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Original Research

Effects of staff education and standardizing dosing and collection times on vancomycin trough appropriateness in ward patients

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Abstract

Background: Many institutions have guidelines for initiation and monitoring, but not timing, of vancomycin.
Objective: Our objective was to evaluate vancomycin trough collection appropriateness before and after an initiative to change the dosing and trough collection times in ward patients.
Methods: A retrospective cohort study of ward patients from May 2014-16 who received scheduled intravenous vancomycin was performed. Nurse managers and pharmacists provided staff education. Differences between pre- and post-intervention groups were compared using student's t-test for continuous data and chi-square test for categorical data.
Results: Baseline characteristics were similar between the pre-intervention (n=124) and post-intervention (n=122) groups except for weight-based maintenance dose (15.3 mg/kg vs. 16.5 mg/kg, p=0.03) and percentage of troughs collected with morning labs (14% vs. 87%, p<0.001). Patients in the pre- and post-intervention groups received a similar frequency of loading doses (14.5% vs. 16%, p=0.68). There was no significant difference in percentage of vancomycin troughs collected appropriately at 30 (40% vs. 42%, p=0.72), 60 (57% vs. 63%, p=0.35), or 75 (60% vs. 68%, p=0.22) minutes from the scheduled time of the next dose.
Conclusion: Staff education and standardizing collection of vancomycin troughs with morning blood collections did not affect the percentage of appropriately collected vancomycin troughs.

Keywords

Vancomycin; Drug Monitoring; Pharmacists; Dose-Response Relationship, Drug; Plasma; Pharmacokinetics; Quality Improvement; Retrospective Studies; United States

INTRODUCTION

Vancomycin is used in empiric medication regimens for disease states such as hospital-acquired and ventilator-associated pneumonia[1] and is a preferred therapy for the treatment of methicillin resistant Staphylococcus aureus (MRSA) and Staphylococcus epidermidis. Numerous dosing strategies for vancomycin have been identified and are routinely used in practice.[2] In each dosing strategy, attaining identified target concentrations, such as a vancomycin trough of 15-20 mcg/mL for complicated infections caused by MRSA, is an important component in providing safe and effective care.

Although vancomycin has long been trusted for its activity against MRSA, appropriate use is necessary to reduce the risk of adverse effects. Numerous risk factors exist for vancomycin-associated nephrotoxicity, including vancomycin trough concentrations[3] ≥15 mcg/mL, concomitant exposure to other nephrotoxins, such as aminoglycosides[4] and piperacillin/tazobactam[5-13], duration of exposure,[12,14-16], and total daily dose.[15,17] Due diligence is necessary when vancomycin is used in patients.

In many institutions there are established clinical practice guidelines for the initiation and therapeutic drug monitoring (TDM) of vancomycin.[18] However, the percentage of institutions that use a standard time for scheduling doses of vancomycin and collecting serum vancomycin concentrations is unknown. Without established guidelines, this can lead to inappropriate collection of vancomycin troughs, which often results in concentrations that are difficult or impossible to interpret and poor patient outcomes.[19] Investigators have offered vancomycin and TDM education to nurses, phlebotomists, and other health care professionals and compared pre- and post-education timing of collecting vancomycin trough levels.[20,21] Swartling *et al*. found a 19% increase in appropriately collected vancomycin troughs after educational interventions (p<0.03).[20] Coleman *et al*. found a non-significant increase of 5% in appropriately collected troughs after educational interventions (p=0.20).[21] These investigators did not comment on the effect this collection may have had on attaining a target trough concentration. Implementation of a standardized vancomycin dosing and

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trough collection schedule coupled with education for clinical staff could possibly reduce inappropriate timing of trough collection. The purpose of this research was to assess the appropriateness of vancomycin trough collection after clinical staff education and standardizing the time of vancomycin dosing and blood collections for vancomycin trough collection in ward patients.

METHODS

The research was approved by the University of Arkansas for Medical Sciences institutional review board (#205589).

On August 1, 2015, a policy change was implemented allowing pharmacist consultation to manage vancomycin therapy. At the same time but separate to the policy, standard administration times that included a dose at 05:00 were instituted. As part of this policy change, pharmacists who were consulted on a vancomycin regimen were provided the authority to dose, monitor, and adjust administration times for vancomycin. Prior to this initiative, standard administration times were 08:00 or 09:00 whenever possible for all dosing intervals. Before and after this initiative, vancomycin doses that were off of the standard administration schedule were treated as exceptions and had trough concentrations ordered prior to the third, fourth, or fifth dose rather than at the standard trough collection time (i.e., morning blood draws and 08:00 or 09:00). Education for the day and night shift nurses regarding the changes in times for morning doses of vancomycin and trough collection was provided verbally by pharmacists and nursing managers. Phlebotomists were not provided education because they were not readily accessible. The duration of education was 2-5 minutes and did not involve administration of a post-education competency assessment. Pharmacists provided more of the education to day shift nurses, and nursing managers provided more of the education to night shift nurses. Formal education sessions occurred during August 2015, and thereafter only informal discussions were performed in small groups or one-on-one to remind individuals of the changes as nurse managers and pharmacists identified individuals needing remediation.

This was a retrospective, observational cohort study of all patients admitted to a non-ICU setting at a single 452-bed academic medical center from May 2014 to May 2016 who received intravenous vancomycin at a scheduled interval. Patients who received their first dose of vancomycin before the implementation date were included in the pre-intervention group, and those who received their first dose on or after the implementation date were included in the post-intervention group. Patients were eligible for inclusion if they were admitted to our institution, received at least 24 hours of intravenous vancomycin therapy, and had at least one serum vancomycin trough concentration drawn between 00:01 to 11:59 recorded in the electronic health record. Patients were excluded if they were receiving renal replacement therapy at the time of admission or were admitted to an intensive care unit before the first serum vancomycin trough concentration was collected. Standard dosing intervals were defined as scheduled vancomycin dosing every 12 or 24 hours. Non-standard dosing intervals that were used in patients were scheduled vancomycin dosing every 8, 36, and 48 hours. The dose of vancomycin for which a blood collection was performed to collect a trough concentration occurred between 00:01 and 11:59 and may have been performed before, with, or after the morning blood collection.

The primary outcome was the percentage of interpretable vancomycin trough concentrations, defined as a trough concentration collected within 30 minutes of the next scheduled dose of vancomycin as long as the vancomycin dose had not been administered yet. This trough concentration could have been drawn at any time between 00:01 and 11:59 as long as there was a scheduled vancomycin dose during that time as well. The sensitivity of this outcome was tested by defining an interpretable vancomycin trough concentration as one collected within 60 and 75 minutes of the next scheduled dose. Differences between pre- and post-intervention groups were compared using Student's t-test for continuous data and Pearson chi-square test for categorical data. The data were analyzed using STATA 14 (StataCorp LP, College Station, TX). Continuous data were reported as mean ± standard deviation, and categorical data were reported as count (percentage). To detect a 15% change in the percentage of serum vancomycin trough concentrations that were interpretable with 80% power and an alpha value of 0.05, 122 vancomycin trough concentrations in each group needed to be evaluated.

RESULTS

All patients (n=79) who were evaluated against the inclusion and exclusion criteria were included, resulting in 246 trough concentrations. Baseline characteristics were similar between the pre-intervention (49 patients, 124 trough concentrations) and post-intervention (30 patients, 122 trough concentrations) groups except for the weight-based maintenance dose (15.3 mg/kg vs. 16.5 mg/kg, p=0.03) and the percent of troughs collected with morning labs (14% vs. 87%, p<0.001). Patients in the pre- and post-intervention groups received a similar frequency of loading doses (14.5% vs. 16%, p=0.68). Standard dosing intervals

Table 1. Baseline and clinical characteristics.

Characteristics	Pre-intervention (n=124)	Post-intervention (n=122)	p-value
Actual body weight, kg (mean, SD)	77.4 (32.5)	71.7 (17.3)	0.09
Loading dose, n (%)	18 (14.5)	20 (16)	0.68
Initial maintenance dose, mg (mean, SD)	1076 (299)	1148 (217)	0.04
Initial maintenance dose, mg/kg (mean, SD)	15.3 (4.8)	16.5 (3.5)	0.03
Initial dosing interval (Q12H or Q24H), n (%)	94 (76)	102 (84)	0.13
Therapy initiated on a weekday, n (%)	92 (74)	87 (71)	0.61
Trough drawn on a weekday, n (%)	92 (74)	93 (76)	0.71
Trough drawn with morning labs, n (%)	17 (14)	106 (87)	<0.001

Q12H: every 12 hours; Q24H: every 24 hours; SD: standard deviation

Table 2. Outcomes

Characteristics n (%)	Pre-intervention (n=124)	Post-intervention (n=122)	p-value
Trough drawn appropriately,			
± 30 minutes from next scheduled dose, n (%)	49 (40)	51 (42)	0.72
± 60 minutes from next scheduled dose, n (%)	71 (57)	77 (63)	0.35
± 75 minutes from next scheduled dose, n (%)	75 (60)	83 (68)	0.22
New trough ordered within 24 hours of last trough, n (%)	17 (14)	20 (16)	0.56

were used in the majority of patients (76% vs. 84%, p=0.13). (Table 1)

There was no significant difference in the percentage of interpretable vancomycin troughs as determined by a blood collection within 30 minutes of the next scheduled dose (40% vs. 42%, p=0.72). Similarly, there were no differences in percentage of blood collections within 60 (57% vs. 63%, p=0.35) or 75 (60% vs. 68%, p= 0.22) minutes from the next scheduled dose. Between the pre-intervention and post-intervention groups, there was no difference in the number of new troughs ordered within 24 hours of the last trough (14% vs. 16%, p=0.56). (Table 2)

DISCUSSION

Standardization of vancomycin trough collection to be with morning labs did not change the percentages of interpretable vancomycin troughs or the need to order a new trough for a subsequent dose because of a missed blood collection. These findings suggest that health care professionals in both groups were afforded a similarly low percentage of vancomycin troughs that could be assessed without extrapolation to a true trough value. Additionally, minimal redrawn troughs in both groups indicate that inappropriately collected troughs minimally affected patient decisions. Although many measured vancomycin trough concentrations may be extrapolated to a true trough concentration, this requires time and training for the clinical pharmacist and patient characteristics (e.g., stable renal function) that are not always present.

Less than two-thirds of vancomycin troughs that were supposed to have been drawn with a morning blood collection within 60 minutes of the 05:00 dose were drawn in this time interval, likely owing to a large percentage (29%) of morning blood collections occurring earlier in the day than anticipated by the investigators. A component of the education provided to nurses suggested morning blood collections be performed as close to 05:00 as possible; however, collecting blood earlier than 05:00 is a long-standing practice that may require further education to rectify or a change to earlier vancomycin trough collection times is warranted. The most likely reasons for similar rates of interpretable vancomycin troughs between groups was inadequate education and reeducation was provided to clinical staff who ordered and collected vancomycin troughs and earlier than expected morning blood collections were not recognized by practitioners in the post-intervention group. Consistent education related to the importance of this initiative as it relates to efficiency and productivity as well potentially improving patient satisfaction should be emphasized in future discussions with individuals who collect patient blood to improve the outcomes from this intervention.

In previous studies, the time of vancomycin trough collection was kept the same but education for nurses and phlebotomists was provided in order to improve understanding for the importance and appropriate timing of blood collections.[20,21] In the study by Swartling *et al*., an increase in appropriate blood collections from 51% to 78% was observed after a longitudinal educational intervention was provided; however, this was not the case in our study. The lack of consistent, scheduled reeducation for clinical staff by nurse managers and pharmacists may have affected ordering and collecting of vancomycin troughs according to the new schedule in our study. Now that the dosing and collection times are standard practice at our institution, evaluation of a new educational effort may be warranted.

There are several potential benefits to standardizing the time of vancomycin dosing and trough collection with morning blood collections. This practice would allow for trough concentrations to be collected and ready to assess prior to morning rounds, which would allow for more timely interventions on patients. Pharmacists at our institution manage vancomycin therapy through a consult service, and preparation of consult notes can be incorporated into the workflow more effectively by having this information available sooner. Although this was not captured in this data analysis, if a vancomycin trough collection were missed or not sent initially with the morning laboratory collection, it could have been ordered as an add-on to this collection, which would have reduced the need to recollect the trough with a later dose and potentially delay intervention. By including the trough collection with the morning blood collection, the result was one less blood collection for a patient and one less percutaneous access, which can increase patient satisfaction.[22] Also, standardized timing of vancomycin trough collection could improve workflow for nurses. For example, there are usually fewer medications ordered at the end of a night shift compared to the beginning of a day shift, which could diminish the overlap of medications requiring intravenous access, mitigate compatibility issues, and reduce the number of nursing activities at the beginning of a day shift.[23]

Standardizing the time of vancomycin trough collection to be with morning blood collections comes with potentially detrimental effects. Because vancomycin doses will be provided before the day-shift staff are available to assess the appropriateness of continuing the therapy or the development of nephrotoxicity, there may be a greater risk of patients receiving a vancomycin dose that otherwise would not be given if assessed later in the morning. Although it is not standard practice to routinely hold doses while awaiting morning laboratory values at our institution, other institutions may have a different policy on this

practice. Each institution should evaluate its specific workflow and pharmacy practice model prior to implementing a change in standardized timing of vancomycin doses and measuring of serum concentrations.

This study is not without limitations. It was a retrospective study design, which can lead to numerous biases, including the inability to assess all variables of interest because they were not collected at the time care was provided and potential differences in the study cohorts. There was inconsistent reeducation for clinical staff, which may have affected the timing of blood collections and should be investigated further following reeducation. Additionally, the time from the previous vancomycin dose to collection of the trough concentration may have been a more appropriate outcome to evaluate than the time from trough collection to the expected next dose of vancomycin, which necessitated the assumption that dosing intervals were stable and the scheduled administration times were appropriate. Vancomycin trough concentrations were not assessed, as this was outside the scope of this study. A previous investigation into the effect of inappropriately collected vancomycin trough concentrations observed that a sizable proportion of vancomycin troughs were collected early, resulting in an overestimation of true vancomycin trough concentrations and likely vancomycin under-dosing.[24] Following reeducation of clinical staff, the effects of inappropriately collected vancomycin trough concentrations should be evaluated for safety, effectiveness, and cost-effectiveness.

CONCLUSIONS

Implementation of a universal vancomycin trough schedule with morning blood collections did not appear to reduce the percentage of inappropriately collected vancomycin troughs. This finding may be the result of a change in time for collection of vancomycin trough concentrations mitigating the effects of educational efforts, which resulted in the morning blood collections occurring earlier than desired. The change in timing of trough collection showed no appreciable harm to patients while pharmacists and other health care providers may have realized benefits in workflow management. Based on the results of this study, we will recommend to continue collecting vancomycin troughs with morning blood collections but will standardize the time of these collections, reeducate clinical staff on this practice and evaluate their understanding with a post-education competency assessment, and evaluate the impact of further education and specific effects on workflow for clinical staff and patient-centered outcomes.

CONFLICT OF INTEREST

There are no real or perceived conflicts of interest for any of the authors.

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References

1. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, O'Grady NP, Bartlett JG, Carratalà J, El Solh AA, Ewig S, Fey PD, File TM Jr, Restrepo MI, Roberts JA, Waterer GW, Cruse P, Knight SL, Brozek JL. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61-e111. doi: 10.1093/cid/ciw353
2. Rybak MJ, Lomaestro BM, Rotschafer JC, Moellering RC, Craig WA, Billeter M, Dalovisio JR, Levine DP. Vancomycin therapeutic guidelines: a summary of consensus recommendations from the Infectious Diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists. Clin Infect Dis. 2009;49(3):325-327. doi: 10.1086/600877
3. van Hal SJ, Paterson DL, Lodise TP. Systematic review and meta-analysis of vancomycin-induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. Antimicrob Agents Chemother. 2013;57(2):734-744. doi: 10.1128/AAC.01568-12
4. Bentley ML, Corwin HL, Dasta J. Drug-induced acute kidney injury in the critically ill adult: recognition and prevention strategies. Crit Care Med. 2010;38(6 Suppl):S169-S174. doi: 10.1097/CCM.0b013e3181de0c60
5. Hammond DA, Smith MN, Li C, Hayes SM, Lusardi K, Bookstaver PB. Systematic review and meta-analysis of acute kidney injury associated with concomitant vancomycin and piperacillin/tazobactam. Clin Infect Dis. 2017 [ahead of print]. doi: 10.1093/cid/ciw811
6. Burgess LD, Drew RH. Comparison of the incidence of vancomycin-induced nephrotoxicity in hospitalized patients with and without concomitant piperacillin-tazobactam. Pharmacotherapy. 2014;34(7):670-676. doi: 10.1002/phar.1442
7. Davies SW, Efird JT, Guidry CA, Dietch ZC, Willis RN, Shah PM, Sawyer RG. Top guns: the "Maverick" and "Goose" of empiric therapy. Surg Infect (Larchmt). 2016;17(1):38-47. doi: 10.1089/sur.2015.104
8. Fodero KE, Horey AL, Krajewski MP, Ruh CA, Sellick JA Jr, Mergenhagen KA. Impact of an antimicrobial stewardship program on patient safety in veterans prescribed vancomycin. Clin Ther. 2016;38(3):494-502. doi: 10.1016/j.clinthera.2016.01.001
9. Gomes DM, Smotherman C, Birch A, Dupree L, Della Vecchia BJ, Kraemer DF, Jankowski CA. Comparison of acute kidney injury during treatment with vancomycin in combination with piperacillin-tazobactam or cefepime. Pharmacotherapy. 2014;34(7):662-669. doi: 10.1002/phar.1428
10. Hammond DA, Smith MN, Painter JT, Meena NK, Lusardi K. Concomitant vancomycin and piperacillin-tazobactam does not increase acute kidney injury in critically ill patients. Pharmacotherapy. 2016;36(5):463-471. doi: 10.1002/phar.1738

11. Kim T, Kandiah S, Patel M, Rab S, Wong J, Xue W, Easley K, Anderson AM. Risk factors for kidney injury during vancomycin and piperacillin/tazobactam administration, including increased odds of injury with combination therapy. BMC Res Notes. 2015;8:579. doi: 10.1186/s13104-015-1518-9
12. Navalkele B, Pogue JM, Karino S, Nishan B, Salim M, Solanki S, Pervaiz A, Tashtoush N, Shaikh H, Koppula S, Koons J, Hussain T, Perry W, Evans R, Martin ET, Mynatt RP, Murray KP, Rybak MJ, Kaye KS. Risk of Acute kidney injury in patients on concomitant vancomycin and piperacillin/tazobactam compared to those on vancomycin and cefepime. Clin Infect Dis. 2017;64(2):116-123. doi: 10.1093/cid/ciw709
13. Sutton JD, Mynatt RP, Kaye KS, Murray KP, Rybak MJ, Pogue JM. Nephrotoxicity comparison of two commercially available generic vancomycin products. Antimicrob Agents Chemother. 2015;59(9):5470-5474. doi: 10.1128/AAC.00388-15
14. Ragab AR, Al-Mazroua MK, Al-Harony MA. Incidence and predisposing factors of vancomycin-induced nephrotoxicity in children. Infect Dis Ther. 2013;2(1):37-46. doi: 10.1007/s40121-013-0004-8
15. Hidayat LK, Hsu DI, Quist R, Shriner KA, Wong-Beringer A. High-dose vancomycin therapy for methicillin-resistant Staphylococcus aureus infections: efficacy and toxicity. Arch Intern Med. 2006;166(19):2138-2144. doi: 10.1001/archinte.166.19.2138
16. Lodise TP, Patel N, Lomaestro BM, Rodvold KA, Drusano GL. Relationship between initial vancomycin concentration-time profile and nephrotoxicity among hospitalized patients. Clin Infect Dis. 2009;49(4):507-514. doi: 10.1086/600884
17. Lodise TP, Lomaestro B, Graves J, Drusano GL. Larger vancomycin doses (at least four grams per day) are associated with an increased incidence of nephrotoxicity. Antimicrob Agents Chemother. 2008;52(4):1330-1336. doi: 10.1128/AAC.01602-07
18. Davis SL, Scheetz MH, Bosso JA, Goff DA, Rybak MJ. Adherence to the 2009 consensus guidelines for vancomycin dosing and monitoring practices: a cross-sectional survey of U.S. hospitals. Pharmacotherapy. 2013;33(12):1256-1263. doi: 10.1002/phar.1327
19. Steinmetz T, Eliakim-Raz N, Goldberg E, Leibovici L, Yahav D. Association of vancomycin serum concentrations with efficacy in patients with MRSA infections: a systematic review and meta-analysis. Clin Microbiol Infect. 2015;21(7):665-673. doi: 10.1016/j.cmi.2015.04.003
20. Swartling M, Gupta R, Dudas V, Guglielmo BJ. Short term impact of guidelines on vancomycin dosing and therapeutic drug monitoring. Int J Clin Pharm. 2012;34(2):282-285. doi: 10.1007/s11096-012-9614-6
21. Coleman LK, Wilson AS. Impact of nursing education on the proportion of appropriately drawn vancomycin trough concentrations. J Pharm Pract. 2016;29(5):472-474. doi: 10.1177/0897190014568381
22. Howanitz PJ, Cembrowski GS, Bachner P. Laboratory phlebotomy. College of American Pathologists Q-Probe study of patient satisfaction and complications in 23,783 patients. Arch Pathol Lab Med. 1991;115(9):867-872.
23. Miller AD, Piro CC, Rudisill CN, Bookstaver PB, Bair JD, Bennett CL. Nighttime and weekend medication error rates in an inpatient pediatric population. Ann Pharmacother. 2010;44(11):1739-1746. doi: 10.1345/aph.1P252
24. Morrison AP, Melanson SE, Carty MG, Bates DW, Szumita PM, Tanasijevic MJ. What proportion of vancomycin trough levels are drawn too early?: frequency and impact on clinical actions. Am J Clin Pathol. 2012;137(3):472-478. doi: 10.1309/AJCPDSYS0DVLKFOH