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Therapeutic Drug Monitoring and Its Association with the Reason for Therapeutic Drug Monitoring Ordered: An Observational Study at Tertiary Care Hospital.

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ABSTRACT

Therapeutic drug monitoring (TDM) is the quantifiable practice of measuring particular drugs at designated intervals to maintain a stable concentration in a bloodstream of patient and can use to design individualised dosage regimens. The aim of the present study was to assess the TDM level and its association with the reason for therapeutic drug monitoring. An observational study which was carried out for a period of two years at a rural tertiary care hospital in India. Reports of patients who were advised for TDM at our hospital were analysed in terms of reason for the TDM and interpreted with the TDM level as sub-therapeutic, Therapeutic, toxic and negligible range. . All analyses were carried out using EpiInfo version 7 and a p value < 0.05 was considered significant. Total 80 samples were collected.44 samples for routine monitoring.22 because of suspected sub therapeutic , 9 and 5 suspicious toxicity and checking compliance respectively. Sub-therapeutic suspicious group had 31.82% sub-therapeutic range routinely monitored group had (52.27%) normal therapeutic level .Suspicion of toxicity had 29.55% Toxic range, compliance group had (40%) negligible range. Association were found between the reason for sending samples for TDM level and measured drug levels i.e.45%. That is why clinicians should not be too reliant only on the clinical presentation and TDM should be recommended to all patients taking drugs which have narrow therapeutic index and require TDM. TDM is useful tool to measure the drug level in bloodstream and optimise the individual dosage regimen.

Keywords: Drug Monitoring,reason ,Therapeutic range,compliance.

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INTRODUCTION

Therapeutic drug monitoring (TDM) is a branch of clinical chemistry and clinical pharmacology that focuses on the measurement of drug concentrations in blood to maintain a constant concentration in a patient's bloodstream, in that way optimizing individual dosage regimens. [1] 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 is performed mainly for monitoring of drugs with narrow therapeutic ranges, drugs with marked variability in pharmacokinetic, drugs for which target concentrations are difficult to monitor, and drugs known to cause therapeutic and adverse effects and toxicity. The science of TDM introduced a new aspect of clinical practice in the 1960s after the publication of initial pharmacokinetic studies linking mathematical theories to patient outcomes [2].

The drugs for which TDM is performed in developing countries are selected on the basis of total workload, cost effectiveness and cost benefit [3]. Therapeutic drug monitoring (TDM) is thoroughly based on the assumption that, if there is a relationship between the concentration of a drug in a biological fluid and its effect, then the measurement of the biological fluid drug concentrations may be useful for patient care. It is defined as a measurement made in the laboratory, which is applied to a small group of drugs in which there is a direct relationship between serum drug concentration and pharmacological response [4]. Most extensively TDM of Antiepileptic drugs have been performed. The most common indication for TDM has been non response to a standard dose of drug. Appropriate dosage adjustment and achieving therapeutic concentrations [3]. TDM level use to compare with normal therapeutic range and differences exist between laboratories and validated target ranges should accompany results to assist clinicians with safe and effective prescribing [5].

MATERIAL AND METHOD

An observational study which was carried out for a period of two years from October 2013 to September 2015 at and Acharya Vinoba Bhave Rural Tertiary Care Teaching Hospital JNMC,Sawangi (Meghe), Wardha, Maharashtra, India.Data of the patients who were advised for TDM at our hospital were collected in terms of reasons such as for routine monitoring, because of compliance, for suspected toxicity and suspected sub-therapeutic.collected data were analysed in terms of reasons for TDM and its association with measured drug level as sub-therapeutic, Therapeutic, toxic and negligible range. All analyses were carried out using EpiInfo version 7 and a p value < 0.05 was considered significant.the study protocol was approved by Institutional Ethics Committee.

RESULT

Table 1: Distribution of patients according to Reason for TDM

Reasons for therapeutic drug monitoring	patient	Percentage (%)
Routine monitoring	44	55%
Suspected toxicity	09	11.25%
Suspected sub-therapeutic	22	27.5%
Compliance	05	6.25%
Total	80	100%

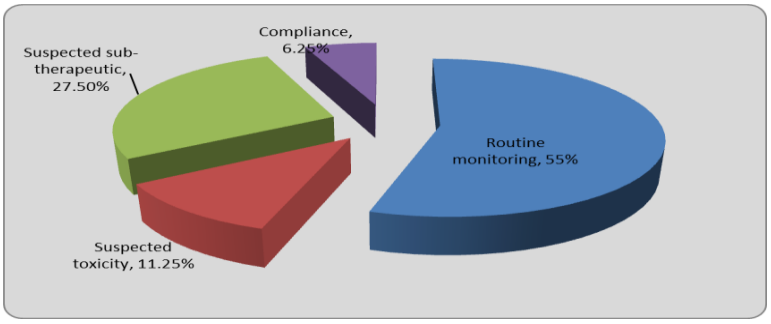

Figure 1: Distribution of patients according to Reason for TDM

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There were total 80 patients who were advised for TDM.Out of the 80 patients, 44 were male (55.0%) and were 36 female patients (45%). There were four main reasons for which clinician advised TDM.44 number of patients were ordered TDM for routine monitoring.22 patients ordered because of suspected sub therapeutic level of drug. While 09 number of patients ordered because of suspicious toxicity. Only 5 patients were ordered for checking compliance.(table1)

Patients who were advised therapeutic drug monitoring in order to check for compliance, had drug levels in the subtherapeutic range (60%) or negligible range (40%).Sub-therapeutic suspicious group had sub-therapeutic range in 31.82% therapeutic range in 54.54% while 9.1% had toxic range. 55.56% patients with clinical suspicion of toxicity had AEDs levels at toxic level.33.33% had therapeutic range and 11.11% had sub therapeutic range. Only 52% patients who were advised TDM routinely had normal therapeutic level . 29.55% and 18.18% patients advised for routine monitoring had toxic and sub-therapeutic range respectively.(Table2). The reason for which TDM was advised and level of TDM obtained according to same reason was calculated.Approximate only 45% association were there in between reasons For TDM order and measured drug levels. There is significance correlation between reason for TDM advised and obtained TDM level (p-value=0.0001)

Table 2: Association Between Reasons For Therapeutic Drug Monitoring Order And Measured Drug Levels.

Reason for TDM advice	Sub therapeutic Range	Therapeutic Range	Toxic Range	Negligible Range	Total
Routine monitoring	08(18.18%)	23(52.27%)	13(29.55%)	00(0%)	44(100%)
Suspected toxicity	01(11.11%)	03(33.33%)	05(55.56%)	00(0%)	09(100%)
Suspected sub-therapeutic	07(31.82%)	12(54.54%)	02(9.1%)	01(4.54%)	22(100%)
compliance	03(60%)	00(0%)	00(0%)	02(40%)	05(100%)
Total	19(23.75%)	38(47.5%)	20(25%)	03(3.75%)	80(100%)

- א2-value=34.49,p-value=0.0001, S,p<0.05

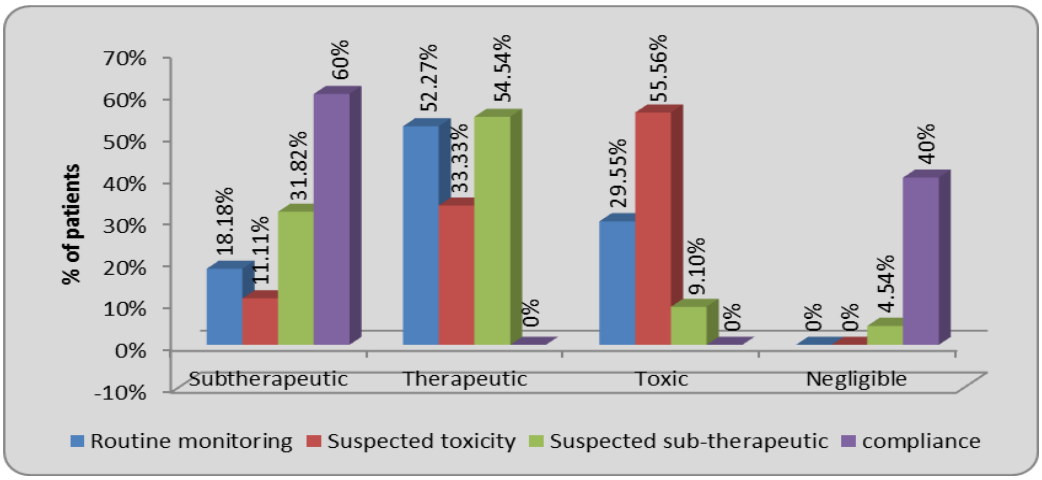

Figure 2: Reasons for Therapeutic Drug Monitoring Order and Measured Drug Levels.

DISCUSSION

None of the patients who were advised therapeutic drug monitoring in order to check for compliance, had drug levels in therapeutic range, falling either in the subtherapeutic range (60%) or negligible range (40%). Sub-therapeutic suspicious group had sub-therapeutic range in 31.82% therapeutic range in 54.54% while shockingly 9.1% had toxic range .55.56% of patients with clinical suspicion of toxicity had drug levels at toxic range. Only 52% patients who were advised TDM routinely had normal therapeutic range .These findings are compatible with the findings of study by Sunee Lertsinudom et.al [6] In their study, 58.25% patient had normal Therapeutic range who went for routine monitoring; Sub-therapeutic range were shown in 38.94% with

clinical issue of sub-therapeutic suspicion, clinical suspicious of toxicity had 40% toxic range .We found the almost similar result in that Sub-therapeutic suspicious group had sub-therapeutic range in 31.82% while .55.56% of patients with clinical suspicion of toxicity had drug levels at toxic range.we also found that patients advised for routine monitoring had toxic and sub-therapeutic range 29.55% and 18.18% respectively.

The association of the reason for TDM advised and measured drug range was found to be approximately 45%. Study by Sunee Lertsinudom et.al. [6] found 66.67% Associations between reasons of sending samples for drug level monitoring and the measured drug levels, This finding underlines the belief that clinicians should not be too reliant only on the clinical presentation and therapeutic Drug monitoring should be recommended to all patients taking drugs which have narrow therapeutic index and require TDM. Drug levels highlights the utility of TDM in patients. Gupta V.et al, 2012) also suggested that Plasma drug levels should be monitored when: A drug has a narrow, well defined therapeutic range, noncompliance is suspected, the desired therapeutic effect is not achieved, there are large inter individual variations in drug utilization or metabolism [7].

CONCLUSION

The results of the study suggest the importance of routine TDM to Detection of non-compliance, toxicity and failure of adequate response because of below reference range. There is only 45% association between reasons for Therapeutic Drug Monitoring ordered and measured drug levels. That is why clinicians should not be too reliant only on the clinical presentation and therapeutic Drug monitoring should be recommended to all patients taking drugs which have narrow therapeutic index and require TDM.

TDM can be help to identify problems with medication compliance among noncompliant patient cases. This study suggests that the result of TDM will be helpful to optimize the dose of drug for the better clinical outcome of patients.

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