

## Need To Be 'Vigilant' About Pharmacovigilance Studies

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Pharmacovigilance, as defined by WHO is - detection, assessment, understanding and prevention of adverse reactions [ADRs] or any medication related problems.

Studies to evaluate safety profile of medications were instituted in early 2002 [2]. Considering the fact that no medication is inherently safe, the treatment objectives to outweigh the benefits over the unwanted reactions of medications was emphasized including the need to monitor their safety profile.

It is true that – globalization coupled with explosion in availability of medications and access to information through internet facility on medicinal products has tremendously influenced the use of medicinal substances. In addition, with the recent 'mushrooming' of manufacturing units and simultaneous increase in the number of new medications there is a need to be alert about the ADRs.

Studies directed at detecting and assessing safer use of medications, appear mandatory to prevent ADRs and achieve rational therapeutic practices. Such activity requires collective and co-ordinated efforts from all the healthcare professionals such as – doctors, nurses and pharmacists. In addition dissemination of ADR data among – consumer groups and pharmaceutical firms also becomes necessary.

Well established guidelines are made available by WHO. Several regional and national centers have been set up in our country by Ministry of Health and Family Welfare to report ADRs.

While, it is clearly understood that safety is as important as the efficacy of therapeutic agent, following aspects need serious evaluation and consideration which may help us achieve our goal of reducing ADRs, but are often overlooked/ignored. Hence an attempt has been made to highlight the same in following paragraphs:

- A huge Pharmacovigilance data has been generated over a decade, by several researchers from innumerable labs / hospitals / organizations /sources, but the medications producing serious adverse effects are still being marketed, at times with a cautionary note for example – Nimesulide, Terfenadine, Coxibs etc.
- Patients reporting with ADRs having co-existing disorders/illnesses as co-morbid conditions are often not

taken into account or considered, while analyzing the ADRs data. Thus leading to misinterpretation of the data.

- While, FDA guidelines for 'IDEAL' data collection are available, often the present method of collection ADRs data does not meet the necessary criteria, therefore may lead to wrong conclusions.
- Most of the studies publish the ADR data which is often analyzed descriptively and do not have a proper control to compare the total number of patients who received a particular medication, thus giving an erroneous value of the study outcome for incidence and magnitude of ADRs.
- Since, genetic variations among individuals to a large extent contribute to a variation in response to a medication the occurrence of ADRs tends to vary from individual to individual / among patients. Hence there is a need for considering this aspect during method of evaluation of ADR data to avoid generalizing occurrence of ADRs and giving a wrong message regarding a particular medication producing ADR.
- Also, such interpretation may lead to refraining / denying, other individuals / patients being prescribed medication producing an ADR. It is possible that other individuals / patients may have a favorable outcome.
- Recording and reporting of ADR monitoring for every drug that is subjected to clinical trial has been made mandatory and forms a part of routine clinical trial protocol. However, attempts to evaluate accurately and build the causal relationship seem to be inadequate.
- In the Indian context, patients are often on multiple drugs including alternative systems of medication. Hence it is often difficult to identify the drug that will have produced the reported ADR, unless proved through objective testing for drug levels or an attempt is made to confirm the absence of other factors contributing to occurrence of ADRs.
- The spontaneous reporting of ADR data is considered ideal and appropriate, but it is rarely practiced, either due to lack of interest, motivation and/or management of such reactions by the attending clinician.
- It is often, difficult to differentiate between ADRs from

drug interactions or drug toxicity in the absence of detailed data collection or drug level monitoring.

- While, investigators are engaged merely in collecting the data, it is the consulting physician who offers immediate treatment for ADRs – either by stopping the drug or by replacing a suitable alternative drug. Therefore, there is a huge time gap between collection of ADR data, its analysis and finally availability of this data to treating physician for suitable action. Hence, such data may not be practically meaningful.
- In addition to confirming a claim that a drug has produced an ADR, it may require supportive Pharmacogenetic studies and re-challenge or de-challenge, which are presently not carried out or are lacking.
- Lastly, despite the fact that voluminous data has been accumulated on ADRs from various centers the practical utility / dissemination of this data appears to be lacking, since no action has been taken thus far.

In summary unless the Pharmacovigilance studies are carried out taking into account the confounding factors such as: an appropriate control group, co-existing co-morbid clinical conditions / illnesses, a deeper history into consumption of co-medications / alternative systems of medicine, follow steps in 'IDEAL' data collection defined by FDA and lastly, a complete objective assessment of the said reaction along with pharmacogenetic analysis, there are more likely chances that it will be subjected to misinterpretation. Hence, the present methods of collecting data on ADRs and extrapolation of results obtained from such studies to the entire population, on the incidence of ADRs may not lead to meaningful conclusions to abandon a medication. Therefore, there is strong need for collective efforts from consumers – to report, prescribers – to identify, manufacturers and regulatory authorities to be proactive, coupled with educational intervention at the 'grass root' level as one of the simplest, essential tools to amplify prevention or minimize ADRs.

In conclusion, looking at the present scenario, we seem to be spending more resources, man power and time than that would be actually necessary in treating the ADRs!

Thus there is a need to plan and introduce an appropriate system in place for data collection, analysis and execute an immediate action against the medications producing serious / fatal adverse reactions, failing such measures our studies will remain only as mere data bases with no therapeutic and practical implications to prevent or minimize the ADRs.

There is certainly a need to be 'vigilant' about Pharmacovigilance studies.

## REFERENCES

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