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Research Article

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The role of Therapeutic Drug Monitoring (TDM) in medication safety. Doctors knowledge and Practice, Taif, KSA

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Abstract

Therapeutic drug monitoring is a branch of clinical chemistry related with medication safety for patients via measurement of its level in blood, particularly drugs of narrow therapeutic range. The use of serum (or plasma) drug concentrations as a guide for monitoring drug therapy has continued to gain increased acceptance. This study aimed to evaluate and reflect opinions of physicians towards its role in some Taif City hospitals in Saudi Arabia. **Design &Methods:** A cross-sectional questionnaire was carried out among physicians, covering three areas: Physician's demographic characteristics, knowledge, and practices on therapeutic drug monitoring. **Results:** Most of the interviewed physicians agreed that it is a tool that can guide the clinician to provide effective and safe drug therapy, and clinical pharmacist to play important role to guide the team work services. The study indicated that male physicians were more knowledgeable about therapeutic drug monitoring. **Conclusion:** physicians almost agreed that therapeutic drug monitoring can play essential role for providing effective and safe drug therapy to the patient.

Keywords: Medicines level measurement, Drug errors, Doctors' understanding and Perception, Taif Hospitals.

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Introduction

Therapeutic drug monitoring (TDM) plays an important role in the development of safe and effective therapeutic medications and individualization of these medications. Patients admitted to the hospital may receive multiple medications and each administration occurrence carries with it the risk of error or misadventure. Then, questions will be raised: How can that be? Why is the medication process so prone to error? TDM is a branch of clinical chemistry that specializes in the measurement of medication levels in blood. Its service is widely used all over the world. However, among hospitals and institutions which provide this service there are variations in the clinical activities. Therefore, it could play a significant role in medication safety as, e.g., it can detect poisoning with any of the administered drugs, particularly those of narrow therapeutic range. Part of the TDM team personnel includes doctors and nurses who participate in patient care (Spector et al, 1988; Shirrell et al, 1999; Gross, 2001; Shenfield, 2001; Marshall and Bangert, 2008). Millions of serious medical errors were reported annually by health care organizations worldwide. These organizations are trying to improve patient safety and move health care quality framework in the right direction by offering solutions and to make good on the patient safety (Thomas et al, 2020; Oyebode, 2013; Helo and Moulton, 2017; Robertson and Long, 2018; James, 2013).Many different professionals (physicians, pharmacists, nurses, medical laboratory scientists, etc.) are involved with the various elements of drug concentration monitoring, which is a truly multidisciplinary process(Burton et al, 2006).

TDM is one of the drug and therapeutics committees (DTCs) within a hospital or primary care clinic that are responsible for evaluating the clinical use of drugs, developing policies for managing drug use and administration, and managing the formulary system, in addition to evaluate and discuss all aspects of drug therapy, they advise the medical, nursing, administrative and pharmacy departments on drug-related issues, also, assessing drug use to identify potential problems, promoting and conducting effective interventions to improve drug use (including educational, managerial and regulatory methods), and to manage adverse drug reactions, and manage medication errors (WHO, 2003; Lazarou et al, 1998; Tomson et al, 2007; Warner and Annesley, *http://www.nacb.org*; Greco, 2005; Bottorff, Bottorff,2005; Labcorp, 2001). In some developed countries, studies have shown that TDM can have a significant impact in promoting rational drug use, monitoring drug use and controlling drug side effects and costs (Weekes and Brooks, 1996; Soumerai and Avorn, 1984).

This survey study was conducted in some Taif hospitals (KSA), mainly to reflect physicians' knowledge and opinion towards therapeutic drug monitoring, and to evaluate the practice of the TDM service in medication safety in hospitalized patients and specifically to:

- know how the doctor determines how much drug to give to his patient when prescribing a dosage quantity and frequency.
- measure the difference between Doctors in their level of knowledge and perception towards the role of TDM in medication safety.
- identify Doctors differences in perception of indication and service optimization of TDM.

Experimental

Study design and setting

This was a cross–sectional survey conducted in most of Taif City governmental hospitals in the western part of Saudi Arabia during three months period. Participants were a total of one hundred physicians in these hospitals. Convenient method of sampling was adopted. Data was collected by trained pharmacy students from physicians. Face-to–face interview method was used and responses were recorded in a pretested semi-structured questionnaire. All physicians were recruited. Verbal informed consent was obtained from them.

The questionnaire was adapted from a survey monkey programme (*http://www.surveymonkey.com/*). The questionnaire was composed of three parts to collect data on physicians' demographics(Gender, Age in year, Nationality, Graduation year and Specialty), knowledge on therapeutic drug monitoring and practices related to the use of TDM. The questionnaire was pretested with a group of 20 physicians. Minor modifications were suggested and adopted in the final questionnaire.

Responses to the questions were recorded as 'agree', 'disagree' and 'don't know'. Other part of questions were answered as 'yes' or 'no' response. Another part of Questions 'under physician's practice on TDM was designed to be answered as 'yes' or 'no'.

Descriptive statistics of all studied variables was presented in frequencies and percentages/proportions. The chi-squared or Fischer exact tests were used to examine the association between different variables when appropriate. The significance level was set at $p<.05$. All analysis was performed using Statistical Package for Social Sciences (SPSS) software for Windows (version 21).

Results

Physician's Demographics:

A total of one hundred physicians were included in this study, of them 75 (75 %) were males and 25 (25 %) were females. Their ages were between 25-59 years, 62% of them were less than 40 years old. Only 31 of participated doctors were Saudis; their graduation years between 1978 –2014 (Table 1).

Table 1: Demographic Date of Physicians Participated in the Study:

Demographic Characteristics	N	%
Gender		
Male	75	75
Female	25	25
Age		
Less than 40	62	62
More than 40	38	38
Nationality		
Saudi	31	31
Non-Saudi	69	69
Specialty		
Specialist	32	32
Consultant	24	24
Registrar	24	24
General Practitioner	19	19
House Officer	1	1

Almost three-quarters of the interviewed physicians had satisfactory knowledge on topics related to the role of TDM in medication safety. They agreed for TDM as a team work service.

Figures 1 and 2 demonstrated their agreement that TDM is a tool that the clinical pharmacist can play an important role to guide the TDM team work services, and to provide effective and safe drug therapy in the individual patient. Also, importance of TDM to patients taking other medicines that affect drug level through drug-drug interactions.

Table 3 significantly indicated that better understanding of the role of TDM towards medication safety is associated with higher education and experience among the interviewed physicians' specialties.

Physician's knowledge on TDM:

Table 2: Doctors' knowledge about drug therapeutic drug monitoring by gender:

Knowledge	Gender		Total	P value
	Male	Female		
TDM is a tool that can guide the clinician to provide effective and safe drug therapy in the individual patient	79.5%	20.5%	100 %	.027
TDM is a team work services	80.5%	19.5%	100 %	.028
If a direct relationship exists between the drug or drug metabolite levels in plasma and the pharmacological or toxic effect.	79.7%	20.3%	100 %	.042
If the drug therapeutic effect cannot be readily assessed	80.0%	20.0%	100 %	.047
If appropriate analytical techniques are available to determine the drug and its metabolite level	79.1%	20.9%	100 %	.022
When clinical outcome is unrelated either to dose or to drug plasma concentration	80.0%	20.0%	100 %	.02

Although it is well understood that TDM is used mainly for monitoring drugs with narrow therapeutic range, more than 80% of the physicians agree of the important role of TDM in case of drugs of wide therapeutic range, while only 67% agreed that drugs with narrow therapeutic index range TDM is useful.

Table 3: Doctors' knowledge about drug therapeutic drug monitoring by specialty:

Knowledge	Specialty				Total	P-value
	Specialist	Consultant	Registrar	Practitioner		
1-TDM is a tool that can guide the clinician to provide effective and safe drug therapy in the individual patient	33.7%	24.1%	21.7%	20.5%	100 %	.023
2-TDM is a team work services	32.5%	22.1%	23.4%	22.1%	100 %	.014
3- The clinical pharmacist can play an important role to guide the team	34.1%	22.7%	22.7%	20.5%	100 %	.012
4-TDM is important for patients who have other disease that can affect drug levels	32.6%	24.4%	23.3%	19.8%	100 %	.003
5-TDM is important for patients who take other medicines that affect drug level through drug-drug interaction	32.9%	22.4%	23.5%	21.2%	100 %	.022
6-For patients suspected of symptoms of drug toxicity, the best time to draw the blood specimen is when the symptoms are occurring	31.8%	34.1%	15.9%	18.2%	100 %	.02
7-If the drug in question has narrow therapeutic index range	29.9%	23.9%	25.4%	20.9%	100 %	.036
8-In order to optimize TDM service knowledge of relevant patient's profile is important	32.4%	22.5%	19.7%	25.4%	100 %	.045

A summary of survey results were displayed on the following figures and tables:

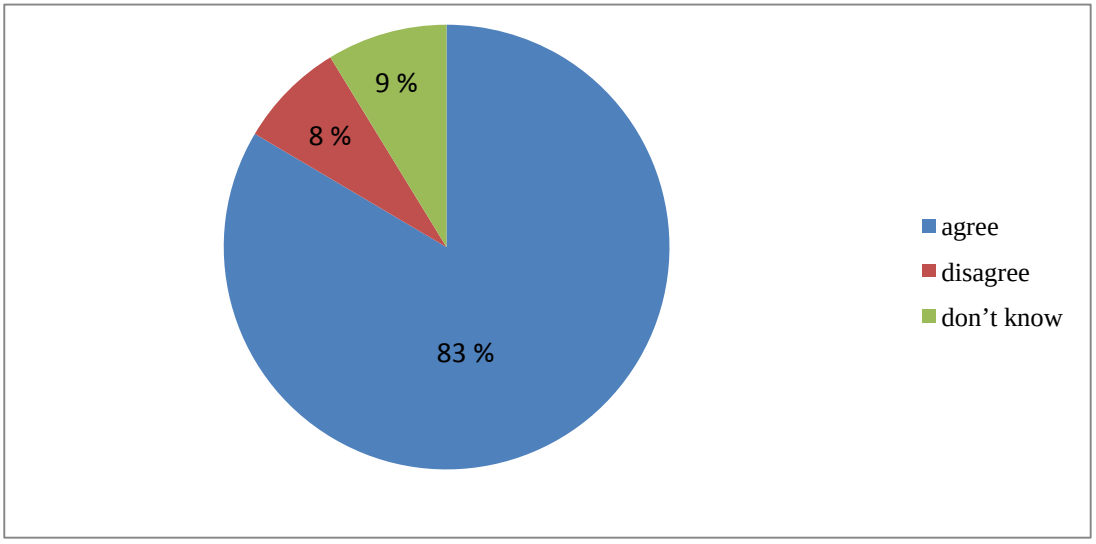

Figure 1: TDM as a tool to provide safe drug therapy

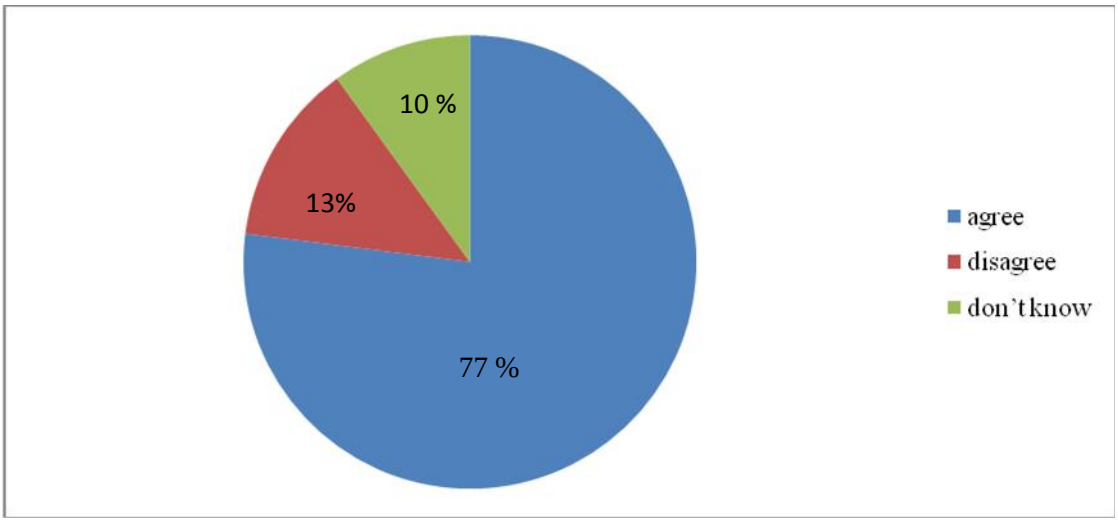

Figure 2: Physicians opinion towards TDM as a team work service

Table 4: Opinion of Physicians for TDM Indication:

Indication	Frequency	Percent
Low therapeutic index	68	68%
Poorly defined clinical end point	34	34%
Non-compliance to therapy	50	50%
Therapeutic failure	63	63%
Drug with saturable metabolism	22	22%
Wide variation in the metabolism of drug.	40	40%
Major organ failure	72	72%
Prevention of adverse drug effect	58	58%

Table 5: Importance of TDM service optimizations:

Indication	Frequency	Percent
Measurement of patient's serum or blood drug concentration must be taken at appropriate time after drug administration	71	71%
Knowledge of relevant patient's profile like demographic data, clinical status, laboratory and other clinical investigation	71	71%
Knowledge of pharmacological and pharmacokinetic profiles of the administered drug	75	75%
Interpretation of serum drug concentration after consideration of all above information and individualizing drug regimen according to the clinical needs of the patient	59	59%

Table 6: Physicians Knowledge regarding the reference ranges for commonly monitored drugs:

Indication	Frequency	Percent
Sometimes the reference range depends on drug indication	55	55%
Drug concentrations within the usual reference range do not rule out drug toxicity in a given patient	57	57%
Many adverse effects are dose-dependent (or not related to serum drug concentration	48	48%
Many factors alter the effect of drug concentration at the site of action	54	54%
In certain life-threatening situations, higher than normal concentrations may be required or even recommended	52	52%

Results of Physician's Practice on TDM:

Table 7: Physicians practices of how often they carry out TDM:

Indication	Frequency	Percent
Daily	10	10%
Two or Three times per a week	13	13%
Weekly	20	20%
Two or three times a month	6	6%
Monthly	16	16%
Others	35	35%
Total	100	100%

Table 8: Doctors Attitude towards their ability to understand and interpret the data of TDM:

Indication	Frequency	Percent
Not confident	18	18%
Slightly confident	36	36%
Confident	37	37%
Very confident	9	9%
Total	100	100%

Table 9: Opinion of Participated Physicians when some drugs should be monitored

Indication	Frequency (Percent %)			
	Gentamicin	Digoxin	Carbamazepine	Phenobarbital
As initial monitoring for new patient	48	45	48	47
Suspected toxicity: if repeated, should not be less than one half-life of previous sample	62	66	45	52
No or inadequate response	23	33	34	30
Suspected noncompliance	48	33	44	40
Suspected drug-interaction	41	44	37	39
After a change in dose regimen	39	36	36	35
Within 6 h after seizure recurrence			36	34
Every 6–12 months in stable adults and every 4–6 months in stable children			41	38

The most frequent drugs requested by the participated Physicians for TDM in the three months before the survey include Digoxin (38%), Carbamazepine (29%), Gentamycin and Phenytoin (24% each).

Drugs requested by participated physicians for TDM in the three months before the survey were shown below:

Indication	Frequency	Percent
Lithium	15	15%
Digoxin	38	38%
Phenytoin	24	24%
Carbamazepine	29	29%
Gentamycin	24	24%
Others	24	24%

Discussion

TDM has become a routine method to maintain “therapeutic” concentrations of numerous drugs. In the current study, most of the interviewed participant doctors agreed that TDM is a tool that can guide the clinician to provide effective and safe drug therapy in the individual patient (Fig. 1).As known worldwide, almost more than 80% of samples from various hospitals departments and other healthcare centers were sent to TDM service, but in Taif hospitals this was not the case, because the interviewed physicians had fair knowledge and background about the role of TDM in medication safety. They had almost poor attitude towards TDM as a tool that can guide the doctor to provide effective and safe therapy to the individual patient. However, it requires drug concentrations to be interpreted for each patient’s complete clinical, pharmacokinetic, and pharmacodynamic information. Unfortunately, most local laboratories report concentration

without complete and accurate medical and drug dosing information. When done poorly, as in a "concentration numbers only" laboratory, TDM may not been effective and could be dangerous (Hisham and Abdelrahim, 2008; *http://psnet.ahrq.gov/glossary.aspx*).Worldwide, adverse events in hospitals are found to be a major problem, as demonstrated by studies such as the Harvard Medical Practice Study (Brennan et al, 1995), the Quality in Australian Health Care Study (Roughead and Semple, 2002)and the Institute of Medicine Report(Kohn et al, 1999).

A survey of 157 TDM laboratories, mainly from Europe, Asian and African countries found that different reporting procedures were used in these laboratories. They ranged from producing hard copy reports, phone calls, and fax, to using online computer reporting. Some of these laboratories reported that insufficient information in the TDM request form was the main problem faced by the TDM service (Flynn et al, 2002; Larry, 2013).

Establishment of TDM and pharmacokinetic surveillance laboratories is essential to offer and ensure safe, private and high-quality healthcare environment for medical staff and patients. Tables 4 - 6 indicate the fairly poor knowledge of the participated physicians about the benefits of TDM in the medication safety and welfare of patients.

For cases requiring TDM indication (Table 4), showed that low therapeutic drug indices was the most frequently requested for TDM, followed by therapeutic failure cases, while drugs with saturable metabolism showed only 22% of physicians opinion.

Tables 5 and 6 showed knowledge of physicians towards importance of TDM service optimizations. More than 70 % of the interviewed doctors indicated that measurement of patient's serum or blood drug concentration must be taken at appropriate time after drug administration, knowledge of patient's profile, and pharmacological and pharmacokinetic profiles of the administered drugs were the most important for TDM services.

Schumacher and Barr (1998) adapted a total TDM testing process for the regularity environmental relation between the TDM team work services in the healthcare.

From Table 3, Specialists were the most knowledgeable about the role of TDM on medication. This may be due to their long medical services experience in hospitals.

Conclusion

This work investigated physicians' knowledge and perceptions toward the role of TDM in medication safety at Taif hospitals (KSA). Findings from this study reveal, in general, there was variation in total knowledge on understanding the role of TDM medication use and safety among the interviewed physicians. It seems necessary to establish educational programmes in the field of TDM services.

From the present investigational survey, there was lack of Pharmacokinetic laboratories in most Taif hospitals; therefore establishment of these laboratories is essential to avoid medical errors. The medical administration and physicians must cooperate with the clinical pharmacist due to his important role in the pharmacokinetic lab. Also, it is essential to establish workshops for health practitioners to educate them about the role of TDM and pharmacokinetic laboratories in controlling and monitoring sound therapeutic process.

Recommendations

The number of actual medication errors that occur in Saudi Arabia healthcare system is, by most accounts, considerable. Therefore, as almost no TDM services were available in Taif hospitals, it is recommended the:

1. Establishment of Drug and Therapeutics Committees (DTCs) in hospitals to act as agents of change.

2. Strategies for physician education regarding implementation optimal use of TDM programs at the hospital.

3. Establishment of educational programmes and drug and therapeutics committees within the hospital and healthcare professionals which may lead to better understanding to improve the medication safety issue and to reduce medication errors.

4. Establishment of workshops for health practitioners to educate them about the role of TDM and pharmacokinetic laboratories in controlling and monitoring sound therapeutic process.

5. Establishment of Pharmacokinetic laboratories in all Taif hospitals except Alhada hospital to avoid medical errors.

Therefore, it is important the establishment of medication safety event management which consists of providing care to the patient, notifying the physician, reporting the event to pharmacy, via a Query/View/Report (QVR), verbally, or otherwise, as appropriate.

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