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Assessment of the Need for Incorporation of Therapeutic Drug Monitoring in Second MBBS Practical.

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ABSTRACT

This study was conducted to assess the level of knowledge and the knowledge gap about Therapeutic drug monitoring(TDM) in second M.B.B.S Students and M.B.B.S interns and to conclude regarding the need of inclusion of Therapeutic drug monitoring in the curriculum of second M.B.B.S.It was a Cross-Sectional Questionnaire Based Study where 100 second M.B.B.S medical students and 50 M.B.B.S. interns were surveyed with a questionnaire Proforma after taking an informed consent. 75% of second M.B.B.S students and only 42% of M.B.B.S interns had good level of knowledge about what happens to a drug in the body. 54% of second M.B.B.S students and 26% of M.B.B.B interns had good knowledge regarding the need to monitor therapeutic level of a drug. Only 2% of second M.B.B.S Students and 8% of M.B.B.S interns given correct answer about the investigation of TDM. No second M.B.B.S student and M.B.B.S interns had the knowledge of instrument used for TDM. 65% of second M.B.B.S. students and 76% of M.B.B.S interns thought that TDM is a new term to them in Pharmacology and affirmed the need for incorporation of TDM in second M.B.B.S curriculum. The present study shows that there is a substantial gap of knowledge about Therapeutic drug monitoring(TDM) in second M.B.B.S students and M.B.B.S interns ,so there is a need of incorporation of Therapeutic drug monitoring(TDM) in second M.B.B.S curriculum.

Keywords: Second M.B.B.S., M.B.B.S. Interns, Therapeutic Drug Monitoring, Curriculum.

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INTRODUCTION

Therapeutic Drug Monitoring (TDM) can be defined as the use of drug measurements in Biological Fluids as an aid to the management of patients receiving drug therapy for the alleviation or prevention of diseases[1].

TDM as a service was introduced towards the mid and late 1980s and the last 10 years have seen it grow, along with the growth of separate clinical pharmacology departments. The service is being improved each year to include more and more drugs and the number of requests for TDM is increasing. Despite this, TDM in several centres remains within the confines of clinical biochemistry departments that provide only the 'measuring' (assay only) and not the 'monitoring' (assay and clinical interpretation) service[2].

The ideal TDM team—a clinical pharmacologist, clinical pharmacist and analytical scientist exists in only a few places. In addition data on levels obtained are limited and physicians are not adequately trained to interpret and use the results optimally. In developing countries TDM services are broadly of two types: one is like in large teaching hospitals where the service is available through departments of clinical pharmacology, while the other is in the private sector, where the drug estimations are performed by the clinical biochemistry departments. The high performance liquid chromatography (H.P.L.C.) technique, which is used by teaching hospitals, is labour intensive, technically demanding and the turnaround time is high. However, as the consumables are available locally, the recurring cost is low. As the TDM service is provided by utilizing the same infrastructure as for other academic and commercially required studies (e.g. new drug pharmacokinetics, bioavailability); it can be offered at very low charge to the patient[3].

Results reported from the clinical biochemistry laboratories give the values and the 'normal' or reference range. In services run by departments of Clinical Pharmacology, laboratory values, interpretation, remarks, and advice are also given. Herbal medicines are being used by an increasing number of patients worldwide, who may not necessarily advise their clinicians of the concomitant use. Interaction with conventional drugs have been documented for licorice, ginseng, tannic acids, plantain, uzara root, hawthorn and kyushin all of which may be prescribed by practitioners of the alternative systems[4].

Ill health is a serious problem impeding progress in most developing countries[5]. This includes diseases highly prevalent in these countries such as infections, diarrhoea, worm infestations, tuberculosis, neurocysticercosis and nutritional deficiencies, plus a higher proportion of patients with diabetes and AIDS. Patients often seek treatment late in their illness. Nutritional deficiencies are often subclinical and escape detection and they have been shown to affect drug pharmacokinetics[6].

The fact that inter population variations in drug pharmacokinetics can result in higher or lower plasma drug concentrations is well known. For example, the metabolism of phenytoin via para-hydroxylatio anticonvulsant dosage may be lower in Indians than in Europeans[7], while

other authors have indicated that ethnic differences may have a significant influence on the plasma clearance of phenytoin.

For TDM programs, quality control is vitally important[2] and in developing countries there are hardly any procedures for laboratory accreditation or external quality control. In India, one centre in Southern India offers an external quality control program (for biochemical tests). For drug levels, however, there is none and most departments and laboratories such as ours use overseas quality control programs although this increases the cost of running the laboratory.

In developing countries, there is a constant attempt to provide drugs to the majority of the population at low cost and bioavailability studies are done only at the time of obtaining marketing approval. Authors have already reported from Pakistan and Vietnam that quality of drugs used may be substandard and need additional quality control[8,9]. Given that generic drugs are freely available in developing countries, quality assurance of manufacturing practice is essential[10]. The TDM service can be used to provide an important early indication of substandard drugs.

The drugs for which TDM is performed in developing countries are selected on the basis of total workload, cost effectiveness and cost benefit. Anticonvulsant drugs are monitored most extensively. The most common indication for TDM of anticonvulsants has been nonresponsive to a standard dose of drug. Appropriate dosage adjustment and achieving therapeutic concentrations results in over 70% of epileptic patients getting good seizure control[11].

TDM of anti-mycobacterial drugs offers the clinician a chance to ensure that the patient achieves a serum concentration above the minimum inhibitory concentration[12]. The Madras Tuberculosis Centre has developed a urine test to identify noncompliance with isoniazid therapy[13].

Lithium monitoring in developing countries has focused on aspects such as compliance, patient education, ethnic differences, and predicting response to treatment. Shanming (1981) considered that one of the reasons for the restricted use of lithium in China may be the lack of facilities for monitoring serum lithium levels[14]. It has been emphasized that there is an urgent need to improve available laboratory facilities in mental health institutions, to encourage research in biological psychiatry and allow for cross cultural comparisons between the developed and the developing countries[15].

A Pharmacoeconomic analysis which calculated the direct and indirect costs of the service and the cost to the patient showed a significant benefit in those in whom therapeutic drug monitoring was carried out.

Developing countries differ from developed ones in having weak health-care structures, inadequate financial resources, unreliable supply and quality of pharmaceuticals, lack of adequate drug legislation and policy and a high rate of inappropriate self-medication[16].

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Priorities for health services in developing countries are radically different from those in developed nations; for example TDM of anticonvulsants has a very low priority and may not be asked for even once during the entire treatment period in a patient with epilepsy. At a time when cost considerations in the west have led to pooling of resources between clinical biochemistry and clinical pharmacology departments[17], in developing countries, the discipline of clinical pharmacology is still fairly new with only a few hospitals having fully-fledged departments. The ability of this discipline to be able to contribute in practically every area of medicine and add 'value' to the existing facilities remains its greatest asset.

Even after the area of TDM being so significant in the form of management of the patients, there is hardly any inclusion of the detailed aspects of the TDM and functioning of TDM team in the second year M.B.B.S. curriculum in theory and practical or in the final year M.B.B.S. curriculum.

The present study is the assessment of knowledge and the gap of knowledge of TDM in fifth semester students of second M.B.B.S. and M.B.B.S interns to answer the question of whether therapeutic drug monitoring should be incorporated in the second year M.B.B.S. curriculum for theory and practical.

AIM AND OBJECTIVES

Aim:

The aim of this study was to assess the need for incorporation of therapeutic drug monitoring in second year M.B.B.S curriculum.

Objectives:

The objectives of this study was **t**o Assess the level of knowledge and knowledge gap of Therapeutic Drug Monitoring in second M.B.B.S Students, to Assess the level of knowledge and knowledge gap of Therapeutic Drug Monitoring in M.B.B.S interns and to conclude regarding the need of inclusion of Therapeutic Drug Monitoring in the form of theory and practical in the curriculum of second M.B.B.S.

MATERIALS AND METHODS

Locus of Study:

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Type Of Study: A Cross-Sectional Questionnaire Based Study.
Duration of Study: Six months
Subjects: Students of second M.B.B.S. and M.B.B.S. interns.
Sample Size: We surveyed 100 second M.B.B.S medical students and 50 M.B.B.S. interns during this Study.

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Ethical Committee Approval: It was taken from institutional ethics committee of the institution.

Informed consent: Before giving questionnaire to student's informed consent was taken.

A questionnaire focusing on concept of drug metabolism, pharmacokinetic and pharmacodynamic action of a drug, therapeutic index, monitoring plasma therapeutic levels of a drug, investigation measuring the therapeutic level of a drug, orientation to the term TDM and TDM team, lab facility and instruments for TDM was distributed to the 100 fifth semester students of second M.B.B.S. and 50 M.B.B.S interns. The questionnaire consisted specific questions regarding knowledge about TDM and opinion about TDM.

Data Analysis:

The data obtained was carefully fed into the computer and analyzed using Microsoft Excel. Results were expressed using descriptive statistics.

QUESTIONNAIRE

1. What happens to a drug in the body?
2. What do you mean by pharmacokinetic and pharmacodynamic action of a Drug?
3. Do you know about therapeutic index of a drug?
4. a.YES b.NO
5. If yes,then what do you know about it? Explain?
6. Is there any need to monitor plasma therapeutic level of a drug?
   a.YES b.NO
7. If yes then why?
8. Do you know any investigation that measures the therapeutic level of a drug?
   a.YES b.NO
9. If yes,then which investigation?
10. What sample, in what quantity and at what point of time we should send sample for estimation of concentration of drug?
11. Are you oriented to the term Therapeutic Drug Monitoring (TDM)?
    a.YES b.NO
12. What do you know about TDM?
13. Is the facility for TDM available in your institute?
    a.YES b.NO
14. Which of the following group of drugs frequently need TDM?
    a.Antifungal Drugs b.Antimalarial Drugs
    c.Antihelmenthic Drugs d.Antiepileptic Drugs
15. Which common instrument is used for TDM?
16. Do you think that TDM is a new term to you in pharmacology and need to be incorporated in second M.B.B.S syllabus?
    a.YES b.NO

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RESULTS

Results were summarized in table number 1 and table number 2.

Table 1: Responses of Second MBBS Students to the Questionnaire on TDM

Question Sr. No. (No. of Students)	Correct Answer/ YES (%)	Wrong Answer/ NO (%)	Unattempted (%)
NO.1 (100)	75	11	14
NO.2 (100)	75	13	12
NO.3 (100)	50 (YES)	43 (NO)	07
NO.4*	44	56	_
NO.5 (100)	82 (YES)	11 (NO)	07
NO.6**	54	46	_
NO.7 (100)	16 (YES)	65 (NO)	19
NO.8***	02	22	76
NO.9 (100)	01	99	00
NO.10 (100)	41 (YES)	45 (NO)	14
NO.11 (100)	13	21	66
NO.12 (100)	42 (YES)	18 (NO)	40
NO.13 (100)	06	94	00
NO.14 (100)	00	06	94
NO.15 (100)	65	18	17

* - 50 students who answered question no.3 positively. ** - 82 students who answered question no.5 positively. *** - 16 students who answered question no.7 –Yes

Table 2: Responses of MBBS interns Students to the Questionnaire on TDM

Question Sr. No. (No. of Students)	**Correct Answer/ YES (%)**	**Wrong Answer/ NO (%)**	**Unattempted (%)**
NO.1 (100)	42	34	24
NO.2 (100)	72	12	16
NO.3 (100)	76 (YES)	18 (NO)	06
NO.4*	46	54	_
NO.5 (100)	86 (YES)	08 (NO)	06
NO.6**	26	74	_
NO.7 (100)	12(YES)	72 (NO)	16
NO.8***	08	04	88
NO.9 (100)	02	98	00
NO.10 (100)	62 (YES)	26 (NO)	12
NO.11 (100)	54	22	24
NO.12 (100)	34 (YES)	50 (NO)	16
NO.13 (100)	78	22	00
NO.14 (100)	00	01	49
NO.15 (100)	76	04	20

* - 38 students who answered question no.3 positively. ** - 46 students who answered question no.5 positively. *** - 06 students who answered question no.7 –Yes.

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01. In answer to question number one, a) 75 % Second M.B.B.S students gave correct answer and 11% gave wrong answer,14 % did not attempted the question, b) 42 % M.B.B.S interns gave correct answer and 34% gave wrong answer,24 % did not attempted the question.

02. In answer to question number two, a) 75 % of second M.B.B.S students gave correct answer and 13 % of students gave wrong answer,12 % did not attempted the question, b) 72% of M.B.B.S interns gave correct answer , 12% gave wrong answer and 16% did not attempted the question.

03. In answer to question number three, a) 50 % of second M.B.B.S students answered positively(Yes) and 43% negatively (No) and 7 % did not attempted the question, b) 76 % and 18 % of M.B.B.S interns answered Yes and No respectively whereas 6% did not attempted the question.

04. In answer to question number four, 44% of M.B.B.S students answered correctly and 56 % answered wrongly of 50 second M.B.B.S students who answered question number three positively, b) 46 % of M.B.B.S interns answered correctly and 54 % of interns gave the wrong answer of 38 interns who answered question number three positively.

05. In answer to question number five about, is there any need to monitor plasma therapeutic level of a drug, a) 82 % of second M.B.B.S student gave answer Yes and 11% answered No whereas 7 % did not attempted the question. b) 86 % of M.B.B.S interns answered positively (Yes) , 8 % negatively (No) and 6 % did not attempted the question.

06. In answer to the question number six, a) 54 % of second M.B.B.S students gave the correct answer and 46 % of students gave the wrong answer of 82 second M.B.B.S students who answered question number five positively. b) 26 % of M.B.B.S intern gave the correct answer whereas 74 % of interns answered wrongly of 46 interns who answered question number five positively.

07. In answer to question number seven , a) 16 % students answered Yes, and 65 % second M.B.B.S. students didn't know the investigation whereas 19 % of students kept question unanswered. b) 12 % answered Yes,72 % of interns did not know about the investigation whereas 16 % of interns kept question unanswered.

08. In answer to question number eight, a) only 2% of second M.B.B.S students given correct answer ,76 % of students unanswered the question and 22 % of them gave other vague answer (Irrelevant), of 16 students who answered question number seven Yes. b) 88% of M.B.B.S interns kept question unanswered, whereas only 8% of interns given correct answer and 4 % gave wrong answer of 6 interns who answered question number Yes.

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09. In answer to question number nine,a) only 1% second M.B.B.S students gave correct answer and 99 % of students gave wrong answer ,b) 2 % of M.B.B.S interns gave correct answer and 98 % of interns gave wrong answer .

10. In answer to question number ten, a) 41% of second M.B.B.S. student answered Yes and 45 % answered No, whereas 14 % did not attempted the question, b) 62% of M.B.B.S interns answered Yes and 26 % answered No ,whereas 12 % did not attempted the question.

11. In answer to question number eleven, a) 13 % of second M.B.B.S students gave the correct answer whereas 21 % gave wrong answer, 66 % of second M.B.B.S student gave no answer, b) 54% of M.B.B.S interns gave the correct answer whereas 24% interns gave no answer and 22 % of the interns gave other vague answer.

12. In answer to question number twelve,) 42 % M.B.B.S students answered Yes and 18 % students answered No, whereas 40 % kept question unanswered .b) 34 % of M.B.B.S interns answered Yes, 50 % of interns answered No and 16% of interns kept question unanswered.

13. In answer to question number thirteen, a) 6 % of second M.B.B.S students answered correctly i.e. antiepileptic drugs. b) 78% of M.B.B.S interns answered correctly .i.e. antiepileptic drugs.

14. In answer to question number fourteen, a) 6 % of second M.B.B.S students gave wrong answer and 94 % of students kept question unanswered , b) 1% of M.B.B.S interns gave wrong answer and 49 % of interns kept question unanswered.

15. In answer to question number fifteen, that is do you think that TDM is a new term to you in pharmacology and need to be incorporated in second M.B.B.S. syllabus.a) 65 % of second M.B.B.S. students gave the answer Yes and 18% gave the answer No,whereas 17% of students kept question unanswered.b) 76 % of M.B.B.S interns gave the answer Yes ,4 % gave the answer No and 20% of interns kept question unanswered.

DISCUSSIONS

In this study to assess the level of knowledge, a cut off of 60% was taken. That is only in case if 60% or more students give the appropriate response then there exists no knowledge gap.

Thus for second M.B.B.S students and M.B.B.S interns regarding the knowledge and knowledge gap of Therapeutic drug monitoring, following observations were made -

75% of second M.B.B.S students and only 42% of M.B.B.S interns had good level of knowledge about what happens to a drug in the body.

44% of second M.B.B.S students and 46% of M.B.B.S Interns had good knowledge regarding therapeutic index of a drug. 54% of second M.B.B.S students and 26% of M.B.B.B interns had good knowledge regarding the need to monitor therapeutic level of a drug.

Those questions which were based on Clinical aspects of Therapeutic drug monitoring (TDM).

Only 2% of second M.B.B.S Students and 8% of M.B.B.S interns gave correct answer about the investigation of TDM. Only 1% of second M.B.B.S students and 2% of M.B.B.S interns gave the correct answer about the sample, its quantity, time for sample collection and its processing for estimation of concentration of a drug for TDM.

13% of second M.B.B.S students and 54% of M.B.B.S interns gave correct answer about TDM (definition of TDM and its implication in clinics).

42% of second M.B.B.S students and 34% of M.B.B.S interns did not have knowledge regarding the facility for TDM available in their institute.

Only 6% of second M.B.B.S students and 78% of M.B.B.S interns answered correctly about the group of drugs that frequently need TDM.

No second M.B.B.S student and M.B.B.S interns had the knowledge of instrument used for TDM. 65% of second M.B.B.S. students and 76% of M.B.B.S interns thought that TDM is a new term to them in Pharmacology and affirmed the need for incorporation of TDM in second M.B.B.S practical.

From above it is clear that there exists a substantial knowledge gap regarding the theoretical as well as practical knowledge of Therapeutic drug monitoring amongst second M.B.B.S students and M.B.B.S interns both.

These observations about the knowledge levels suggest that there is fairly good knowledge about the theoretical aspects of TDM like its meaning amongst the second MBBS students and interns both. Regarding the group of the drugs requiring the TDM only MBBS interns had good knowledge. This may be the result of incorporation of concept of TDM in curriculum. But again not a due weightage is given to discussion of TDM in course or in the textbooks.

The level of knowledge about sample ,its quantity, time for sample collection and its processing for estimation of concentration of a drug , TDM team ,instrument of HPLC was very poor amongst both second MBBS students and interns.

The probable reason of this knowledge gap is due to the fact that.

In the second M.B.B.S curriculum recommended by medical council of India, there is no mention of Therapeutic drug monitoring in practical either of second MBBS or final MBBS. To bridge this knowledge gap ,we suggests the incorporation of Therapeutic drug monitoring in the

practical of second M.B.B.S and increasing the weight age given to TDM in theory of second MBBS .

Some of our recommendations of Therapeutic drug monitoring for the incorporation in second M.B.B.S curriculum are-

Topics to be incorporated in practical-
1. Visit to TDM laboratory.
2. Method of collection of sample.
3. Identification of various parts of High Performance Liquid Chromatography (H.P.L.C.).
4. Therapeutic problems based on concept of TDM.

The space required for this incorporation can be provided by deleting some of the pharmacy practicals which have lost their relevance in the modern medical science

Topics to be covered in theory-
1. Definition
2. Background
3. Role of Therapeutic drug monitoring (TDM) in safe drug treatment
4. High Performance Liquid Chromatography (H.P.L.C)
5. TDM team and its functioning.

The same knowledge is carried forward by the student to the final year where resensetization can be done in Medicine and clinical posting hence by the time student enters the internship he or she is well versed with the concept of TDM and its practical implications for the benefit of the patients.

CONCLUSION

The present study concludes that there is a substantial gap of knowledge of Therapeutic drug monitoring(TDM) in second M.B.B.S students and M.B.B.S interns, so there is a need of incorporation of Therapeutic drug monitoring(TDM) in practical of second M.B.B.S curriculum and there is need to increase the weight age given to TDM in theory

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