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Impact of the pharmacist's request for vancomycin dosage in a university hospital: observational study

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Abstract

Objective: Considering the Resolution of the Collegiate Board RDC 586 of 2013, which regulates the clinical actions of the pharmacist, among them the prescription of laboratory tests to monitor the pharmacotherapy, the study aims to evaluate the impact of the request for vancomycin serum concentration by the pharmacist in a university hospital compared to other professionals. **Methods:** Patients who used vancomycin within a four-month period were included, being divided into group A, with patients who underwent the examination having the exclusive prescription by the assistant medical team between July and August 2021, and in group B with the examination prescribed by the pharmacist, between September and October 2021, patient demographic data, laboratory results of creatinine and dosage of vancomycin, number of vancomycin dosages collected, etiology of infections, culture results, and de-escalation of therapy were collected. **Results:** 22 patients were included for group A and 23 for group B. The results of initial and final creatinine, creatinine change, nephrotoxicity and vancomycin trough result in the therapeutic target did not show statistical differences between the groups. The total number of collections and the number of collections until reaching the therapeutic target of each patient differed between the groups, being higher in both for group B (p=0.01), requested by the pharmacist. In addition, the number of patients who reached the therapeutic target was 16 (69.56%) for group B against 6 (27.27%) for group A (p=0.01). **Conclusion**: The findings suggested pharmaceutical action in the follow-up of vancokinemia, as well as the direct prescription of the plasma dosage test of this antimicrobial by this professional, can contribute to greater therapeutic success and obtaining the optimized dosage for the individuality of each patient.

Keywords: Vancomycin, Pharmacist, Drug monitoring, Nephrotoxicity.

Impacto da solicitação de vancocinemia pelo farmacêutico em um hospital universitário: estudo observacional

Resumo

Objetivo: Considerando a Resolução da Diretoria Colegiada - RDC 586 de 2013, normativa que regulamenta as ações clínicas do farmacêutico, dentre elas a prescrição de exames laboratoriais para monitorização da terapêutica, o estudo objetiva avaliar o impacto da solicitação da dosagem sérica de vancomicina pelo farmacêutico em um hospital universitário comparado a outros profissionais. **Métodos:** Foram incluídos pacientes que utilizaram vancomicina no período de quatro meses, sendo divididos em grupo A, com pacientes que realizaram o exame tendo a prescrição exclusiva pela equipe médica assistente entre julho e agosto de 2021, e no grupo B com o exame prescrito pelo farmacêutico, entre setembro e outubro de 2021. Foram coletados dados demográficos dos pacientes, resultados laboratoriais de creatinina e vancocinemia, a quantidade de coletas de vancocinemia, etiologia das infecções, resultados de culturas e realização do Descalonamento da terapia. **Resultados:** Foram incluídos 22 pacientes para o grupo A e 23 para o grupo B. Os resultados de creatinina inicial, final, alteração da creatinina, nefrotoxicidade e resultado da vancocinemia no alvo terapêutica não apresentaram diferenças estatísticas entre os grupos. O número de coletas total e número de coletas até atingir a meta terapêutica de cada paciente divergiu entre os grupos, sendo maiores em ambos para o grupo B (p=0,01), solicitados pelo farmacêutico. Além disso, o número de pacientes que atingiram a meta terapêutico foi de 16 (69,56%) para o grupo B contra 6 (27,27%) para o grupo A (p=0,01). **Conclusão:** Os resultados para o grupo de pacientes analisados sugerem que a atuação farmacêutica no acompanhamento da vancocinemia, bem como a prescrição direta do exame de dosagem plasmática deste antimicrobiano por este profissional, pode contribuir em um maior sucesso terapêutico e obtenção da posologia otimizada para a individualidade de cada paciente.

Palavras-chave: Vancomicina, Farmacêuticos, Monitoramento de Medicamentos, Nefrotoxicidade.

Introduction

Vancomycin is an antimicrobial of the glycopeptide class, which acts in the inhibition of cell wall synthesis and bacterial growth. It is effective against gram-positive bacteria, particularly in the treatment of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Among the adverse effects we can mention fever, erythema, phlebitis, ototoxicity and nephrotoxicity. Frequently and alarmingly, the emergence of microorganisms resistant to vancomycin is observed, such as vancomycin-resistant *S. aureus* (VRSA)[1].

This medication appeared in the mid-1950s and was quickly approved by the FDA due to the absence of alternative therapies against MRSA[2]. In turn, from the 1980s onwards, with the increase in the number of MRSA infections and the use of vancomycin as a treatment, many studies were carried out aimed at tracing a serum target for its concentration, with the objective of achieving the lowest toxicity possible and maintaining its therapeutic efficacy[3]. The 2009 American Entities Consensus for Monitoring Vancomycin in MRSA Infections reports that the recommended trough vancomycin serum concentration for adults is between 15 and 20 mg/L, collected up to one hour before the next administration of the medication during the steady state. In addition to this method, there are modern ones highly recommended in the literature that use the AUC/MIC ratio (area under the vancomycin clearance curve/minimum bacterial growth inhibitory concentration) obtained by software that uses Bayer's Theorem to calculate the patient's individual pharmacokinetic parameters and estimate the ideal dose, or by means of first-order pharmacokinetic equations, estimated by two different collections in the steady state[4].

Collegiate Board Resolution - RDC No. 586 of August 2013, published by the Federal Pharmacy Council (*Conselho Federal de Farmácia*, CFF), regulates pharmacists' clinical duties, assigning these professionals the task of requesting laboratory tests for the purpose of therapeutic monitoring, evaluating its results and promoting dose adjustment when necessary through clinical pharmacokinetics[5]. At the University Hospital of Western Paraná (*Hospital Universitário do Oeste do Paraná*, HUOP), vancocinemia has been performed using the trough collection methodology since May 2019. Initially, the test was only prescribed by attending physicians, with the adjustment accompanied and guided by pharmacists, where the latter professionals often had to suggest the collection prescription and later the dose adjustment, which delayed performance of pharmacotherapy. However, as of September 2021, pharmaceutical professionals were qualified to request the exam, passing on to the assistant team the suggested adaptation after the serum vancomycin dosage, rendering pharmacotherapy monitoring more practical.

In this context, the objective of this study was to evaluate the prescription of the vancocinemia test by pharmacists, observing the impact of the direct request for the dosage by these professionals on therapeutic monitoring when contrasted with that of other professionals.

Methods

This is a retrospective, descriptive and observational study of a quantitative nature, carried out in a University/Teaching Hospital with 371 beds divided into the Internal Medicine, Surgery, Neurosurgery, Obstetrics and Pediatrics specialties.

The study was carried out from July to October 2021 and its population was the group of patients who received vancomycin and had their plasma levels monitored through vancocinemia. The paper was approved by the Unioeste Ethics and Research Committee, under opinion No. 3,552,940 of 09/04/2019.

Patients of both genders, aged at least 18 years old and hospitalized in intensive care areas and wards, who had their serum vancomycin dosage monitored at least once in the period were included. The patients were separated into two groups: Group A, in which the vancocinemia prescription was only assigned to the medical professional from July to August 2021, and Group B, where the vancocinemia prescription was assigned to the pharmaceutical professional, from September to October 2021, as there was no practical change other than the professional who performed the exam prescription. Trough monitoring in the steady state was used for dose adjustment in both groups, as it consisted of the previously standardized methodology at the institution due to the limitations inherent to other methodologies.

Pediatric patients and those undergoing treatment for diseases related to the Central Nervous System (CNS) were excluded, as the therapeutic target in vancomycin use in these populations differs from the adult population with other pathologies in the institutional protocol, as well as patients who already had renal dysfunction before using this glycopeptide, as its pharmacokinetics differs when related to drug excretion and requires differentiated monitoring[6]. To classify as nephrotoxicity caused by the drug, the definition proposed by Rybak *et al*. 2009 was considered, which indicates a 0.5 mg/dL increase in serum creatinine after treatment initiation.

The patients' demographic data were collected, as well as creatinine and vancocinemia laboratory results, number of vancocinemia collections, etiology of the infections, results of cultures and performance of therapy of therapy, which consists in using an antimicrobial with a lower action spectrum, guided by the culture, being part of rational antimicrobial management[7]. The patients were not evaluated for other comorbidities and use of other medications, as they were not segregated in relation to these variables, with the objective of generating a homogeneous sample between the groups.

These data were obtained from electronic medical charts and tabulated in an Excel – Microsoft® Office (Microsoft Corporation, USA) spreadsheet. The statistical analysis of the study was performed using the R Studio v1.4.1717 software, performing the Shapiro-Wilk test for analysis of homogeneity of the variables, the Student's t test for the parametric variables, the Mann-Whitney test for analysis of the non-parametric variables and the Chi-square test for the categorical variables.

Results

A total of 45 patients were included in the study, divided into 22 and 23 patients for groups A and B, respectively. The mean age observed for this population was 46.36 ± 13.35 years old for Group A and 49.43 ± 19.32 for Group B. Group B had 73.91% (17) of male individuals, a higher number when compared to Group A, with 50.00% (11), as can be seen in Table 1.

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Table 1. Characterization of the patients included in the study and results (Paraná, Brazil, 2021).

	A (%) (n=22)	B (%) (n=23)	p-valor
Age (years old), mean (SD)	46.36 (13.35)	49.43 (19.32)	0.51
Male, N (%)	11.00 (50.00)	17.00 (73.91)	0.22
Initial creatinine (mg/dl), median (IQR)	0.58 (0.78)	0.51 (0.41)	0.42
Final creatinine (mg/dl), median (IQR)	0.63 (0.78)	0.60 (0.64)	0.88
Creatinine change, median (IQR)	0.00 (0.30)	0.00 (0.40)	0.21
Nephrotoxicity, N (%)	3.00 (13.63)	5.00 (21.74)	0.75
Vancocinemia result at target, mean (SD)	17.00 (1.67)	17.56 (1.63)	0.50
N collections total, mean (SD)	2.00 (1.50)	3.00 (1.50)	0.01
N collections to reach the target, mean (SD)	1.50 (1.75)	2.00 (1.25)	0.01
N patients who reached the target	6.00 (27.27)	16.00 (69.56)	0.01

A: Group of patients who underwent the vancocinemia test prescribed only by the medical professional; B: Group of patients who underwent a vancocinemia test prescribed by the pharmacist; SD: Standard Deviation; IQR: Interquartile Range.

Baseline creatinine was similar for both groups, with a median of 0.51 and an interquartile range of 0.41 for Group B, and a median of 0.58 and an interquartile range (IQR) of 0.79 for Group A, with no statistical difference between the groups (p=0.42). Final creatinine after the treatment with vancomycin in these groups also showed no statistical difference (p=0.88). The creatinine change considering creatinine at treatment initiation and at its end showed the same median in both groups (0.00 mg/dL), with IQR values of 0.30 for Group A and of 0.40 for Group B. No statistical difference was observed between the groups in this data either (p=0.21). In addition to comparing the medians of the groups, a 0.5mg/dL increase in serum creatinine was considered for monitoring vancomycin toxicity[3], observing 3 individuals (13.63%) in Group A while 5 (21.74%) patients in Group B had nephrotoxicity, with a p-value of 0.75 for this variable.

The mean vancocinemia result when the patients reached the target of 15-20mg/dL was 17.00 ± 1.67 for Group A and 17.56 ± 1.63 for Group B with p-value of 0.50, again showing similarity between the therapeutic targets obtained by the groups and absence of statistical difference. The mean number of collections until reaching the therapeutic target and its standard deviation was higher for Group B, with a median of 2.00 and an IQR of 1.50 when compared to Group A, which obtained 1.50 and IQR of 1.75, showing a difference between the groups (p=0.01). There was also discrepancy in the number of patients who effectively reached the therapeutic target between 15.00 and 20.00 mg/dL, with 16 (69.56%) in Group B versus 6 (27.27%) in Group A (p=0.01).

Observing the number of collections and the serum vancomycin concentration until the therapeutic target is reached in Table 2, it is observed that the patients from Group B had the test collected 7 times so that the target was achieved, while those from Group A did not exceed 3 collections. Group B obtained nine different dosages that resulted in serum vancomycin concentration between 15 and 20 mg/dL, whereas Group A only obtained 3 different dosages prescribed, which can be seen in Table 3.

As can be seen in Table 4, Group B had 20 (86.96%) patients completing the treatment and 2 (8.69%) deaths, while Group A had 15 (65.18%) completions and 5 (22.73%) deaths, but also 2 (9.09%) therapy changes. Each group had pharmacotherapy de-escalation.

Characterizing the infections observed in the study, prevalence of sepsis of undetermined focus was verified, affecting 16 patients (35.56%) in the study, followed by 15 patients (33.33%) with bloodstream infection.

Table 2. Total number of vancocinemia collections from patients who reached the therapeutic target (Paraná, Brazil, 2021).

Total Number of Collections	A (n=6)	B (n=16)	Total (n=22)
1	3.00	4.00	7.00
2	1.00	7.00	8.00
3	2.00	2.00	4.00
4	0.00	2.00	2.00
7	0.00	1.00	1.00

A: Group of patients who underwent the vancocinemia test prescribed only by the medical professional; B: Group of patients who underwent the vancocinemia test prescribed by the pharmaceutical professional.

Table 3. Vancomycin dosage in patients who reached the therapeutic target of 15 to 20 mg/dl (Paraná, Brazil, 2021).

	Dosage that achieved the target	A (n=6)	B (n=16)	Total (n=22)
1	1,000 MG 12/12H	2	2	4
2	1,500 MG 12/12H	0	2	2
3	500 MG 8/8H	0	1	1
4	750 MG 8/8H	0	1	1
5	1,000 MG 8/8H	3	2	5
6	1,250 MG 8/8H	0	1	1
7	1,500 MG 8/8H	1	4	5
8	1,750 MG 8/8H	0	2	2
9	2,000 MG 8/8H	0	1	1

A: Group of patients who underwent the vancocinemia test prescribed only by the medical professional; B: Group of patients who underwent the vancocinemia test prescribed by the pharmaceutical professional.

Table 4. Treatment outcome of patients who used vancomycin in the study (Paraná, Brazil, 2021).

Clinical outcome	A (%) (n=22)	B (%) (n=23)	TOTAL (n=45)
Completed treatment	15 (65.18)	20 (86.96)	35 (77.78)
Death	5 (22.73)	2 (8.69)	7 (15.55)
Therapy change	2 (9.09)	0 (0.00)	2 (4.44)
De-escalation	1 (4.54)	1 (4.38)	2 (4.44)

A: Group of patients who underwent the vancocinemia test prescribed only by the medical professional; B: Group of patients who underwent the vancocinemia test prescribed by the pharmaceutical professional.

The distribution of pathogens observed in this population is shown in Table 5. Of the 45 patients studied, 2 (4.44%) did not have requested cultures (one in each group), while 16 patients (eight in each group) had negative microbiological cultures. Among the positive cultures, gram-negative bacteria were observed in 4 (8.89%), while 24 (53.33%) presented gram-positive etiology. Cultures with vancomycin-resistant microorganisms were not observed during the study period.

Table 5. Etiological and pathological characterization of the infections observed in the study (Paraná, Brazil, 2021).

	A (%) (n=22)	B (%) (n=23)	TOTAL (n=45)
Microorganisms			
Gram -	3 (13.64)	1 (4.34)	4 (8.89)
Acinetobacter baumanii	1 (4.55)	0 (0.00)	1 (2.22)
Enterobacter cloacae complex and Stenotrophomonas maltophilia	1 (4,55)	0 (0,00)	1 (2,22)
Escherichia coli	1 (4.55)	0 (0.00)	1 (2.22)
Pseudomonas aeruginosa	0 (0.00)	1 (4.34)	1 (2.22)
Gram +	11 (50.00)	13 (56.52)	24 (53.33)
Staphylococcus aureus (MRSA)	3 (13.64)	6 (26.09)	9 (20.00)
Staphylococcus hominis	2 (9.09)	3 (13.04)	5 (11.11)
Enterococcus faecalis	2 (9.09)	1 (4.35)	3 (6.67)
Staphylococcus aureus (MSSA)	1 (4.55)	0 (0.00)	1 (2.22)
Staphylococcus capitis	2 (9.09)	0 (0.00)	2 (4.44)
Staphylococcus epidermidis	0 (0.00)	2 (8.70)	2 (4.44)
Staphylococcus haemolyticus	1 (4.55)	1 (4.35)	2 (4.44)
No culture collected	1 (4.55)	1 (4.35)	2 (4.44)
Negative	8 (36.36)	8 (34.78)	16 (35.56)
Type of Infection			
Sepsis of undetermined focus	6 (27.27)	10 (43.48)	16 (35.56)
Bloodstream infection	8 (36.36)	8 (34.78)	15 (33.33)
Pulmonary focus sepsis	1 (4.55)	2 (8.70)	3 (8.89)
Surgical site infection	3 (13.64)	1 (4.35)	4 (6.67)
Osteomyelitis	1 (4.55)	1(4.35)	2 (4.44)
Pneumonia	1 (4.55)	1(4.35)	2 (4.44)
Fournier's gangrene	2 (9.10)	0 (0.00)	2 (4.44)
Cutaneous focus sepsis	1 (4.55)	0 (0.00)	1 (2.22)

A: Group of patients who underwent the vancocinemia test prescribed only by the medical professional; B: Group of patients who underwent the vancocinemia test prescribed by the pharmaceutical professional.

Discussion

According to the patients' demographic results presented in Table 1, we can state that the patients had similar dispositions between both groups, even when related to renal function before and after beginning the therapy with vancomycin. The systematic review by van Hal *et al*. (2013) asserts that nephrotoxicity studies associating the trough serum concentration present a variation from 5.00% to 43.00% of patients who developed such problem, which is influenced by the population under study, for example, critically-ill patients who are using other concomitant nephrotoxic drugs are at a higher risk of nephrotoxicity[8], profiles that were included in the current study.

As the total number of vancocinemia collections and the number of collections until reaching the therapeutic target showed a difference between the groups, it is observed that prescription of the test by pharmacists led to a more assiduous monitoring of the medication dosage adjustment, being collected in the steady state after the previous dose adjustment. In addition to that, this result can also be explained by the discrepancy in the number of patients who effectively reached the therapeutic target, from 6 (27.27%) in Group A to 16 (69.56%) in Group B. This difference was significant, reinforcing the hypothesis that the pharmacists' role in monitoring contributes to achieving the therapeutic targets, which is advantageous for the patients and promotes a more effective and safe use of this therapeutic alternative. A similar study showed an increase in the number of patients who reached the therapeutic target, from 50.50% to 79.70% ($p<0.01$), after the implementation of vancocinemia management by the pharmacists in a teaching hospital, as well as in the number of dosages in the therapeutic target (from 31.66% to 59.18%; $p<0.01$), but with a different therapeutic target (between 10.00 and 20.00 mg/dL)[9]. In 2015, Masuda *et al.* found in their study that 62.70% of the patients reached the same therapeutic target when compared to 41.70%, after the pharmaceutical intervention in the appropriate vancomycin dosage ($p<0.01$)[10]. In turn, in Smith *et al*. (2016), where pharmacists were able to order vancocinemia and other laboratory tests independently, it was observed that the incidence of renal failure dropped from 16.30% to 4.70% ($p=0.02$)[11]. Another factor that should be considered is that the medical team was not trained in dose adjustment by vancomycin monitoring by means of trough collection whereas the pharmacists in fact were, in addition to having developed the monitoring protocol established in the unit.

The distribution of dosages that reached the therapeutic target in the patients from the different groups (Table 3) obtained a greater distribution for Group B. The bias of this observation is that this group has more patients; however, it can be seen that the dosage assertiveness is due to individualization of the vancomycin dose, guided by the exam. The study by Marquis *et al*. 2015 also shows a difference between the dosage regimes after the implementation of a vancomycin dosage guide directed by pharmacists, where prior to implementation the dosage adopted in the institution was 1,000 mg every 12h for almost all patients[12].

It is observed that in Group A there were more than twice as many deaths and change of therapy, when compared to Group B (Table 4). This finding may have been influenced by the adequate drug dosage adjustment, which occurred significantly in the second group, leading to therapeutic effectiveness and eventual clinical complications, toxicity, adverse events and even death. The proper dose can also prevent the medication from being changed to another and more expensive therapeutic alternative. In Table 5, prevalence of growth of positive grain bacteria is observed, mainly MRSA, indicating adequate vancomycin use in this study[4].

As a limitation, we can mention the brief period of time for the analysis of the monitoring by the pharmacists, generating a sample size that may not be sufficient when compared to other similar studies. This is due to the fact that the number of vancomycin

serum dosages is not defined daily by the institution, as it demands from patients using the drug the ideal moment for such laboratory stage – the steady state after each dose adjustment, which demands extended monitoring in order to have a representative sample size. Even so, the results suggest differences between both observed groups. Thus, it is interesting that new studies are developed to assess the pharmacists' influence on the clinical outcomes, as well as the reduction in cases of renal failure caused by the drug.

Conclusion

The study results suggest that the pharmaceutical action in vancocinemia monitoring, as well as the direct prescription of the plasma dosage test of this antimicrobial by these professionals, can contribute to greater therapeutic success and to reaching the optimized dosage for the individuality of each patient. New studies are required to significantly demonstrate the performance of these professionals as active prescribers of exams related to therapeutic monitoring.

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Collaborators

RFE: Writing of the article, data analysis and interpretation; GTS: Conception and design, data analysis and interpretation; FWB AND LFC: Conception and design, data analysis and interpretation; ACS: Relevant critical review of the intellectual content, data analysis and interpretation.

Conflict Of Interest Statement

The authors declare no conflicts of interest in relation to this article.

References

1. James MR, Flower R, Henderson F *et al*. Rang & Dale: farmacologia. 9. ed. Rio de Janeiro: GEN Guanabara Koogan; 2020.
2. Levine DP. Vancomycin: A History. Clin Infec Dis. 2006;42:S5–S12. DOI: 10.1086/491709.
3. Rybak M, Lomaestro B, Rotschafer JC et al. Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Ame Jour of Heal-Syst Pharm. 2009;66:82–98. DOI: 10.2146/ajhp080434.
4. Rybak MJ, Le J, Lodise TP *et al*. Therapeutic Monitoring of Vancomycin for Serious Methicillin-resistant Staphylococcus aureus Infections: A Revised Consensus Guideline and Review by the American Society of Health-system Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Clin Infec Dis. 2020;71:1361–1364. DOI: 10.1093/cid/ciaa303.
5. Conselho Federal de Farmácia. Resolução- RDC nº 586, de 29 de agosto de 2013. Brasil: Regulamenta as atribuições clínicas do farmacêutico e dá outras providências; 2013; 1–11.
6. Drew RH, Sakoulas G. Vancomycin: Parenteral dosing, monitoring, and adverse effects in adults - UpToDate. 2017. Available in: https://www.uptodate.com/contents/vancomycin-parenteral-dosing-monitoring-and-adverse-effects-in-adults. Accessed on: 5st Jan 2022.
7. ANVISA. Diretriz Nacional para Elaboração de Programa de Gerenciamento do Uso de Antimicrobianos em Serviços de Saúde. 2017.
8. 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. Ant Agen and Chem. 2013;57:734–744. DOI: 10.1128/AAC.01568-12.
9. Momattin H, Zogheib M, Homoud A *et al*. Safety and Outcome of Pharmacy-Led Vancomycin Dosing and Monitoring. Chemotherapy. 2016;61:3–7. DOI: 10.1159/000440607.
10. Masuda N, Maiguma T, Komoto A *et al*. Impact of pharmacist intervention in preventing nephrotoxicity from vancomycin. Inter Jour of Clin Pharm and Therap. 2015;53:284–291. DOI: 10.5414/CP202274.
11. Smith AP, Millares-Sipin CA, James M *et al*. Impact of a Pharmacist-Initiated Vancomycin Monitoring Program. The Cons Pharm. 2016;31:505–510. DOI: 10.4140/TCP.n.2016.505.
12. Marquis KA, DeGrado JR, Labonville S *et al*. Evaluation of a Pharmacist-Directed Vancomycin Dosing and Monitoring Pilot Program at a Tertiary Academic Medical Center. Annals of Pharm. 2015;49:1009–1014. DOI: 10.1177/1060028015587900.