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The effects of missed doses of antibiotics on hospitalized patient outcomes



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ABSTRACT

Background: Missing doses of antibiotics in hospitalized patients is a well-described but inadequately recognized issue. We hypothesized that missing doses of antibiotics decreases quality of care.

Methods: Retrospective study on patients admitted to the Shock Trauma ICU from February to June 2015. Patients prescribed a multidose course of antibiotics were evaluated. A missed antibiotic dose was one ordered but never given (a completely missed dose) or a dose that was not given within an hour before or after the planned time (an off-schedule missed dose). Patient outcomes included a positive culture, ventilator, ICU and hospital length of stay (LOS), and mortality. Multiple statistical methods were used as appropriate; significance was set as $P < 0.05$.

Results: For the 5-mo study period, 280 patients were admitted and 200 met inclusion criteria. Eight percent of patients (16/200) did not miss any antibiotic doses, 39% (77/200) had only off-schedule doses, 2% (4/200) had only completely missed doses, and 51% (103/200) had both off-schedule and completely missed doses. For the 200 patients, 8167 doses were ordered and 2096 (26%) were missed. Adjusting for age, gender, BMI, injury severity score, and doses of antibiotics showed that those who miss doses off-schedule had longer LOS than those who do not miss doses of antibiotics. There was a significant nonlinear relationship between LOS and frequency of early (P -value = 0.02) and late (P -value = 0.01) doses.

Conclusions: To reduce length of hospital stay and optimize quality, methods to improve compliance with antibiotic dosing schedules should be investigated.

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Background and significance

Clinicians order medications to improve the outcome of their patients, and most assume that in hospitalized patients 100% of ordered medications will be administered. Unfortunately, there is a growing appreciation that missed doses occur with unanticipated frequency.

Multiple studies have shown the deleterious effects of missed medication doses on patient outcomes. Louis *et al.* determined missing doses of Enoxaparin during therapy strongly correlates with incidence of deep-vein thrombosis in trauma and general surgery patients.¹ A similar result was ascertained in a study determining the effects of interrupted antibiotic therapy in TB treatment. Patients who missed more than 10% of their medications had higher risks of failing to convert to a negative TB culture.² Finally, in a study regarding missed doses of all medication irrespective of indication, decreasing missed doses lowered hospital mortality by 16.2%.³ It appears that missed doses of medication is more common than many realize and that minimizing missed doses can improve quality of care and patient outcomes.

Among all classes of medication, antibiotic doses are the most commonly omitted.⁴ In a study of 18,527 patients conducted by the UK National Patient Safety Agency, missing medication doses was fatal for 27 patients and placed 68 patients into severe harm.⁵ Missing doses of medication was of low or moderate harm to an additional 5405 of the 18,527 patients.⁵ Of the patients that died from missing medication doses, 33% died from missed doses of antibiotics.⁵ Recently, Seymour *et al.*⁶ demonstrated the significant clinical effect of not missing, but delayed infusion of antibiotics in septic patients. Missing doses or lack of adherence to antibiotic scheduling is not uncommon and negatively impacts patient care.

Taken together, it is clear that missing doses of medications, and especially antibiotics, is detrimental to optimal patient outcomes. However, there are two ways to miss doses of medication: delayed initiation of therapy and missing doses of medication once ordered or prescribed. Whereas studies have shown that delayed initiation of antibiotics increases sepsis related mortality, this study will look into the effects of missed doses of already prescribed antibiotics on patient outcomes. We hypothesized that the rate of missed doses of antibiotics in hospitalized patients affects outcomes.

Methods

Ethical review

This study was approved by the UHealth institutional review board. Because this retrospective study was of minimal risk to patients, a waiver was given for informed consent.

Patient selection

A retrospective chart review of patients admitted to the Memorial Hermann Shock Trauma ICU (STICU) from February 2015 to June 2015 was conducted. A course of antibiotic was

defined as an order of antibiotics that included at least two consecutive doses. Patients who were only prescribed topical, prophylactic, or one dose of an antibiotic were excluded from the study. Antibiotics prescribed as continuous infusion courses were also excluded because without a scheduled time of administration for each dose, there is no consistent method to determine if a dose was given on time or missed. Inclusion of patients was not affected by the antibiotic ordered; all antibiotics prescribed were included in the study. Erythromycin, when prescribed for its enteric motility instead of its antibacterial properties, was not included. Thus, of the 280 patients reviewed during the 6-mo study, 200 patients were included in the study.

Study variables

Data collected for the study were separated into two categories: data collected for each dose of antibiotic prescribed and data collected for patient-level outcomes. Patient charts were used to gather the data collected for each dose prescribed. These data include name of the antibiotic, planned date, day (i.e., weekday or weekend) and time the dose was to be given, actual date and time the dose was administered, duration between planned and actual time the dose was given, route of administration of the antibiotic (IV, PO, etc.), dosing schedule of the antibiotic (number of doses of the antibiotic prescribed per day), and whether the dose of antibiotic was missed.

A missed dose of antibiotic was defined as a dose of antibiotic that was either never given (a completely missed dose) or a dose given but not within an hour of the scheduled time (an off-schedule missed dose). Because giving doses plus or minus 1 h of the scheduled time was the standard protocol in the STICU, an off-schedule dose was considered a missed dose. To establish the number of hours the dose was off-schedule, the number of minutes the dose was early or late was rounded down to the nearest hour. Nurse's notes were primarily used to ascertain the reason a dose was completely missed. If a patient was in the operating room when a dose was missed, anesthesia records were screened to see if the missed dose was administered during surgery. Doses missed in the STICU but given in the OR were not completely missed. Rather, the time the dose was given in the OR was recorded as the actual time the dose was given. Plus and minus 30 min of CT or MRI results and start/end times for physical therapy and procedures were used as the time frame for which a patient was out of the ICU for radiology, physical therapy, or procedures. If a patient was not in any of these categories when a dose was missed, laboratory values were checked for trough levels and possible toxicity. If no reason was found for the missed dose, "no reason" was recorded for the reason the dose was missed.

The reasons for completely missed doses were divided into two categories: valid or nonvalid. Valid medical reasons for missing a dose included doses held by a physician, hypotension, an NPO order, a change in order, a schedule conflict between orders, and high vancomycin trough levels. Nonvalid reasons include late, early, inappropriate time, prior late dose, medicine unavailable, patient in procedure, physical therapy,

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