



Forensic Pharmacovigilance: An Overview

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ABSTRACT

The primary goal of forensic pharmacovigilance is to provide risk assessment, signal detection and collection of evidence the drug which are misuse/ abuse/ nonapproved. Pharmacovigilance offers its wide scope in forensic sciences by putting forward its expertise on adverse profile of drugs which may be instrumental in solving the cases and bringing the justice forth. Pharmacovigilance, as a medical discipline, is used in forensic cases in a variety of ways. The main themes are: could this drug (or chemical) have caused this harmful effect in this person (these people), and did it cause the effect either 'beyond all reasonable doubt? Distilling all the evidence available to the pharmacovigilance expert in a clear, unbiased way to help the court is a major challenge. After this, the other hurdle for the pharmacovigilance expert is often to offer comment on various aspects of professionals' behavior on what was the state of knowledge, when and how should that knowledge have been used in the prevention and management of harm.

Keywords: Pharmacovigilance, Forensic Science, Medico legal case, Signal management.

INTRODUCTION

Forensic science is the application of a broad spectrum of sciences to answer questions of medicolegal case (interest to a legal system which is related to crime).²

Medicolegal Case: A medico-legal case is one where besides the medical treatment; investigations by law enforcing agencies are essential to fix the responsibility regarding the present state/condition of the patient. The case therefore has both medical and legal implications.¹⁴

The main functions of Forensic department are

- Analyze evidence from the police
- Prepare reports describing their results
- Provide testimony in court

Pharmacovigilance also known as drug safety, the pharmacological science relating isto the *collection, detection, assessment, monitoring, and prevention* of pharmaceutical adverse effects with products²¹.

Forensic Pharmacovigilance is a branch of pharmacovigilance uses the expert knowledge of adverse drug effects related to illicit drugs and resolved legal questions or un cover criminal act¹⁵.

The example for the forensic pharmacovigilance is given as:

Cases of Contaminated Heparin in USA: As example of forensic pharmacovigilance is the discovery and investigation in to the adverse drug reactions caused by contaminated heparin in USA in 2008.

The raw material for the recalled heparin batches was processed in China from pig's intestines by the American Pharmaceutical firm Scientific Pacific Laboratory.

The U.S. Food and Drug Administration was quoted as stating that at least 81 deaths were believed to be linked to a raw heparin ingredient imported from the People's republic of China and that they had also received 785 reports of serious injuries associated with the drug's use^{8,20}.

Need of Forensic Pharmacovigilance

Law and medicine have in common that both disciplines are involved in making serious decisions with long term consequences on information that is heterogeneous and often incomplete. Evidence used in court ranges over several kinds of scientific discipline that underpin observations made by both experts and members of the public.

Pharmacovigilance, as a medical discipline, is used in forensic cases in a variety of ways. The main themes are:

Could this drug (or chemical) have caused this harmful effect in this person (these people), and did it cause the effect either 'beyond all reasonable doubt?'

The pharmacovigilance expert must help the Court understand the different sorts of scientific evidence available and alert the Court to the relative weight that such evidence commands. At the same time the pharmacovigilance expert must have regard to the evidential test that the Court will apply and be prepared to help the Court relate the evidence in the case (with its different probative weight) to the test that the Court applies. This is the point at which most scientists and



clinicians find themselves in difficulty -because the Court has to weigh evidence not in a vacuum but having regard not just to the evidence itself but also to the role it is fulfilling and the relative position of the litigating parties.

Distilling all the evidence available to the pharmacovigilance expert in a clear, unbiased way to help the court is a major challenge. After this, the other hurdle for the pharmacovigilance expert is often to offer comment on various aspects of professionals' behavior on what was the state of knowledge, when and how should that knowledge have been used in the prevention and management of harm⁶.

Ethics Involve in Forensic Pharmacovigilance

Epidemiology on Drug Facilitated crime in the different countries

Drug facilitated crime is a general term that includes robbery, money extortion, deliberate maltreatment of vulnerable people (children including Munchausen by proxy syndrome, the elderly, the disabled and mentally ill people), rape and sexual assault is a subset of DFC (drug facilitated crime).

Substances used in DFCs are usually odorless or test less, dissolve readily in beverages are fast acting, effective at low dose, have a short plasma half life, are potent central nervous system depressant, mimic severe alcohol intoxication or sedation.

The different countries Forensic department like Canada (Royal Canadian Mounted Police), Ireland (National Police Service of the Republic of Ireland), Germany (Munich Department of Forensic Medicine, Bonn Department of Forensic Medicine) and USA (US department of Justice) etc along with their health authority did survey on drug facilitated crime and drug facilitated sexual assault.

The case report (2000-2010) revealed that alcohol either alone or combination with other drugs was by far the commonest drug substance found in 67% of criminal.

Cannabis was the second most prevalent drug, present in 30.3 % criminal.

The remaining positive drugs finding were composed of benzodiazepines (4.8 %), cocaine (2.8 %), amphetamine (1.9 %), opiates (0.7 %) and propoxyphene (0.3 %) ^{4,15,22}.

Scope

In Illicit drug

Illicit drug use cases seek the expert opinion on drugs and their possible adverse events.

The illegal drugs use is on rise since few decades. The number of intentional and unintentional deaths from prescription drugs overdose is now greater than the deaths from heroin and cocaine combined.

A large part of the problem is the use of pain-killers without a prescription or misusing a prescribed drug to get "high." Improving the way prescription painkillers are

prescribed can reduce the number of people who misuse, abuse or over dose these drugs, while making sure patients have access to safe and effective treatment^{3,10}.

In 2011, legislation to create a Prescription Drug Monitoring Program was passed in Maryland to make comprehensive information on prescribed and dispensed Controlled Dangerous Substances available to doctors, pharmacists and other healthcare providers⁵.

Discrimination between Serious and Severe Reaction

There is a thin line of demarcation between serious and severe drug reactions which are misunderstood many a times. Court proceedings may be in a need to judge the gravity of problem in terms of seriousness and severity.

Severe reactions should never be confused with serious reactions. For instance, in any drug related injury in clinical trials compensation is granted to the victim for which judiciary needs to ascertain whether the injury was serious or not.

There is a criterion almost universally accepted for determining the seriousness of drug reaction. If the ADR (adverse drug reaction) falls in to the bracket of that criterion then it should be designated as serious event. A reaction is said to be serious if it 1) results in death, 2) is life threatening, 3) requires inpatient hospitalization or prolongation of existing hospitalization, 4) results in persistent or significant disability/incapacity, 5) results in congenital abnormality, and 6) is any other medically important condition.

Severity of the ADR's deals with the intensity of the reaction graded as mild, moderate, and severe. Severe is never synonymous with serious e.g. headache may be severe in grade but not of great medical significance for seriousness²¹.

Discrimination between Adverse drug reaction and Adverse Event

- There are several causality assessment scales i.e. Naranjos's scale, WHO causality assessment scale and Bayesian scale adopted by the pharmacovigilance experts to assign the level of correlation.
- This scale's use for determining the likelihood of whether an ADR (adverse drug reaction) is actually due to the drug rather than the result of other factors¹.

Medication Error and Medical Negligence

Pharmacovigilance department play a pivotal role to solve those cases which occur due to medical negligence or medication error. Here some examples of case related to medication error were given as:

Case 1

Sriniva Srinivasaragavan et al., reported a case report of medical negligence which is given as



A 49 year old patient was brought to the casualty and admitted in the ward at 10:50 PM with alleged history of road traffic accident. Clinically there was no evidence of pelvic, long bone and spinal bone injury as per the medical record. Neurosurgeon opinion obtained and suggested CT Brain. Since the patient became hemodynamically unstable with progressive fall in BP (80/60) and tachycardia (120/min), he had not been shifted for the CT brain investigation. Dopamine drip and IV fluids started. Later around 11:50 PM, Patient developed sudden cardio respiratory arrest and was revived. He was put on mechanical ventilator support. Patient developed second episode of cardio respiratory arrest. Death was declared. The clinical cause of death was "Severe head injury as a result of road traffic accident."

Since it was a medico-legal case, the body was sent for autopsy to find out the actual cause of death. Autopsy was conducted on the body of the deceased on 21/4/2011 morning. The autopsy report revealed that the death was caused by cardio respiratory arrest¹⁸.

Case 2

WHO reported many cases occur due to medical negligence or medication error. One example of the case is given as:

A 10-year-old leukemia patient in Britain who had to be given a chemotherapy injection. The boy died due to a wrong injection being given to him. The boy ate food that was prohibited before the procedure; he was hence taken hours later by a different department than the cancer doctors. "The injections were given in a particular order but that day due to the mix-up he got the wrong injection and died five days later." The committee exonerated the doctor because it found the other factors -the when, where and how -had all played a role in the boy's death⁹.

Signal Detection of Prohibited Products

Illicit drug use cases seek the expert opinion on drugs and their possible adverse events. The illegal drugs use is on rise since few decades. The number of intentional and unintentional deaths from prescription drugs overdose is now greater than the deaths from heroin and cocaine combined. A large part of the problem is the use of pain-killers without a prescription, or misusing a prescribed drug to get "high." Improving the way prescription painkillers are prescribed can reduce the number of people who misuse, abuse or overdose these drugs, while making sure patients have access to safe and effective treatment. In 2011, legislation to create a Prescription Drug Monitoring Program was passed in Maryland to make comprehensive information on prescribed and dispensed Controlled Dangerous Substances available to doctors, pharmacists and other healthcare providers^{3,11}.

Signal detection of controlled substance like narcotic product and ergogenic or performance enhancing agent include anabolic steroids, narcotic analgesics,

diuretics, beta blockers, growth hormone, oral peptide hormones, amphetamines, caffeine, cocaine, sympathomimetic agents, and erythropoietin done by pharmacovigilance with the help of federally sponsored data sources of quantitative (community level) information include report from the National Institute on Drug Abuse (NIDA), Community Epidemiology Working Group (CEWG), the Drug Enforcement Administration (DEA), National Drug Intelligence Center (NDIC) and the National Institute of Justice (NIJ)¹⁰.

Challenges of pharmacovigilance

Though pharmacovigilance is set to offer its application in forensic sciences but there are few challenges before the pharmacovigilance to be met. Increased globalization of drugs, exponential rise in volume of drugs used and polypharmacy are few elements which make the pharmacovigilance a complex discipline. Under the light of these challenges, pharmacovigilance now should be understood beyond merely reporting the harms; rather it should be a rigorous risk benefit assessment. Few standards of quality in pharmacovigilance have been set and good pharmacovigilance practices (GVP) is a citable example of that. It is imperative to adhere to such standards while implementing pharmacovigilance in forensic areas.

CONCLUSION

In the light of increasing medicolegal cases, there is a substantial need of contribution of drug expertise in solving the criminal and civil cases involving the drugs at one or other stages. Pharmacovigilance can cater to the needs of legal framework to mine the cases involving the drugs by differentiating the serious and non serious reactions, establishing the causal relationship between drug and adverse event. Proliferating role of pharmacovigilance has now sprawled over the arena of legal medicine giving birth to newer branch of science known as forensic pharmacovigilance which offers a wide range of its scope and application and warrants a cautious execution of this exercise else it may deviate from the intended use.

REFERENCES

1. Agbabiaka T.B., Savovic J., Ernst E. Methods for causality assessment of adverse drug reactions a systematic review. *Drug Saf*, 31(1), 2008, 21e37.
2. Ballantyne KN, Edmond G, Found B., Peer review in Forensic science. *Forensic Science Int.*, 277, 2017, 66-76.
3. Dasgupta N., Schnoll Sidney H., Signal detection in post-marketing surveillance for controlled substances. *Drug and Alcohol Dependence*, 105S, 2009, S33–S41.
4. Djezzar S., Richard N., Deveaux M., Epidemiology of Drug-Facilitated Crimes and Drug-Facilitated Sexual Assaults. *Toxicological Aspects of Drug-Facilitated Crimes*. 2014, 0-12-416748-3.
5. Drug induced deaths. Maryland: Department of Mental Health and Hygiene (2012).



6. Edwards IR. and Body D., Forensic Pharmacovigilance, International Journal of Risk & Safety in Medicine., 24, 2012, 1-2.
7. Edwards IR., Considerations on causality in pharmacovigilance. Int J Risk Saf., 2012, 2441e54.
8. <https://www.heparinscience.com/contamination>
9. Iyer M., Medical errors in top 10 killers: WHO., The Times Of India Delhi, 2011, pp 1
10. Jerry L., Forensic pharmacovigilance and substandard or counterfeit drugs. International Journal of Risk & Safety in Medicine., vol. 24, no. 1, 2012, pp. 37-39.
11. Jonsson A.K., Soderberg C., Espnes K.A., Ahlner J., Eriksson A., Reis M., Druid H., Sedative and hypnotic drugs- Fatal and non-fatal reference blood concentrations. Forensic Science International, 236, 2014, 138–145.
12. Malve HO.,Forensic pharmacology: An important and evolving subspecialty needs recognition in India. J Pharm Bioallied Sci, 8(2), 2016, 92-7.
13. Medhi B., Singh P.K., Bansal Y.S, Setia P. Forensic pharmacokinetics: a new dimension for drug related medico legal cases. J Forensic Res, 2, 2011, 128.
14. Medical Guidelines for Patient Care, Medico legal Cases- What, When and How, Medical Division, BARC (2009).
15. Persauda N. and Healy D., Epidemiological evidence in forensic pharmacovigilance. International Journal of Risk & Safety in Medicine, 24, 2012, 31–35.
16. Rouve Nadege, Bagheri Haleh, Telmon Norbert, Pathak Atul, Franchitto Nicolas, Schmitt Laurent, Rouge Daniel, Lapeyre-Mestre Maryse, Montastruc Jean-Louis, Prescribed drugs and violence: case/noncase study in the French Pharmacovigilance Database., Eur J Clin Pharmacol, 67, 2011, 1189–1198.
17. Sewal Rakesh K., Saini Vikas K., Medhi B. Forensic pharmacovigilance: Newer dimension of pharmacovigilance. Journal of Forensic and Legal Medicine, 34, 2015, 113e.
18. Srinivasa ragavan N., Kadhiraazhagan, Thunder chief K., Magendran J., Death due to Medical Negligence: A Case Report. J Indian Acad Forensic Med., 35 (3), 2013, 288-289.
19. Steven B. Karch MD., Peer review and the process of publishing of adverse drug event reports. Journal of Forensic and Legal Medicine, 14, 2007, 79-84.
20. Tremblay J.F., Making heparin safe: Although manufacturing fraud remains possible, Chinese firms have upgraded their processes to meet stricter U.S. regulations, American Chemical Society, 94 (40), 2016, 30-34
21. World Health Organization, Collaborating Centre for International Drug Monitoring. The importance of pharmacovigilance safety monitoring of medicinal products. Geneva: World Health Organization (2002).
22. Yadav PK., Ethical issues across different fields of forensic science. Egypt J Forensic Sci., 7 (1), 2017.

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