



Medication safety in intensive care unit patients with renal impairment: assessing the potential for interventions to prevent adverse drug events

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1. Background & Objectives

Background: Renal impairment affects about 30% of ICU patients, leading to challenges in drug clearance and an increased risk of drug accumulation and toxicity^{1,2}. Despite the general recognition of overdose-related medication errors, the extent of their impact on patient safety and the requisite preventive measures remain obscure^{3,4}. Commonly used medications require dose adjustments to minimize overdose risks and potential adverse drug events (ADEs) in these vulnerable patients⁵.

Objectives: This study aims to (1) identify overdosing incidents of selected renally eliminated drugs, digoxin, vancomycin, meropenem, and rosuvastatin (2) assess associated ADEs, and (3) propose preventive measures to improve medication safety in ICU settings.

2. Methods

Study Design: A retrospective, observational cross-sectional study conducted in four Swiss ICU centres between 2021 and 2022.

Population: The study included 6,325 ICU patients with documented renal function data. Patients were evaluated for renal impairment (defined as eGFR \leq 60 ml/min) and included if they had been prescribed one or more of the four drugs of interest.

Drug Selection and Dosing Criteria:

The drugs analyzed were selected due to their dependence on renal excretion, established dose adjustment guidelines for renal impairment, and potential for severe toxicity upon overdosing. Dosing recommendations were based on Swiss Summary of Product Characteristics (SmPC) guidelines, supplemented by FDA prescribing information and other verified resources.

Data Collection and Analysis: Patient data, including demographics, medication administration records, and renal function measures, were extracted from COPRA PDMS, the clinical information system used for ICU documentation. Each patient's administered daily drug doses were compared with recommended doses adjusted for their eGFR at the time of administration. Renal function was estimated using both creatinine-based and cystatin C formulas when available.

Overdose and ADE Identification: Overdosing was defined as any administered dose exceeding recommended daily amounts for the respective eGFR level, even if only on a single day. ADEs were assessed by examining patient records for clinical signs of toxicity, such as high digoxin or vancomycin blood levels, elevated CK levels (for rosuvastatin), or liver enzyme abnormalities (for meropenem).

3. Results

Study Population: Of 6,325 ICU patients studied, 1,483 received at least one of the drugs of interest, with 36.4% of the overall population having signs of renal impairment (eGFR \leq 60 ml/min).

Overdosing Incidence: Among patients receiving target drugs, 11% experienced at least one instance of overdosing. Overdosing rates by drug were as follows:

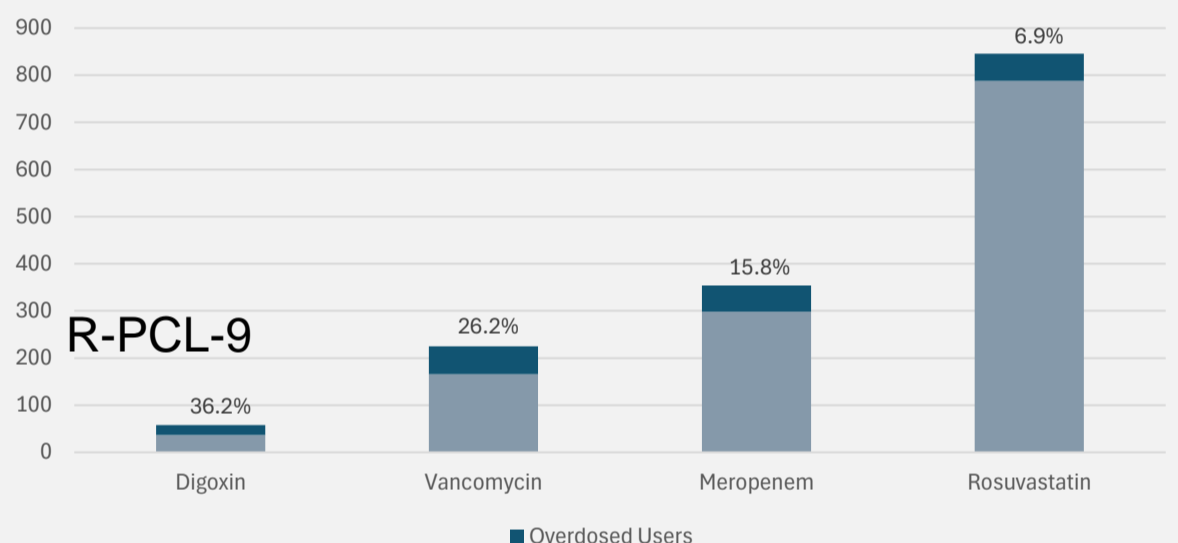


Figure 1: Overdosing rates by drug of interest

Adverse Drug Events: ADEs linked to overdosing were identified in 4 cases, each showing clinical signs of toxicity (Table 1).

Table 1: Patient cases with drug-induced toxicity

Case	Target	KDIGO Category	Day of treatment	Toxicity signs & symptoms	Causality assessment
A	Digoxin	3a	7	Hyperkalemia of unclear etiology, visual disturbances	Possible
B	Vancomycin	3b	6	Declining renal function	Possible
C	Meropenem	2-3a	17	10-fold increase of liver enzymes	Certain
D	Rosuvastatin	4	5	CK = 14,141 U/l, necrotizing myopathy biopsy	Probable

5 Conclusion

Our study reveals a substantial occurrence of overdosing in renally impaired ICU patients, with a notable incidence of adverse ADEs associated with improper dosing. Specifically, the observed cases of toxicity highlight the risk of serious complications when recommended renal dosing guidelines are not followed. These findings underscore the importance of **regular renal function monitoring, accurate dose adjustments, and clinician education on renal dosing guidelines**. Implementing these targeted interventions could reduce the risk of toxicity and significantly improve patient safety in ICU settings.

References

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