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Kidney biopsy findings in vancomycin-induced acute kidney injury: a pooled analysis

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ABSTRACT

Vancomycin represents a tricyclic glycopeptide that is widely administered to patients with Gram-positive infections. Acute kidney injury is considered as an important adverse effect, as it commonly leads to significant morbidity and high rates of treatment discontinuation. Vancomycin has been suggested to be associated with acute tubular necrosis and tubulointerstitial nephritis; however, evidence regarding kidney lesions is currently scattered, coming exclusively from case reports. The aim of this study is to accumulate literature studies with biopsy-proven cases of vancomycin-induced nephrotoxicity and assess the effects of histological findings on renal prognosis. Survival analysis is planned to be performed in order to identify which kidney lesions are linked to lower rates of renal recovery.

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KEYWORDS

vancomycin, biopsy, nephrotoxicity, acute kidney injury

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- 1 Background: Vancomycin represents a tricyclic glycopeptide that is widely administered to patients with Gram-positive infections. Acute kidney injury is considered as an important adverse effect, as it commonly leads to significant morbidity and high rates of treatment discontinuation. Vancomycin has been suggested to be associated with acute tubular necrosis and tubulointerstitial nephritis; however, evidence regarding kidney lesions is currently scattered, coming exclusively from case reports. The aim of this study is to accumulate literature studies with biopsy-proven cases of vancomycin-induced nephrotoxicity and assess the effects of histological findings on renal prognosis.
- 2 Study design The meta-analysis will be conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
- 3 Search strategy: Medline, Scopus, CENTRAL, Web of Science and Clinicaltrials.gov will be systematically searched from inception. Google Scholar will be searched to provide grey literature coverage. The full reference list of the retrieved studies will also be searched to identify potential additional sources ("snowball" method). Search will be based on Medical Subject Headings (MeSH) terms ("Vancomycin", "Biopsy", "Acute Kidney Injury", "Kidney Tubular Necrosis, Acute", "Nephritis") combined with a list of keywords ("histology", "AKI", "tubular necrosis", "nephritis", "renal failure", "renal impairment", "nephrotoxicity"). No date or language restrictions will be applied.
- 4 Study selection: All studies reporting kidney biopsy findings of patients with vancomycin-associated acute kidney injury will be held eligible. Cases without data about renal histology or with acute kidney injury caused by factors unrelated to vancomycin therapy will be excluded.
- 5 Data extraction Data extraction will be performed independently by two researchers. The following data will be extracted: name of first author, publication date, age, sex, comorbidities, symptoms, eosinophilia, urinalysis findings, vancomycin dosage, indication for vancomycin therapy, co-administration of other antibiotics, acute kidney injury stage (according to the KDIGO guidelines), need of renal replacement therapy, renal recovery, follow-up period and histological findings (background, mesangial expansion, Tubulitis, eosinophilic infiltration, tubular dilatation, atrophy, necrosis, casts, interstitial edema, interstitial fibrosis, epithelial sloughing, granulomas, intimal fibrosis, arteriolar hyalinosis, immunofluorescence and electron microscopy findings).
- 6 Quality assessment Risk of bias of case reports will be evaluated by judging the potential risk of bias concerning the domains of selection, ascertainment, causality and reporting (Murad et al. BMJ Evidence-Based Med 2018;23:60–3. <https://doi.org/10.1136/BMJEBM-2017-110853>).
- 7 Data analysis Statistical analysis will be performed in R-3.6.3 and will be explorative in nature since it is the first study in the field to evaluate the association of kidney histology findings with renal prognosis. Renal recovery will be set as the outcome of interest. Statistical significance will be detected as p-value <0.05. The normality of data will be evaluated using the Shapiro-Wilk test. Continuous data will be compared using the t-test or the Mann-Whitney U-test test based on the distribution of data. Survival analysis will be performed by applying a Cox proportional hazards regression model. Kaplan-Meier curves will be constructed.