard approaches used for evaluating antimicrobial therapies of acute maxillary sinusitis.

- Future studies will further validate the hypothesis that drug exposure at the infection site can be used to predict clinical success and failure with more robust information than standard approaches used for evaluating antimicrobial therapies of acute maxillary sinusitis.

- The results of this study may be used to inform the design of future clinical trials using comparable patient populations.

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