Journal of Infection and Public Health xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

Comparison of the incidence of acute kidney injury during treatment with vancomycin in combination with piperacillin–tazobactam or with meropenem

Majed S. Al Yami [a,b,*]

[a] King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[b] The University of Arizona, College of Pharmacy, Tucson, USA

ARTICLE INFO

Article history:
Received 19 July 2016
Received in revised form 17 October 2016
Accepted 18 November 2016

Keywords:
Acute kidney injury
Nephrotoxicity
Vancomycin
Piperacillin–tazobactam
Meropenem

ABSTRACT

The purpose of this study was to evaluate the observed incidence of acute kidney injury (AKI) in adult patients receiving either piperacillin–tazobactam (PT) and vancomycin or meropenem and vancomycin for at least 48 h. In this retrospective cohort study, we included adult patients with no known renal dysfunction who received either the combination of PT-vancomycin or meropenem–vancomycin for at least 48 h. The study's primary outcome was the incidence of acute kidney injury (AKI), defined by the Kidney Disease: Improving Global Outcomes (KDIGO) in patients with baseline normal renal function as an increase in serum creatinine (Scr) by ≥0.3 mg/dl within 48 h. A total of 183 patients were evaluated for AKI. The incidence of AKI was higher but not statistically different in the PT-vancomycin group (7.41%) compared with the meropenem–vancomycin group (5.33%). This study was not able to detect a statistically significant difference in AKI between the two treatment groups. A larger prospective study is warranted.

Introduction

The development of acute kidney injury (AKI) is associated with poor outcomes in hospitalized patients, with increased morbidity and mortality in these patients [1,2]. Drugs are among the most common causes of AKI in both hospital and community settings. Risk factors for drug-induced AKI include underlying renal disease, diabetes, hypotension, sepsis, volume depletion, human immunodeficiency virus and advanced age [3].

Vancomycin is a glycopeptide antibiotic that has been used in clinical practice for more than fifty years. It is commonly prescribed to treat Gram-positive infections, particularly those caused by methicillin-resistant *Staphylococcus aureus* (MRSA). The use of vancomycin alone has been associated with a 5%–43% incidence of AKI [3,4]. Piperacillin–tazobactam (PT), an antipseudomonal β-lactam/β lactamase inhibitor antibiotic is frequently used in combination with vancomycin for empiric therapy in hospitalized patients. According to PT's manufacturer, the product has a less than 1% incidence of AKI [5]. However, published data have shown a higher rate of AKI when PT is used alone (11%) or in combination with vancomycin (16%–49%) [6–10].

Meropenem is a carbapenem antibiotic that is also used concomitantly with vancomycin as part of an empiric broad spectrum antibiotic regimen. According to its manufacturer, the incidence of AKI in patients receiving meropenem is less than 1% [11]. However, there are limited data regarding the incidence of AKI when meropenem is used in combination with vancomycin.

Purpose, hypotheses, and rational

We compared the observed incidence of AKI between PT-vancomycin and meropenem–vancomycin in adult patients without documented impaired renal function. To our knowledge, no retrospective studies have evaluated the effect of meropenem on kidney function when used in combination with vancomycin. We hypothesize that the incidence of AKI in patients receiving meropenem-vancomycin is less than that in patients receiving PT-vancomycin.

Methods

Study setting

This study was conducted at two hospitals: Banner-University Medical Center Tucson, a 479-bed tertiary academic hospital and Banner-University Medical Center South, a 245-bed academic med-

* Tel.: 857 4882525.
E-mail address: mshry2003@gmail.com

http://dx.doi.org/10.1016/j.jiph.2016.11.007

Please cite this article in press as: Al Yami MS. Comparison of the incidence of acute kidney injury during treatment with vancomycin in combination with piperacillin–tazobactam or with meropenem. J Infect Public Health (2017), http://dx.doi.org/10.1016/j.jiph.2016.11.007

Table 1
Comparison of clinical characteristics and outcomes.[a]

Characteristics	PT-vancomycin (n = 108)	Vancomycin–meropenem (n = 75)	p
Mean ± S.D. age, yr	52.4 ± 17.29	54 ± 18.46	0.7
Male, no. (%)	71 (65.74)	50 (66.67)	0.5
Mean ± S.D. weight, kg	84 ± 21.2	77.9 ± 23.9	0.03
Mean ± S.D. vancomycin trough concentration	15.7 ± 9.2	16.9 ± 8.6	0.8
Mean ± S.D. Scr at start of antibiotics	0.8 ± 0.2	0.8 ± 0.2	0.3
Mean ± S.D. Scr at 48 h	0.8 ± 0.4	0.7 ± 0.3	0.1
Mean ± S.D. estimated Clcr at baseline, ml/min	100.6 ± 37.6	98.8 ± 41.6	0.3
Critically ill patients, no (%)	19 (17.6)	13 (17.3)	0.56
Systemic infection	35 (32.4)	27 (36)	0.36
Comorbidities			
Diabetes mellitus, no. (%)	19 (17.59)	27 (36)	0.004
Heart failure, no. (%)	7 (6.48)	4 (5.33)	0.5
Hypertension, no. (%)	44 (40.74)	33 (44)	0.38
Malignancy, no. (%)	19 (17.59)	22 (29.33)	0.04
Other comorbidities, no. (%)	93 (86.11)	72 (96)	0.02
Diagnosis of sepsis, no. (%)	21 (19.44)	18 (24)	0.2
Use of pressors, no. (%)	13 (12)	15 (20)	0.1
Mean ± S.D. length of antibiotic treatment	4.36 ± 1.9	5.42 ± 3.0	0.9
Concomitant nephrotoxic drugs			
Contrast, no. (%)	45 (41.67)	24 (32)	0.12
NSAID, no. (%)	14 (12.96)	4 (5.33)	0.07
ACE inhibitor, no. (%)	9 (8.33)	7 (9.33)	0.5
Aminoglycosides, no. (%)	0	0	–
Antibiotic indication, no. (%)			
Bacteremia, no. (%)	3 (2.77)	1 (1.33)	…[b]
Skin and soft tissue infection, no. (%)	20 (18.52)	7 (9.33)	…
Respiratory tract infection, no. (%)	37 (34.26)	24 (32)	…
Intra-abdominal infection, no. (%)	5 (4.63)	3 (4)	…
Urinary tract infection, no. (%)	3 (2.78)	3 (4)	…
Empiric therapy, no. (%)	32 (29.63)	14 (18.67)	…
Endocarditis, no. (%)	0	1 (1.33)	…
CNS infection, no. (%)	0	2 (2.67)	…
Bone and joint infection, no. (%)	8 (7.41)	8 (10.67)	…
Neutropenic fever, no. (%)	0	12 (16)	…

[a] Scr = serum creatinine, Clcr = creatinine clearance, NSAID = nonsteroidal anti-inflammatory drug, ACE = angiotensin-converting enzyme, CNS = central nervous system.
[b] Data unavailable.

ical center in Tucson, Arizona. This study was approved by the Human Subjects Protection Program Institutional Review Board (IRB) of the University of Arizona.

Study design and population

A retrospective cohort study was conducted, including eligible adult patients admitted to medical/surgical units and the medical/surgical intensive care units at the two hospitals between November 1, 2013 and November 30, 2014. Data obtained from the electronic health record system Epic were reviewed and analyzed for each patient. Patients were included in the study if they were at least 18 years of age, had a baseline Scr within 24 h of admission, and had received either PT-vancomycin or meropenem–vancomycin for at least 48 h. Patients were excluded if they were currently receiving renal replacement therapy or if they had a history of underlying renal dysfunction (defined as a serum creatinine > 1.5 mg/dl, structural kidney disease, or post-kidney transplant).

Study endpoint

The primary outcome measured in this study was the incidence of AKI, defined by the Kidney Disease: Improving Global Outcomes (KDIGO) in patients with baseline normal renal function as an increase in Scr by ≥0.3 mg/dl within 48 h.

Statistical analysis

A sample size of 180 (90 patients in each arm) was required to achieve a statistical power of 80% based on the estimates of a 25% rate of AKI in the PT-vancomycin group and 10% in the meropenem–vancomycin group. Descriptive and demographic categorical variables were compared using Fisher's exact test. Continuous outcome variables were compared using an unpaired Student's t-test. A p value of less than 0.05 was considered statistically significant. STATA 14.0 (StataCorp, College Station, TX) was used for statistical analyses.

Results

183 patients met the inclusion criteria and were included in the study (108 in the PT-vancomycin group and 75 in the meropenem–vancomycin group). Overall, patients who received PT-vancomycin had a higher mean body weight compared to those who received meropenem–vancomycin. Table 1 summarizes the baseline demographic characteristics of the two groups. There was a comparable proportion of critically ill patients in both groups. There was no significant difference in the rate of systemic infection vs organ related infection in both groups. There was no significant difference between the two groups in terms of comorbidities, such as heart failure and hypertension. However, the meropenem–vancomycin group included more patients with diabetes mellitus and malignancy compared with PT-vancomycin group. No significant differences were found between the two groups in terms of the use of concomitant nephrotoxic agents (e.g., ACE inhibitors, intravenous radiocontrast, NSAIDS or aminoglycosides). Between the two groups, no significant differences were observed in the mean estimated creatinine clearance Clcr at baseline, mean vancomycin trough concentration, mean Scr, Scr at 48 h, and number of treatment days. In the PT-vancomcin group, 8 of

Please cite this article in press as: Al Yami MS. Comparison of the incidence of acute kidney injury during treatment with vancomycin in combination with piperacillin–tazobactam or with meropenem. J Infect Public Health (2017), http://dx.doi.org/10.1016/j.jiph.2016.11.007