Assessment of Therapeutic Drug Monitoring of Gentamicin

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SUMMARY. The objective of study was to assess therapeutic drug monitoring (TDM) of gentamicin. A retrospective review of documents forms of 108 patients receiving gentamicin were reviewed in drug information centre, King Saud Medical City Hospital (KSMC), Riyadh. 82 patients were subjected to TDM. Although sampling time is crucial for computing data for TDM process, in study it was recorded only once (0.9%). Other medications were found in 93 (86.1%) patients. Regarding the documentation of gentamicin serum level, both gentamicin peak and trough levels were documented for 55 (50.5%) patients, peak level was documented only for two (1.8%) patients and for five (4.6 %) patients only trough level was documented, whereas for 46 (42.2 %) patients neither of peak nor trough levels were documented. Among the patient specific characteristics serum creatinine was recorded for 98 (90.7%) patients, although creatinine clearance was calculated for 91 (84.3%) patients. The reason for ordering the TDM was missing from all the patient records. Time of sampling and indications were found to be inadequate in almost all requests, necessitating measures initiated to educate and train the team involved in TDM process to as to have a meaningful monitoring of data.

INTRODUCTION
Therapeutic drug monitoring (TDM) is an established useful clinical service in pharmacotherapy. It helps in identifying alternations in drug disposition, adjusting drugs’ dosage regimen and minimizing adverse effects. Therapeutic drug monitoring (TDM) involves not just measurement of drug concentration, but also demands precise and complete interpretation of drug concentrations in biological fluids.

KEY WORDS: appropriateness of therapeutic drug monitoring (TDM) criteria, sampling time TDM, indication TDM, gentamicin TDM.

When pros and cons are put together TDM is probably highly beneficial, but increasing evidence suggests that current use is suboptimal affecting patient outcome resulting in wastage of scarce fund on measuring values which cannot be interpreted and do not assist patient management. In this study, because of toxicity (nephrotoxicity and ototoxicity) of Gentamicin, for that reason we need TDM.

In previous studies, up to 70-80% of drug
quantifications performed in inpatients have been inappropriate, as ideally drug levels are requested only when there is an appropriate indication. Significant limitations in benefits and toxicity may result if monitoring is performed without proper indication or with incorrect timing.

The present retrospective study was undertaken to find the proportion of gentamicin level determinations in hospitalized patient fulfilling accepted criteria for appropriate gentamicin level monitoring which could be a medium to further the quality of TDM services.

MATERIAL AND METHODS

Study design
This work has been performed retrospectively as a cross-sectional descriptive study, gaining the required information from the request forms of gentamicin monitoring in the drug information center, King Saud Medical City Hospital (KSMC), Riyadh. The study protocol was approved by the Research Ethics committee of KSMC Hospital. As many as 108 medical records of patients treated with gentamicin were used for data collection in a period from the start of August till end of December 2012.

Data collection
Patients receiving gentamicin for presumptive or laboratory diagnoses of gram-negative bacterial infections and in whom TDM was initiated by their respective clinicians who sent serum samples for gentamicin determination were included in the study. Fluorescence polarisation immunoassay (TDxR, Abbott Lab., USA) was employed to determine gentamicin concentrations. Dosage adjustment was recommended, if the trough and/or peak concentration(s) fell out of a predetermined range. Subsequent serum samples for gentamicin concentrations were obtained to ensure attainment of therapeutic levels.

Patient records and request forms were reviewed for the appropriateness of TDM using the demographics of patients: name, gender, age, weight, and height. Medication related information included time of first dose, time of blood sampling in relation to the last dose, duration of the treatment with the current dose, dosage regimen, other drug(s) taken by patient, relevant biochemical tests (serum creatinine, serum urea, creatinine clearance), and clinical related information of patient indication (e.g., toxicity, non-compliance).

Statistics
Descriptive statistics were used and the results were presented as percentages of cases and analyzed using MS Office Excel for Windows.

RESULTS
Among the 108 patients analyzed, 82 were male. It was observed that demographic details of all patient records had age, gender and weight, except one patient. Time for the start of dose was provided for 103 patients. TDM of gentamicin was mentioned for 82 patients.

Although sampling time is crucial for computing data for TDM process, in our study it was recorded only once (0.9%) for one patient. Other medications were found in 93 patients (Fig. 1).

Regarding the documentation of gentamicin serum level, both gentamicin peak and trough levels were documented for 55 (50.5%) patients, peak level was only documented for two (1.8%) patients and for five (4.6%) patients only trough level was documented, whereas for 46 (42.2%) patients neither peak nor trough levels were documented.

Among the patient specific characteristics serum creatinine was recorded for 98 (90.7%) patients, but not monitored. Serum creatinine was recorded and monitored in nine (8.9%) patients and for one patient serum creatinine was not recorded at all, for whom we will not be able to calculate creatinine clearance.

Although creatinine clearance was calculated for 91 (84.3%) patients, creatinine clearance was...
calculated correctly for 85 (78.7%) patients out of 91 patients.

Dose adjustment was done for 50 patients, whereas wrong dose calculation was done for four patients.

Diagnosis for which gentamicin prescribed was made known in 92 (85.2%) medical records, which were *Pseudomonas aeruginosa*, post traumatic, post meningitis, diabetic foot, burn, gynaecological infections, intra abdominal infections, osteomyelitis, septicemia, soft tissue infections/wounds, subacute bacterial endocarditis, urinary tract infection. The reason for ordering (indication) the TDM was missing from all the patient records.

**DISCUSSION**

Appropriate TDM service always requires sufficient information. TDM is a multidisciplinary function. Accurate and clinically meaningful drug concentrations can only be obtained by collaboration between clinicians, nurses and pharmacists and requires excellent communication. Unfortunately, still ignorance persists, without realizing that the information is very important for constructing a good interpretation. A clinical interpretation enhances and evolves therapeutic drug measuring service into TDM service. The measured concentration must always be interpreted in tandem with clinical response, the demographics and clinical status of individual patient, the dosage regimen used, the indication for TDM and pharmacokinetic characteristics of drug. The blood sampling should be done in appropriate time by considering the moments when the drug attains its peak, trough, and steady-state levels in plasma. Failure to do this may result in little benefit or may be harmful to the patient. The clinicians who apply the TDM should consult the clinical pharmacologists or clinical pharmacists who are well trained for this job. The timing of blood collection and indication are two crucial elements of drug monitoring requests, which rely on the specific purpose of the TDM. Incorrect sampling time, coupled with inaccurate interpretation, may expose the patient to harmful effect. Previous studies have documented that inappropriate measurements and indications have wasted significant proportion of resources spent on TDM. The requesting physician needs to provide required associated critical information which would facilitate accurate interpretation.

This study demonstrates that documentation of relevant information and following steps of gentamicin TDM is crucial to optimize gentamicin TDM practice to ensure maximum benefits of the TDM. Patient demographics are necessary to assess contribution of age, disease state, ethnic group to interindividual variation in pharmacokinetics and pharmacodynamics can be considered. In our study this need has been totally addressed. Time for starting a dose was almost completely taken care of among TDM patients. About three fourth of patients had documented dosage regimens, other medications prescribed and kidney function tests.

Appropriateness of sampling time and indication were observed to be negligible and are a cause of concern as both of these have a crucial part to play in optimization of drug regimen. While evaluating appropriateness of indication and sampling time for gentamicin in a similar study appropriateness of indication and sampling were 56.7 and 61.7%, respectively.

Requesting TDM service routinely without clear indications among in-patients could result in unnecessary costs.

Jennifer et al. in his study on gentamicin monitoring practice on two hospitals found that 20% of gentamicin concentrations were collected at inappropriate times or had incomplete documentation of dose administration times. Both lead to ineffective dosing.

It is a general norm that physician orders blood sample for TDM and nurses withdraw the sample and dispatch it to laboratory. There is a possibility that due to their unawareness on the importance of the required items of request forms they would have missed the necessary data.

If TDM pharmacist participates routinely during rounds together with the physicians at hospital this may help in consultation especially on indications of the TDM service. A clinical pharmacist’s involvement in TDM has been shown to decrease inappropriateness and monitoring costs. Presence of pharmacist in a pediatric setting, decreased inappropriate indications and samplings from approximately 15 to 0%.

Majority of the patients had serum creatinine measured and recorded but not monitored which indicates improper monitoring, exposing the patients to adverse effect of the gentamicin on the renal function (nephrotoxicity) which is one of the chief benefits of TDM of gentamicin.

Although for the majority of the patients’ creatinine clearance was calculated correctly there were some patients whose creatinine clearance
was calculated incorrectly and some patients their creatinine clearance wasn’t calculated at all. All these factors will not only make gentamicin TDM costly, but also cause undue pain and suffering for the patient.

Limited resources require that drug assays should only be performed when they meaningfully contribute to patient management, as therapeutic drug monitoring service has a far greater role than just therapeutic drug measuring 8.

The cost of performing TDM is expensive. It is important for blood samples to be obtained and the results interpreted appropriately to contain the costs of health care. TDM pharmacists need to consider implementing more comprehensive and long-term educational programmes for nursing staff, laboratory personnel, physicians and pharmacists has already been documented.

All the approaches discussed for changing physician behavior traditional education, formal TDM services, multidisciplinary quality-improvement efforts, and computerized approaches can improve the use of TDM 10.

**CONCLUSION**

This study demonstrates that the trough or pre-dose, level and a one hour post-dose or peak level were below the expected standards along with other requirements which will pose an obstacle in correct interpretation of serum drug concentration. The active participation of pharmacist in TDM process is indispensable by provision of all TDM team members with the role they need to play for ensuring better patient outcome.

**REFERENCES**