Efficacy and Safety of Ceftazidime-Avibactam Comparative Dosage Regimens in Patients with Kidney Injury: A Retrospective Cohort Study

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Background

Limited data are available for Ceftazidime-avibactam (CAZ-AVI) dosing in patients with chronic kidney diseases. High rate of treatment failure was found among patients with chronic kidney diseases for which renally adjusted doses has been used[(1)]. In our institution, Off-Labeled High Adjusted Dosing regimens (OLHAD) has been used for the treatment of severe infections. Doses were driven from ceftazidime adjusted dosing regimens in CKD patients. Therefore, we aimed to compare the efficacy and safety between labeled and OLHAD regimens of CAZ-AVI in CKD patients.

We aimed to evaluate the efficacy and safety of OLHAD of CAZ-AVI compared to labeled adjusted dosing (LAD) in renal impaired patients.

Estimated Creatinine Clearance (mL/min)	Labeled Adjusted Doses (LAD) of CAZAVI(a)	Off-Labeled High Adjusted Doses (OLHAD) of CAZAVI
Greater than 50	2.5g (2g /0.25g) every 8 hrs	2.5g every 8 hrs
31 to 50	1.25g (1g /0.25g) every 8 hrs	2.5g every 8 hrs
16 to 30	0.94g (0.75g /0.19g) every 12 hrs	1.25g every 8 hrs
6 to 15	0.94g every 24 hrs	0.94g every 12 hrs
Less than or equal 5	0.94g every 48 hrs	0.94g every 24 hrs

Primary Outcome

- To assess the clinical cure of OLHAD compared to LAD, defined as: complete or partial resolution of fever (temperature > 38.3 °C) and leukocytosis (white blood cell count > 12x10 9) for more than 24 hr.

Secondary Outcome

I. To evaluate 30-days mortality due to infection in renally impaired patients receiving LAD and OLHAD of CAZ-AVI
II. Determine the ICU and hospital discharge rate.
III. Clostridioides difficile incidence to be detected from laboratory by stool molecular C.diff PCR that occurred during CAZ-AVI course and within and 30 days after CAZ-AVI course completion.

Methods and Materials

A retrospective cohort study was conducted between June 2018 and December 2020 in King AbdulAziz Medical City- Jeddah, Saudi Arabia (850 bed, tertiary hospital).

Inclusion criteria:

- Patients ≥14 years old who has chronic kidney disease in any stage (CrCl ≤ 50 ml/min) or on dialysis (in-hospital or outpatient setting)
- Received at least 48 hours of CAZ-AVI

Exclusion criteria:

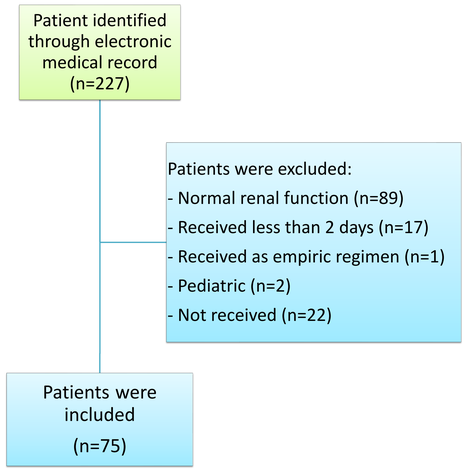
- Patients with cultures resistant to CAZ-AVI other than Metallo- beta-lactamase (MBL) isolated organisms
- Received empirical CAZ-AVI
- Received CAZ-AVI less than 2 days or with incorrect dose.

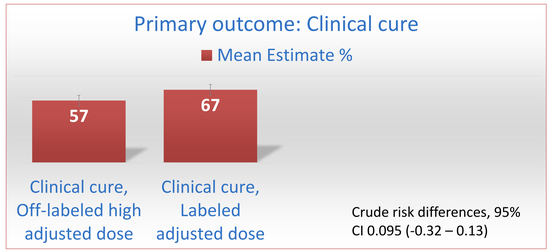
Statistical Analysis: Descriptive analysis used for baseline characteristics. Crude risk difference and contingency table analysis were used as appropriate.

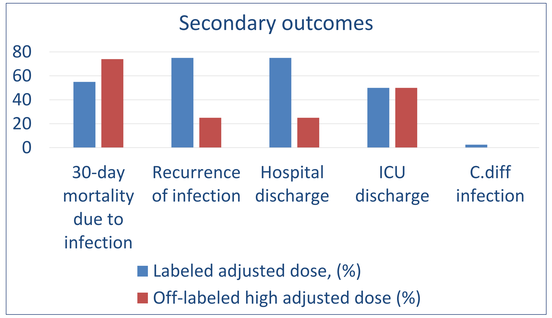
Ethical approval for this study was granted from the research ethics committee in King Abdullah International Medical Research Center.

Results

Study Algorithm







Result

Characteristic	Labeled adjusted n= 40	High adjusted n= 35
Age (mean ± SD)	70 ± 10.4	68.3 ± 15.1
Gender (male/female)	21/19	22/13
Past medical history, n (%)		
Diabetes mellites	31 (77.5)	26 (74.3)
Hypertension	35 (87.5)	27 (77.1)
Dyslipidemia	6 (15)	4 (11.4)
Cerebrovascular accident	17 (42.5)	11 (31.4)
Coronary artery disease	15 (37)	12 (34.29)
Heart disease	18 (45)	19 (54.29)
Liver disease	6 (15)	3 (8.5)
Seizure	3 (7.5)	6 (17.1)
Lung disease	6 (15)	5 (14.29)
Hemodialysis, n (%)	21 (52.2)	17 (48.5)
IHD	7 (17.5)	6 (17.4)
CRRT, n (%)	14 (35)	11 (31.4)
Loading dose, n (%)	11 (27.5)	8 (22.86)
CAZ-AVI duration (median, IQR)	14, (7.5- 18.5)	13, (8- 15)
Primary diagnosis		
Ventilator Acquired Pnumonia	2 (5)	1 (2.8)
Hospital Acquired Pnumonia	17 (42)	15 (42.8)
Community Acquired Pnumonia	0	1 (2.8)
Intra-abdominal infection	7 (17.5)	9 (25.7)
Urinary Tract Infection	9 (22.5)	5 (14.2)
Skin and soft tissue infection	5 (12.5)	4 (11.4)
Types of bacteria, n		
Klebsiella	38	26
Pseudomonas	0	1
E.coli	0	1
Type of Gene resistance, n		
OXA-48	16	11
NDM	0	1
KPC	0	0
OXA-48 and NDM	3	2
No report	21	21

Conclusions

The efficacy and safety of both studied dosing regimen of CAZ-AVI in renally impaired patients were almost comparable. Patients' severity of illness and further regression analysis will be conducted to better evaluate safety. Larger sample size needed to answer the study question on the use of OLHAD than LAD.

References

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