The Utilization of Critical Values (Vancomycin) Reporting System of Siriraj Hospital: A Pilot Study

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ABSTRACT

Objective: The critical values of the drug level are defined as the drug concentrations which are greater or lower than therapeutic values. These greater values can cause drug toxicity while the lower values lead to inadequate treatment, and both require immediate attention from physician. Critical values are reported to physician by telephone, but the utilization of critical values and physician's intervention has not been recognized. The present study was to determine the utilization rate of the critical values (vancomycin) reporting system and to identify the incidence of false positive result of critical values of vancomycin blood level.

Methods: The nurses who worked in 8 medicine wards, Siriraj Hospital were interviewed by telephone questionnaires including two main questions for 3 months.

Results: The results showed that the utilization rate of the critical values reporting system was 88.81%. After critical values were reported, the physician adjusted dosage of vancomycin 60.63%, drug discontinuation 23.62% and adjusted nothing 15.75%. The incidences of false positive result of critical values (vancomycin) were 1.38%.

Conclusion: The critical values reporting system remains important to help physicians in dose adjustment in critically ill patients or problematic patients such as abnormal drug clearance (liver and kidney diseases) or drug interactions. However, the therapeutic drug monitoring should be used carefully and correlated with clinical signs and symptoms due to the presentation of false positive of the critical values of vancomycin blood level.

Keywords: Critical value; Vancomycin; therapeutic drug monitoring (Siriraj Med J 2017;69: 190-193)

INTRODUCTION

The definition of critical values for therapeutic drugs is blood concentrations of the drug which are higher or lower than therapeutic ranges and requires immediate attention.[1] It is usually related to drug toxicity which varies from mild to probably lethal. The system of critical value reporting was initiated in 1972.[2] Nowadays, the International Organization for Standardization also includes critical value reporting in its clinical laboratory standard ISO 15189.[3] The critical values are commonly reported by telephone to wards or to physicians.[4] The data of critical values reporting at Siriraj poison control center, Siriraj hospital showed that vancomycin has the most frequently reported critical values. Statistical data from the overall drug monitoring between January to December 2014, showed a total of 4,549 vancomycin tests, and 1,767 tests showed within the range of critical values.

Vancomycin is a glycopeptide antibacterial drug which is widely used for the treatment of gram-positive cocci infections.[5] Therapeutic drug monitoring of vancomycin has been suggested to avoid ototoxicity and nephrotoxicity.[6] The incidences of ototoxicity are 1.4-5.5%. Reversible ototoxicity is usually related to vancomycin concentrations >40 mg/L. Irreversible ototoxicity is rare and typically encountered with concentrations >80 mg/L. The incidence of nephrotoxicity to vancomycin are 5-15%, although this will increase to 25-35% in patients receiving concomitant

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nephrotoxics. Vancomycin-induced nephrotoxicity occurs when vancomycin concentrations are greater than 20 mg/L and is typically reversible. For evaluation of the efficacy and the toxicity of vancomycin, it should be monitored at the lowest drug concentrations (trough level) in blood sample before giving the next dose of vancomycin after at least 30 minutes. Vancomycin trough level should be in the range of 5-15 mg/L.[7,8] However, McClain *et al*, demonstrated 14 laboratories reported vancomycin critical values which varied between 15 -100 mg/L with median critical value of 20 mg/L.[9]

At present, clinical toxicology laboratory has many services including therapeutic drug monitoring throughout 24 hours to immediately alert the physicians or nurses when drug level is in the critical values. However, there have not been any studies about association between the critical values reporting system and its utilization for adjusting drug dosage. Moreover, the false positive of the critical values may occur if blood is drawn shortly after recently giving vancomycin.

Therefore, the present study was to determine the utilization rate of the critical values reporting system and to identify the incidence of false positive result from the critical values of vancomycin blood level.

MATERIALS AND METHODS

Trough serum vancomycin concentrations are the most accurate and practical method for monitoring efficacy. Blood was drawn for the subject at the steady state of vancomycin and within 30 mins of the next dose. In this study, all patients who received prolonged courses of vancomycin and the routine monitoring of serum vancomycin concentrations over than 20 mg/L were used. The critical values of vancomycin were selected from the Laboratory Information System, (HCLAB) Sysmex Corp., after 1 day of drug level reporting and only reports from 8 medicine wards. Subjects were nurses who worked at these 8 medicine wards. Nurses who were interviewed, answered the question by opening the patient's medical record to prevent the recall bias. A telephone questionnaire was used for interviewing which comprised of two main categories as follows; the first category was the time of blood sample collection. Trough level was the drug concentrations which were drawn at 30 minutes prior to the next dosage. Peak levels were drug concentrations from blood that was collected after the completion of vancomycin dosage for 1 to 2 hours. The incidence of false positive critical values is the number of peak level to the total of critical values. The second category was utilization of critical values that were classified into 2 groups. (1) The critical values reports were not interpreted and (2) were interpreted to help physician in clinical judgment (dose adjustment, no dose adjustment, and drug discontinuation). The utilization rate was the number of the critical values reports which were interpreted to the number of trough levels. The study period was three months during November 2015 to January 2016. Data analysis was performed using frequency with percent on Statistical Package for the Social Sciences program, IBM Corp (SPSS). This study was rated as exempt from procedural review and approved by the Siriraj Institutional Review Board (Si. 308/2558).

RESULTS

A total of 145 critical values of vancomycin were studied. The median (Interquartile Range) critical value of vancomycin was 24.9850 (8.28) mg/L which ranged between 20.02 to 63.67 mg/L. The time of blood sampling is very crucial. The evaluation in therapeutic efficacy and toxicity of vancomycin should be monitored at the lowest concentrations using blood samples before the next dose or trough level. Therefore, critical values should be reported which were only trough levels higher than 20 mg/L. The Table 1 shows the times of blood sampling. The result showed that the incidences of false positive critical values of vancomycin were 1.38 %. The utilization rate of the critical values reporting system was 88.81%. After the medical laboratory technicians reported the critical values, the physicians' actions were dose adjustment 60.63 %, drug discontinuation 23.62%, and no dose adjustment 15.75% as shown in Table 2.

TABLE 1. Time of blood samplings.

Time of blood sampling	Number (percent)
After given vancomycin (Peak level)	2 (1.38%)
Before given vancomycin (Trough level)	143 (98.62%)
Total	145

TABLE 2. Utilization of vancomycin critical values for clinical decision.

Utilization of vancomycin critical values	Number (percent)
Use critical value in consideration	127 (88.81%)
Dose adjustment	77 (60.63%)
No dose adjustment	20 (15.75%)
Drug discontinuation	30 (23.62%)
Do not use critical value in consideration	16 (11.19%)
Dead	1 (6.25%)
Hemodialysis	6 (37.50%)
Stopping after one dose	9 (56.25%)

DISCUSSION

In Table 1, peak level was only 1.38% compared with the trough level (98.62%) because sample time of the trough level is more accurate than sample time of the peak level. In general practice, the trough level is used for monitoring the vancomycin dosage and interval. Measured concentrations and time of collection are used to calculate a "true" peak and trough to guide additional dosing. Therefore, recording the actual collection time is important.[8] In Table 2, this study demonstrated that about 88.81% of critical values reports influenced therapy. The critical value consideration for dosage adjustment was 60.63% in 88.81% of use drug monitoring, by therapeutic drug monitoring services in the hospital. Dosage adjustment was provided by the physicians who used pharmacokinetic parameters in vancomycin drug monitoring. Then, in case of dosage adjustment, this may be come from drug overdose or under dose. The physicians will provide the new adequate dosage and new fit interval for the next dose. Drug discontinuation may come from drug overdose or need to postpone the next dose. No dose adjustment was meaning the last dose was adequate dosage and fit in the interval. In this study, there were some cases which did not have drug level which might have come from too early to have drug level or early death or change to other antibiotics after the first dose. In the case of hemodialysis, some physicians do not need to have vancomycin drug level because hemodialysis can increase total body clearance of vancomycin which is difficult to estimate. However, it is also recommended that plasma levels of the drug should be monitored. In chronic hemodialysis, the plasma trough levels should be determined before the session. In the continuous hemodialysis, the total body clearance is almost constant, and determination of trough levels may be performed at any time.[10]

This study did not have the data about patient's outcome after using this reporting system. This was because the objective of this study was only to investigate the utilization rate of the critical values reporting system which was a pilot study of vancomycin. However, in further study of another drug, we will study and compare data about patients' outcomes before and after using this reporting system.

CONCLUSION

The critical values reporting system remains important to help physicians in dose adjustment in critically ill patients or problematic patients such as abnormal drug clearance (liver and kidney diseases) or drug interactions. However, the therapeutic drug monitoring should be used carefully and correlated with clinical signs and symptoms due to the presentation of false positive of the critical values of vancomycin blood level.

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