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A survey of therapeutic drug monitoring in a teaching hospital

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ABSTRACT

Objectives: Therapeutic drug monitoring (TDM) is one of the tools that aim to improve and ensure the best therapeutic effects while avoiding drug toxicity. This study aimed to identify the clinical utilization and application of TDM at a major teaching hospital in Jeddah.
Methods: A cross sectional survey of the clinical utilization and application of TDM at King Abdulaziz University Teaching Hospital across nurses in medical, surgical, pediatric, and intensive care units. The sample size (n = 130) represented 30% of the nursing population. The collection of questionnaires started on the 31st of January 2019 and was completed by the 10th of March 2019.
Results: The indication to use TDM was well-known to respondents. However, only 64% of respondents reported collection and measuring of the correct drug levels at a precise sampling time with no specific protocols being followed for each drug. Moreover, only 53% reported that the drug levels were being re-measured and adequately monitored for the right indication and proper sampling time. Regarding the presence of clinical pharmacists, 70% of the respondents indicated that no clinical pharmacist worked in their department.
Conclusion: Results demonstrate that appropriate sampling time was not used for the majority of monitored drugs. In the absence of a TDM request form, this finding probably indicates the lack of national or local TDM guidelines. In conclusion, TDM services, which include standardized forms, references, and an active clinical pharmacist will likely improve the application of TDM.

1. Introduction

Therapeutic drug monitoring (TDM) is one of the tools that aim to improve and ensure the best therapeutic effects while avoiding drug toxicity. It is defined as the use of assay procedures for determination of drug concentrations in blood or other body fluid and to facilitate the interpretation of these measurements with the intention to develop safe and effective drug regimens [1]. Clinical Pharmacokinetic Services or TDM Services involve more than just measuring drug concentration but rather encompass an entire patient-centered process that starts with requesting drug levels followed by obtaining the appropriate biological sample at the appropriate time in addition to the laboratory measurement and then communicating the result to the medical team who interprets the results and make therapeutic decisions [2].

TDM services depend on teamwork among the medical staff. However, it is one of the main responsibilities and competencies of the clinical pharmacist to advise as to the appropriate timing of TDM, evaluate obtained serum drug concentrations, and interpret the outcomes to structure individual dosing regimens [3]. Indeed, many pharmaceutical societies, including the American Society of Health System Pharmacists, The European Association of Hospital Pharmacist, and other healthcare institutions advocate the importance of pharmacists providing TDM as a fundamental part of their pharmaceutical care to selected patients [4]. In medically advanced countries, hospitals have incorporated clinical pharmacists in a broader spectrum of activities that encompass more vital roles. In Saudi Arabia, clinical pharmacy was first introduced in 1970, yet it is only now that it is beginning to be acknowledged and recognized. As a result, only 41% of hospitals in Riyadh, Saudi Arabia had pharmacists regularly monitor serum drug concentrations or their surrogate markers to determine the outcome

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of drug therapy and toxicity [5]. This study aimed to identify clinical utilization and application of TDM at a major teaching hospital in Saudi Arabia.

2. Methods

A cross sectional study was conducted using a paper-based survey that was created and validated by the research group. Construct, content and face validity were verified using two experts in the field to describe the application of TDM services. The survey was handed to nurses working at King Abdulaziz University Hospital (KAUH) in ten different in-patient wards, including male and female surgical wards, male and female medical wards, pediatric medical and intensive care units (ICUs), and specialized ICU. The ethical approval for conducting this study was obtained from the Research Ethics Committee at King Abdulaziz University Faculty of Medicine and the Nursing Department at King Abdulaziz University Hospital (Reference No 462-18).

A paper-based survey was handed to nurses. The survey was designed to ensure the full completion of the questionnaire. All questions were written in English with a cover page that explained the aim of the study. The collection of questionnaires started on the January 31, 2019 and was completed by the March 10, 2019. The survey consisted of open-ended and multiple-choice questions (MCQs) that addressed TDM services. The survey consisted of six different sections: (1) demographics and background, (2) general TDM knowledge, (3) candidate medications for TDM in the unit, (4) frequency of drug sampling, (5) reporting procedures, and (6) the presence or absence of a clinical pharmacist. A pilot study preceded this study and was used to optimize the phrasing of some questions, including additional MCQ answers and elimination of drugs that were not used in the institution, which were removed from the final survey.

Proper application of TDM was measured by the percentage of appropriate sampling times and the correct frequency of monitoring of all drugs combined. Appropriate sampling time was defined as correctly answering both of the two questions: (1) When is the ideal time for initial sampling of drug concentration and (2) what is the name of the monitored level? Correct frequency of monitoring was implemented by the responses to the ideal time for re-measurement. Summary statistics were applied to each question. Descriptive and inferential statistics were used to calculate the difference in individual responses from the mean of all responses. All statistics were conducted using Excel software.

3. Results

3.1. Demographics

A total number of 130 responses with a response rate of 100% were collected from nurses, which represented 30% of the total hospital nursing population. The ages of surveyed nurses ranged between 26 and 59 years with 126 (96.9%) females and only four (3.1%) males. Nationalities varied among Saudi, Indian, Filipino, Jordanian and Pakistani. Education levels were either diploma in 82 (63.1%) or bachelor's in 45 (34.6%) and 3 (2.3%) had post-graduate degrees (Table 1). The average service years for nurses was 9.5 years.

Table 1
Demographics.

Age (years), mean ± (SD)	35.9 ± 8
Female, n (%)	126 (96.9%)
Nationalities, n (%)	
Filipino	30 (23.1%)
Indian	95 (73.1%)
Saudi	3 (2.3%)
Pakistani	1 (0.8%)
Jordanian	1 (0.8%)
Education level, n (%)	
Diploma	82 (63.1%)
Bachelor	45 (34.6%)
Post-graduates	3 (2.3%)

n: number; %: percentage; SD: standard deviation.

3.2. TDM knowledge and utilization

Regarding the indication for TDM, 86 (66.2%) of the respondents reported its use when initiating therapy or adjusting dose, while 56 (43.1%) also chose the application of TDM for critically ill or patients with rapidly changing physiological statuses. Eighty-one (62.3%) claimed that TDM was used to confirm toxicity/lack of effect in a poorly controlled patient in addition to its use as a measure of patient compliance (Fig. 1). More importantly, only 83 (63.6%) reported the collection and measurement of the correct drug levels at a precise sampling time when initiating TDM based on general self-knowledgeable guidelines with no specific protocols being followed for each drug. Also, 69 (53.1%) of the respondents stated that the reported medications were being re-measured and adequately monitored for the right indication and proper timing intervals. Appropriate sampling times and frequencies of sampling for each drug is mentioned in (Table 2).

3.3. Presence of a clinical pharmacist:

Regarding the presence of a clinical pharmacist, 91 (70.0%) of the respondents indicated that no clinical pharmacist was present in their departments, while 26 (20.0%) and 13 (10.0%) of the responds demonstrated that there was a part time and full-time clinical pharmacist, respectively, in their departments.

Moreover, 75 (57.7%) of the respondents mentioned that the physician decides whether the drug level obtained is appropriate, and only 41 (31.5%) reported the involvement of a clinical pharmacist in the drug treatment decision-making.

3.4. Reporting procedure for TDM result

The reporting procedure was almost exclusively 97 (74.6%) done through the hospital's computerized system, which lacks a TDM form or a well-formulated reporting method. On the other hand, 64 (49.2%) of the respondents reported using a medication chart to report the decision and dosing recommendations (Table 3).

4. Discussion

This study is the first to assess TDM knowledge corresponding to the presence or absence of a clinical pharmacist at KAUH. In this study, the purpose was to observe the way in which TDM is utilized at KAUH, Jeddah and the insufficiencies of monitoring in relation to the presence or absence of a clinical pharmacist on the medical team. The survey had questions that reflected the appropriateness of the sampling time used in this institution with more than one third of the respondents indicating that the time of sampling was not adequately undertaken. In addition, the question addressing the sufficiency of sampling frequency demonstrated that almost half of the answers implied that the frequency of sampling was inadequate. In the absence of a TDM request form, this finding probably indicates that the institution lacked national or local TDM guidelines. While not specifically measured by this survey, it has been reported in previous studies that reaching thera-

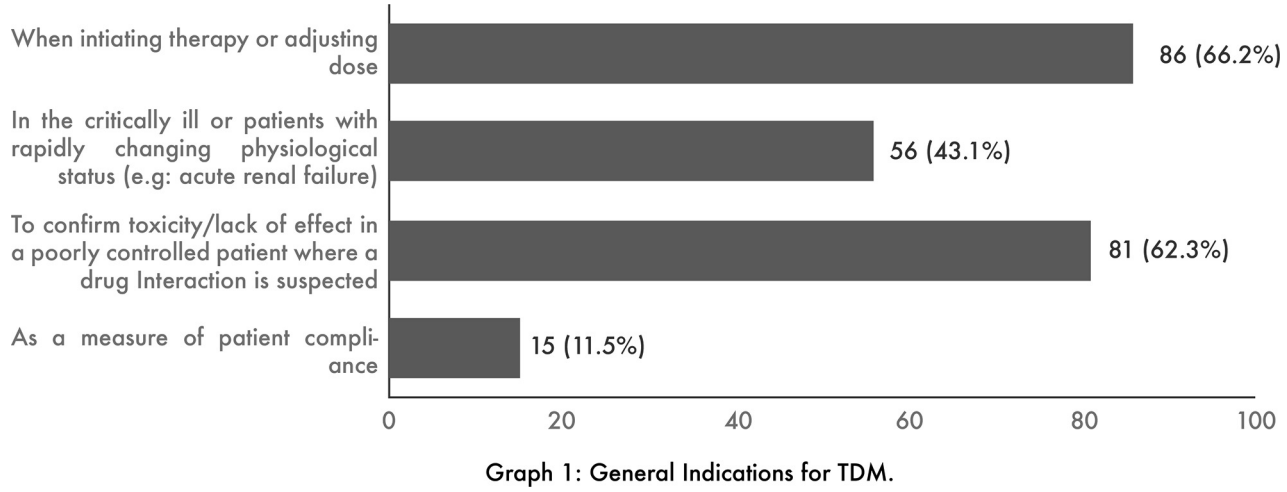

Fig. 1. General indications for TDM.

Table 2
Appropriate sampling times and frequencies of sampling for each drug.

	Aminoglycosides n = 120	Vancomycin n = 128	Digoxin n = 87	Theophylline n = 20	Methotrexate n = 54
Appropriate Sampling time, n (%)	95 (79.2%)	88 (68.8%)	30 (34.5%)	15 (75.0%)	28 (52.0%)
Appropriate Frequency of sampling, n (%)	68 (56.7%)	77 (60.2%)	10 (11.5%)	13 (65.0%)	47 (87.1%)

N: Number; %: percentage; Aminoglycoside: gentamicin, amikacin.

Table 3
Reporting procedure for TDM results.

	By phone, n	TDM request form, n	Hospital's computerized system, n	Medication chart, n
Reporting procedure	28	20	97	64

peutic drug levels, which correlate with clinical efficacy, is approached by practicing TDM according to consensus recommendations of guidelines [6].

In Saudi Arabia, there is a scarcity of information regarding pharmacist involvement in TDM services. The answers from the last section of our survey demonstrated that clinical pharmacists did not have an active role in TDM at the time that the survey was conducted. This finding could be a result of numerous factors, one of which is that they are not present either full or part-time in the majority of departments along with the pharmacy being understaffed. Nonetheless, their absence may be a contributing factor in the inappropriateness of TDM, and as a recommendation based on this study, the presence and active role of a clinical pharmacist in these departments is crucial. Currently, our institution is expanding the clinical services by including more patient care and incorporating TDM services in the near future. Worldwide, numerous studies have assessed the clinical and economic outcomes of pharmacist intervention in TDM. One study concluded that pharmacist intervention in TDM has a significant impact on clinical outcomes and a decrease in the length of hospitalization and unnecessary costs [7]. Pharmacist-led TDM services have been shown to have a positive impact on optimizing the initial dosing for vancomycin, amikacin, and gentamicin [8]. Another study demonstrated that the clinical pharmacist can help in advancing patient care by deciding and prescribing patient specific medications and providing pharmacokinetic and pharmacodynamic consultations [9]. Likewise, clinical pharmacists were found to lead to an increase in the appropriateness of drawn troughs of the immunosuppressant, tacrolimus, in solid organ transplant patients and led to a higher percentage of patients achieving aminoglycoside pharmacokinetic/pharmacodynamic goals [10,11].

In order to improve TDM services in hospitals with a lack or shortage of clinical pharmacists, assigning TDM requirements to members of the pharmacy staff would increase the sufficiency of TDM sampling. On the other hand, educating the nursing staff by performing TDM sessions periodically in each hospital ward would also be beneficial. Last, initiating a TDM protocol supervised and revised by experienced clinical pharmacists, stating the correct sampling time and frequency for every drug, would make a significant difference, help minimize inconsistent results, and aid in delivering the best medical care for patients.

This research however, is subject to a few limitations. First, is the small sample size although the data is considered accurate within the institution, these results may change if the sample size was expanded or extended to a different geographic location. Second, the survey was localized in one institution, which makes the results ungeneralizable. This study has several strengths: (1) it is a novel study in terms of addressing the application of drug monitoring in a transition phase of an educational institution that is slowly expanding pharmaceutical services and care to include therapeutic drug monitoring and (2) applicability; the survey can be used in any institution as a tool to assess the appropriateness of TDM in other institutions.

In conclusion TDM, which only involves measuring drug concentrations, has been shown to be inappropriate. TDM services, which include standardized forms and references and an active role of a clinical pharmacist, will likely improve the application of TDM. In the future we plan to expand our survey to other

medical staff, including physicians and pharmacists, and compare our results to other hospitals in which the pharmacists have a more active role in clinical care. Moreover, a further prospective study; concerning the time of sample collection will enhance our knowledge regarding the appropriateness of TDM in our hospital.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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