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Pharmacist support in the entry of blood drug concentration test order avoids vancomycin-induced kidney injury

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Abstract

Background: Task shifting and sharing have been proposed as strategies to address healthcare staffing shortages and improve patient outcomes. In emergency and intensive care medicine, pharmacist interventions have shown potential to reduce medication errors and improve care quality. However, the precise benefits of pharmacist support in therapeutic drug monitoring (TDM) for emergency center inpatients require further verification.

Objective: To determine the contribution of pharmacist support in entering blood drug concentration test orders to patient safety during anti-methicillin-resistant *Staphylococcus aureus* (MRSA) drug administration in the emergency and critical care center, and investigate the association between this support and the frequency of vancomycin-induced kidney injury.

Design: Single-center retrospective cohort study comparing outcomes 2 years before and 2 years after implementing pharmacist support for blood concentration test order entry.

Methods: Patients receiving intravenous vancomycin with blood concentrations measured at the emergency center were included. Propensity score matching was used to minimize confounding. The primary outcome was the change in frequency of vancomycin-induced kidney injury before and after pharmacist support implementation.

Results: Pharmacist support significantly reduced the frequency of vancomycin-induced kidney injury (from 6.5% to 0.0%, $p = 0.043$) and shortened time to first TDM implementation ($p = 0.019$) in the overall cohort. Similar significant reductions were observed in the propensity score matched cohort (from 11.9% to 0.0%, $p = 0.013$).

Conclusion: Pharmacist support in entering blood drug concentration test orders significantly reduced vancomycin-induced kidney injury frequency and shortened time to first TDM, enhancing patient safety during anti-MRSA medication administration in the emergency and critical care center. This task-shifting approach demonstrates clear benefits for patient care and physician workload.

Plain language summary

Pharmacist support in the entry of blood drug concentration test order avoids vancomycin-induced kidney injury

Why was this study done? This study aimed to evaluate the impact of pharmacist support in entering blood drug concentration test orders on patient safety during anti-MRSA drug administration in emergency and critical care settings. The researchers sought to determine if this task-shifting approach could reduce the frequency of vancomycin-induced kidney injury and improve the timeliness of therapeutic drug monitoring.

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What did the researchers do? A single-center retrospective cohort study was conducted comparing outcomes two years before and two years after implementing pharmacist support for blood concentration test order entry. They included patients receiving intravenous vancomycin with measured blood concentrations in the emergency center. To minimize confounding factors, propensity score matching was used. The primary outcome was the change in frequency of vancomycin-induced kidney injury before and after implementing pharmacist support.

What did the researchers find? Pharmacist support significantly reduced the frequency of vancomycin-induced kidney injury from 6.5% to 0.0% ($p = 0.043$) in the overall cohort, and the time to first therapeutic drug monitoring implementation was shortened ($p = 0.019$). Similar significant reductions were observed in the propensity score matched cohort, with vancomycin-induced kidney injury frequency decreasing from 11.9% to 0.0% ($p = 0.013$).

What do the findings mean? These findings suggest that pharmacist support in entering blood drug concentration test orders significantly enhances patient safety during anti-MRSA medication administration in emergency and critical care settings. The task-shifting approach demonstrates clear benefits by reducing the risk of kidney injury and improving the timeliness of drug monitoring. This study provides evidence supporting the implementation of pharmacist-led interventions in emergency and intensive care medicine to improve patient outcomes and address healthcare staffing challenges.

Keywords: emergency and critical care center, kidney injury, pharmacist, task sharing, task shifting, vancomycin

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Introduction

Background

Task shifting refers to the transfer or delegation of tasks, while task sharing involves the collaboration of healthcare professionals with different training levels for a task.[1] Task shifting and sharing have been touted as strategies to address staffing shortages, empower healthcare professionals, increase job satisfaction, and improve patient outcomes.[2] Promoting task shifting and sharing should reduce the workload of healthcare professionals and improve patient outcomes.[3]

The sophistication and diversification of medical care are constantly advancing, and the level and quality of knowledge and skills required of physicians and other healthcare professionals are increasing. Physicians particularly bear a heavy burden in addressing the increasing sophistication of medical technology. In the field of emergency and intensive care medicine, various medical specialists are expected to maximize their respective expertise and provide a multidisciplinary approach. There have been recent reports of pharmacist interventions in improving the quality of medical care in the emergency and critical care center. Pérez-Moreno et al.[4] and Bakey et al.[5] reported that intervention in the process of medication reconciliation and direct oral anticoagulants selection reduced medication errors. Dietrich et al.[6] reported that intervention in the emergency department (ED) outpatient culture review and ED discharge antimicrobial review significantly reduced healthcare costs. Ibarra[7] reported that an intervention providing a lecture on appropriate vancomycin loading dose significantly increased the appropriate loading dose of vancomycin within 12 h of a patient's arrival. Hammond et al.[8] reported that intervention on antibiotic therapy ordering contributed to improved antimicrobial selection for sepsis and reduced the time-to-first-dose of antimicrobials. Thus, deploying a full-time clinical pharmacist to the emergency and critical care center promotes the appropriate

use of drug therapy, particularly antimicrobials, and improves beneficial care to patients.

Importance

In February 2022, our institution began to support the entry of anti-methicillin-resistant *Staphylococcus aureus* (MRSA) drug blood concentration test orders through a full-time emergency and critical care center pharmacist to reduce the workload of physicians in therapeutic drug monitoring (TDM) of emergency center inpatients. We have previously reported that this support reduces the workload of emergency and critical care center physicians.[9] However, the precise benefit of this support to patients remains partially verified.

Goals of this investigation

This study aimed to investigate the association between the presence or absence of entry support and the frequency of vancomycin-induced kidney injury as a contribution of pharmacist support in the entry of blood drug concentration test orders to safety during anti-MRSA drug administration in the emergency and critical care center.

Methods

Study design and setting

A single-center retrospective cohort study was conducted at the University of Miyazaki Hospital. Pharmacist support in the entry of blood drug concentration test orders was started on February 21, 2022. A retrospective cohort study was conducted to evaluate the effectiveness of this support for 2 years each before (February 21, 2020, to February 20, 2022, pre-task shift) and after (February 21, 2022, to February 20, 2024, post-task shift) the start of the entry support.

The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology statement (Supplemental Material).[10]

Procedure of pharmacist support in the entry of blood drug concentration test order

During the pre-task shift period, blood drug concentration test orders could only be entered by physicians, and pharmacists could only facilitate entry. During the post-task shift period, pharmacists could directly enter blood drug concentration test orders by the following procedure.

Pharmacist support in the entry of blood drug concentration test orders was provided to patients receiving anti-MRSA drugs (vancomycin and teicoplanin) who were hospitalized in our emergency center. First, when TDM was required for the patient, the pharmacist requested the attending physician or the physician in charge of the patient to enter the blood drug concentration test order, representing the doctors. After the request, the pharmacist, in place of the doctors, entered the blood drug concentration test order in the electronic medical record and issued the order. Subsequently, the pharmacist entered a note in the patient's electronic medical record stating that the order was entered on behalf of the doctors. In addition, the attending physician or the physician in charge of the patient was asked to approve the substitute entry order. Next, the pharmacist notified the patient's charge nurse that a blood draw was scheduled to measure blood drug concentrations. The pharmacist, representing the doctor, entered the blood drug concentration test order at the optimal timing based on the latest guidelines. The pharmacist in charge of blood drug concentration test order entry support was a full-time pharmacist at the emergency center.

Blood drug concentrations were measured on the sampling day, analyzed directly by the TDM section in the pharmacy department, and immediately reflected in prescriptions.

Selection of participants

The study participants were patients (aged $\geqslant$18 years) who were started on intravenous vancomycin and had their blood concentrations measured at the emergency center of University of Miyazaki Hospital, between February 21, 2020 and February 20, 2024. Patients who had received vancomycin continuously from their previous physician and those who were receiving renal replacement therapy, such as dialysis, during vancomycin administration were excluded.

Measurements

Information on patient age, sex, height, weight, laboratory data (serum creatinine (SCr), blood

urea nitrogen (BUN), alanine aminotransferase, aspartate aminotransferase, serum K, serum Na), drug prescription history, and vancomycin blood concentrations was collected from the electronic medical records. Using the collected information, the occurrence of acute kidney injury during vancomycin treatment was analyzed. The development of acute kidney injury was determined based on the KDIGO diagnostic criteria[11] and the attending physician's diagnostic history. Specifically, acute kidney injury was defined as a $\geqslant$0.3 mg/dL increase in SCr from baseline at 48 h, or a 1.5× increase within 7 days.

Outcomes and analysis

The primary endpoint was the change in the frequency of vancomycin-induced kidney injury before and after pharmacist support in the entry of blood drug concentration test orders. Participants were divided into the pre- and post-task shift groups before and after the start of the pharmacist support, respectively. In addition, to minimize confounding effects owing to differences in group distribution, propensity score matching (PSM) was performed at a ratio of 1:1 based on the propensity score for one episode using a logistic regression model. The covariates in the propensity score analyses included loading dose implementation, concomitant diuretics, and piperacillin/tazobactam combination. In eligible patients before and after matching, the onset of acute kidney injury was compared. Fisher's exact test was used for nominal variables, and the Mann–Whitney *U* test was used for continuous variables. R v.4.3.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. $p < 0.05$ indicated statistical significance.

Results

Characteristics of the study's participants

This study recorded 180 vancomycin-administered patients, with 107 and 73 belonging to the pre- and post-task shifts, respectively. In addition, there were 118 matched patients, with 59 each in the pre- and post-task shifts. Table 1 presents the pre-vancomycin characteristics of patients. Table 2 presents vancomycin dosing conditions, the onset of acute kidney injury, and the number of days between vancomycin initiation and first TDM implementation in each group.

There were no significant differences in sex, age, or renal function between the two patient groups. The post-task shift group had a significantly higher loading dose rate ($p < 0.001$) and exhibited a higher concomitant diuretics rate ($p = 0.050$). The pre-task shift group had a slightly higher piperacillin/tazobactam combination rate ($p = 0.278$).

In PSM patients, there were no significant differences in sex between the two groups; however, age ($p = 0.020$) and BUN ($p = 0.046$) were significantly higher in the post-task shift group than in the pre-task shift group. However, there were no significant differences between the two groups in the rate of loading dose implementation ($p = 1.000$, standardized difference < 0.001), concomitant diuretics ($p = 1.000$, standardized difference < 0.001), or piperacillin/tazobactam combination ($p = 1.000$, standardized difference < 0.001), and the bias was eliminated completely.

Main results

In the overall patients, pharmacist support significantly reduced the frequency of vancomycin-induced kidney injury (from 6.5% to 0.0%, $p = 0.043$) and shortened the number of days to first TDM implementation ($p = 0.019$, Figure 1(a)). Similarly, a significant reduction in the frequency of vancomycin-induced kidney injury (from 11.9% to 0.0%, $p = 0.013$) and shorter time to first TDM implementation ($p = 0.022$, Figure 1(b)) owing to pharmacist support were observed in PSM patients.

Discussion

This study aimed to investigate the association between pharmacist support in the entry of blood drug concentration test orders and the frequency of vancomycin-induced kidney injury. Support in the entry of blood drug concentration test orders by a full-time pharmacist in the emergency center significantly reduced the frequency of vancomycin-induced kidney injury. This result benefits patients receiving vancomycin, considering safety. Furthermore, it benefits the attending physician, as it reduces the interruption of treatment with

Table 1. Comparison of patient characteristics before and after the start of pharmacist support.

Characteristics	Overall			PSM			
	Pre ($n = 107$)	Post ($n = 73$)	p Value	Pre ($n = 59$)	Post ($n = 59$)	p Value	Standardized difference
Male	78 (72.9%)	52 (71.2%)	0.866[a]	45 (76.3%)	42 (71.2%)	0.676[a]	0.116
Age (years)	70 (19–97)	73 (21–92)	0.266[b]	68 (19–89)	74 (21–92)	0.020[b]	0.378
Body weight (kg)	61.9 (34.4–98.0)	60.4 (35.0–109.4)	0.935[b]	61.9 (37.2–92.2)	60.5 (35.0–109.4)	0.651[b]	0.059
Height (cm)	160.0 (133.0–185.0)	163.0 (139.0–176.0)	0.593[b]	162.0 (133.0–185.0)	163.0 (139.0–176.0)	0.808[b]	0.045
BMI (kg/m^2)	24.3 (16.0–36.4)	23.8 (15.5–41.0)	0.593[b]	24.3 (16.0–33.9)	23.7 (15.9–41.0)	0.344[b]	0.104
Serum creatinine (mg/dL)	0.77 (0.30–2.87)	0.86 (0.28–2.58)	0.110[b]	0.77 (0.30–2.87)	0.82 (0.28–2.58)	0.450[b]	0.053
BUN (mg/dL)	20.2 (3.9–119.2)	24.3 (8.0–100.0)	0.062[b]	18.9 (7.40–94.0)	24.5 (8.0–100.0)	0.046[b]	0.144
CLcr (mL/min)	66.37 (17.71–305.71)	64.02 (11.71–215.39)	0.252[b]	66.50 (28.23–305.71)	64.12 (16.61–215.39)	0.383[b]	0.264
eGFR (mL/min/1.73 m^2)	71.49 (20.53–228.09)	64.18 (15.98–231.67)	0.075[b]	68.07 (20.53–228.09)	64.59 (19.09–231.67)	0.240[b]	0.176
ALT (U/L)	30 (6–891)	29 (3–1216)	0.926[b]	34 (8–283)	29 (4–1216)	0.474[b]	0.178
AST (U/L)	44 (12–425)	39 (9–1380)	0.937[b]	47 (12–277)	39 (12–1380)	0.335[b]	0.130
K (mmol/L)	4.0 (2.6–5.4)	4.0 (2.8–5.5)	0.222[b]	3.9 (2.6–5.4)	4.0 (2.8–5.5)	0.173[b]	0.275
Na (mmol/L)	140 (116–161)	141 (122–153)	0.666[b]	140 (116–161)	141 (129–153)	0.431[b]	0.113
Diuretic	14 (13.1%)	18 (24.7%)	0.050[a]	10 (16.9%)	10 (16.9%)	1.000[a]	<0.001
PIPC/TAZ	44 (41.1%)	24 (32.9%)	0.278[a]	23 (39.0%)	23 (39.0%)	1.000[a]	<0.001

Median (minimum–maximum) or *n* (%).
[a]Fisher's exact test; [b]Mann–Whitney *U* test.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; PIPC/TAZ, piperacillin/tazobactam; PSM, propensity score matching.

Table 2. Comparison of vancomycin dosing and frequency of vancomycin-induced kidney injury before and after the start of pharmacist support.

Characteristics	Overall			PSM			
	Pre ($n = 107$)	Post ($n = 73$)	p Value	Pre ($n = 59$)	Post ($n = 59$)	p Value	Standardized difference
Loading	58 (54.2%)	65 (89.0%)	<0.001[a]	51 (86.4%)	51 (86.4%)	1.000[a]	<0.001
Loading dose (mg)	1500 (1000–2000)	1500 (800–2000)	0.948[b]	1500 (1000–2000)	1500 (800–2000)	0.778[b]	0.003
Loading dose/BW (mg/kg)	25.15 (14.91–31.50)	25.84 (13.75–31.51)	0.725[b]	24.65 (14.91–31.25)	25.48 (13.75–31.51)	0.909[b]	0.055
First trough concentration (μg/mL)	10.65 (1.81–36.63)	11.10 (4.08–25.67)	0.673[b]	10.76 (1.81–36.63)	10.94 (4.08–25.67)	0.989[b]	0.084
Days to first TDM (day)	3 (2–7)	3 (2–5)	0.019[b]	3 (2–5)	3 (2–5)	0.022[b]	0.386
AKI	7 (6.5%)	0 (0.0%)	0.043[a]	7 (11.9%)	0 (0.0%)	0.013[a]	0.519

Median (minimum–maximum) or *n* (%).
[a]Fisher's exact test; [b]Mann–Whitney *U* test.
AKI, acute kidney injury; BW, body weight; PSM, propensity score matching; TDM, therapeutic drug monitoring.

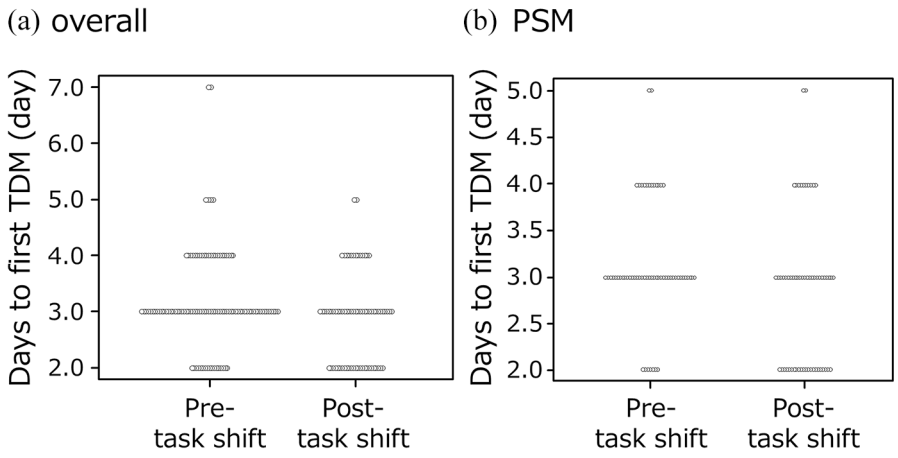

Figure 1. Days between the start of vancomycin administration and first TDM in overall (a) and propensity score matching (b) patients.
PSM, propensity score matching; TDM, therapeutic drug monitoring.

vancomycin and the approach needed for renal impairment.

Among anti-MRSA drugs, vancomycin has a high frequency of inducing kidney injury.[12] Therefore, vancomycin is used with TDM to control blood concentrations.[13] However, kidney injury somewhat persists. The causes include inadequate assessment of renal function and TDM that misses the appropriate time. This also includes special populations that are not recognized until blood concentrations are checked. In our institute, the involvement of a full-time emergency and critical care center pharmacist in supporting the entry of anti-MRSA drug blood concentration test orders has improved pharmacist intervention in designing the vancomycin initiation dose. This may have reduced the inappropriateness of renal function assessment based on the patient's transport opportunity and circulatory dynamics during vancomycin initiation. Similarly, this study showed that pharmacist support reduces the number of days to the first TDM. In a meta-analysis reported by Kunming et al.,[14] a significant reduction in vancomycin-induced kidney injury was observed in patients who received pharmacist intervention. Reported interventions incorporated in this study included dosage recommendations, TDM planning, drug selection, guidance development, staff education, and renal function monitoring. In TDM management, the proportion of initial concentrations drawn at the correct time according to guidelines was significantly improved in the post-intervention period than in the pre-intervention patients.[14] In addition, the post-intervention group showed a shorter number of days to reach a concentration in the target therapeutic range than did the pre-intervention group.[14] This implies that, in our study, patients with special populations who were initiated on vancomycin could have been treated through earlier TDM before the blood concentrations reached abnormal levels.

The risk factors for vancomycin-induced renal injury have been elucidated. Concomitant use of diuretics or piperacillin/tazobactam in patients receiving vancomycin is a risk for acute kidney injury.[15] Therefore, these risks should be appropriately considered when analyzing the impact of pharmacist support in the entry of blood drug concentration test orders on vancomycin-induced kidney injury. Therefore, PSM was used to eliminate these risk biases in the comparison of patient data before and after the start of the pharmacist support. The loading dose implementation was significantly biased in the overall patients, and these risks were adequately eliminated by PSM, and a reduction in the number of days to the first TDM and a lower frequency of vancomycin-induced kidney injury with pharmacist support were shown in PSM patients. In the aforementioned risk-adjusted population, pharmacist

support in the entry of blood drug concentration test orders demonstrated a safety benefit in the use of anti-MRSA medications in the emergency and critical care center. Age and BUN were higher in the post-task shift group of PSM patients. Renal impairment during vancomycin initiation has also been reported as a risk for vancomycin-induced kidney injury.[15,16] Older age and higher BUN may be risk factors for reduced renal function. That is, the post-task shift group may be a group with reduced renal function during vancomycin initiation compared with that of the pre-task shift group. However, pharmacist assistance reduced the frequency of vancomycin-induced kidney injury. These results suggest that our pharmacist intervention (earlier TDM) may significantly benefit patients.

Limitations

This study had some limitations. First, this was a single-center study, limiting the generalizability of the findings. Second, this analysis did not consider the relationship between information on vancomycin blood concentrations in individual patients and the time of onset of acute kidney injury. Third, the therapeutic intensity of vancomycin could not be guaranteed because this analysis did not involve the treatment effects. A more precise multicenter prospective observational study is required to address these limitations.

Conclusion

This study shows that pharmacist support in the entry of blood drug concentration test orders was associated with the prevention of the occurrence of vancomycin-induced kidney injury, enhancing patient safety during anti-MRSA medications. We believe that our task-shift operation and its evaluation results are useful findings that suggest the possibility of pharmacists demonstrating their pharmacy expertise in the emergency/intensive care area and further collaboration among multiple professions and their contribution to patients.

Declarations

Ethics approval and consent to participate

This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Review Committee of the Faculty of Medicine at the University of Miyazaki, Japan (O-1587). Due to the retrospective nature of the study, the Ethics Review Committee of the Faculty of Medicine at the University of Miyazaki waived the need to obtain informed consent.

Consent for publication

Not applicable.

Author contributions

Naoki Yoshikawa: Conceptualization; Data curation; Formal analysis; Funding acquisition; Project administration; Writing – original draft.

Chiaki Miyata: Conceptualization; Investigation.

Hidehiko Koreeda: Conceptualization; Investigation.

Shuichi Nakahara: Investigation.

Yuki Matsusaki: Investigation.

Yusei Yamada: Formal analysis.

Takehiko Nagano: Supervision.

Hidenobu Ochiai: Supervision; Writing – review & editing.

Ryuji Ikeda: Project administration; Supervision; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supplemental material

Supplemental material for this article is available online.

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