Journal of Pharmacovigilance & Drugs Safety

An Official Publication of Society of Pharmacovigilance, India.

Review Article

Environmental Pharmacovigilance (EPV): An emerging branch of Science- A review.

Vyas K[1], Sharma V[2]

[1] Research Officer (Ayu), RARIND, CCRAS, Jaral Pandoh, District Mandi, H.P.
[2] HOD of QA, Torque Pharma, Baddi, District Mandi, H.P.

ABSTRACT

Introduction: *Environmental Pharmacovigilance (EPV) is a developing branch of science relating to the detection, assessment, understanding and prevention of Adverse Environmental Impacts (AEI) of Pharmaceutical products. It identifies risk levels of pharmaceutical residues mainly in water & soil for Environmental Risk Assessment (ERA) and its effective management. These spotting activities are necessary not only after launch of a new pharmaceutical product but also through its whole Life cycle.*

Aims & Objectives: *The branch is aimed to find out significant environmental issues related to Pharmaceuticals in Environment (PIE).*

Review & Discussion: *The main components of Environmental Pharmacovigilance (EPV) are- Environment, Pharmaceutical Product, Product user (Human/ animal)/ dealer and Victims of the risks developed. The victims may be non-targeted human population, wild life species or aquatic inhabitants etc. The documentation of this vigilance search is completely limited as it is quite difficult to differentiate the relative impact of pharmaceuticals and other Environmental stimuli. Moreover, management plans require deep knowledge of Physico-chemistry, pharmacokinetics, toxicology and other sciences, which make it very specific. Though Environmental Risk Assessment is already included in regulatory approval process for new drugs, its implementation is poor in Developing countries.*

Conclusion: *there is great need to focus on this branch of vigilance in order to save the world from fatal hazards.*

Key words*: Environmental Risk Assessment, Pharmaceuticals, Adverse Environmental Impact, Regulatory approval process.*

Corresponding Author

Vyas K
Research Officer (Ayu), RARIND, CCRAS, Jaral Pandoh, District Mandi, H.P.

INTRODUCTION

Pharmacovigilance (PV) is aimed to detect, assess, understand and prevent adverse drug effects or any other drug-related problem.[1] It was arisen after very serious medical disasters like Thalidomide disaster[2] and Eltroxin Case[1]. There are a number of branches of this science including Environmental Pharmacovigilance (EPV) or Ecopharmacovigilance, which is still in developing stage.

RESULTS

Introduction and History

Environment is very much vulnerable to various bi-products and metabolites of pharmaceutical products. When large amount of pharmaceutical residues are released in water or soil, after launch of a new Pharmaceutical product or during any point of its whole life cycle, it puts entire living society at potential risks of toxicity, serious health hazards and even death. Such phenomenon may cause great damage to the ecosystem, wildlife and biofilms, too[3]. Though there are rules & regulations for Environmental safety in good manufacturing practices and disposal, but their monitoring is very poor, especially in lower middle income countries. Hence, it is very crucial to trace out the signals of unsafe quantity of pharmaceutical products in environment and take steps to prevent or minimize the hazards. Environmental Pharmacovigilance (EPV) or Ecopharmacovigilance does the same work[4] and also propagates green Health care. EPV identifies the Pharmaceuticals in Environment (PIE) for ultimate Environmental Risk assessment (ERA)[3]; risks like acute and chronic toxicity, carcinogenicity, interference with hormone and immune systems and drug resistance.[1] Initial evidences of Ecotoxicity were not only surprising but distressing, too. The major examples are as follows:

1. After frequent prescription of Diclofenac Sodium by veterinary doctors, it started to be found in the carcasses of cattle on which vultures feed. Hence, vultures suffered from visceral gout and renal failure. As a result, extreme decline in vulture population was found in Asia, leading to epidemics because of decaying carcasses. Again due to same phenomenon, the number of feral dogs which led to disease threats such as rabies.[4,5]
2. Residues of pharmaceutical products also affect aquatic organisms. Finding of intersex fish in European river without any identifiable specific causes was a major example of it.[4]

3. One laboratory study suggested that antidepressants like fluoxetine could trigger spawning in some shellfish, thereby disturbing the ecological balance.[5]

These examples indicate that understanding the causes of Environmental disasters and developing Environmental Risk Management Plans (ERMPs).

Environmental entry of Pharmaceutical Products

Pharmaceutical products and their metabolites get entered into environment through various means. Some accesses are visible & clear while some may not be observed through naked eyes. The entrances may be[4]-

1. Direct release of product/ metabolites into waste water system by Product makers and Hospitals
2. Improper disposal of unused drugs
3. Excretion of the user (human or veterinary) of drug in to sewage system, either as a parent compound or a metabolite
4. Terrestrial depositions, e.g. sludge application to land, leaching from solid waste landfills, or irrigation with treated or untreated wastewaters

Among all these routes, the excretion of human or animals after therapeutic use is the most affecting one. Again, locally elevated drug concentrations can be found near manufacturing or disposal site and surrounding the release area.

Environmental Risk Assessment (ERA) method and its utility

In many countries, low levels of medicines have been detected in sewage treatment plant (STP) effluents, surface water, sea water, ground water and drinking water.[5] Some data has been collected regarding acute toxic effects of these residues, but subtle chronic hazards are difficult to assess swiftly. Hence, a method is developed by European Union (EU) to assess the environmental risk through generation of risk quotient[4].

ERA = PEC: PNEC

(ERA= Environmental Risk Assessment, PEC= Predicted Environmental Concentration, PNEC= Predicted Non-effect Concentration)

Such assessment is not only helpful in identifying the signals of excessive drug residue in water and soil, but also proves to be a helping hand in diagnosing as well as treating multi-organ symptomatology for clinicians. As per a case report[6], a 13-year-old Hispanic female was treated for multiple complaints since age 9. She was treated in a large metropolitan integrated health system by her pediatrician, a cardiologist, a neurologist, and a gastroenterologist and multiple emergency department visits. All her investigations and scans showed no oddity. At last, it was confirmed that all her complaints & symptoms were due to fumes of an oil making company that was only 30 feet away from her residence.

Again, many house care and routinely used products may also increase the ERA by their heavy metallic and toxic contents. One study, carried out in Nigeria revealed that various detergents, whether liquid or powdered, have unsafe concentrations of Nickel (Ni), lead (Pd) Chromium (Cr) and cadmium (Cd) using Atomic Adsorption Spectrophotometer. Hence, people using the detergents regularly are at risk of developing certain diseases.[7]

Risk assessment for Water and Aquatic organisms

The corrective measures developed to treat water and soil play significant role in preventing the related hazards. But results of water pre-treatment for Potabilization may vary depending on the type of water and some other factors. A study carried out to measure variability of the parameters for safe drinking water in Mexico, showed that turbidity was under statistical control in all 45 samples collected but residual Chlorine & pH were not found in range of Potabilization control. This study points out that the process is affected by water quality, which is variable. This is especially true in the rainy season where there is more turbidity due to the dragging of sediments towards the supply source, in addition to the existence of a relationship between the increase in turbidity of raw water and disinfectant dosage.[8]

Various bio-monitoring studies have been carried out regarding application of metabolomics as an innovative tool for ERA. These demonstrate the effectiveness and high sensitiveness of the environmental metabolomics in elucidating disturbances in a variety of metabolic pathways in aquatic organisms, both fish and invertebrates, from sites with different level of environmental contamination and thus its suitability to be applied in studies of aquatic pollution and toxicology.[9]

Mercury (Hg), a well-established neurotoxin, has more recently been studied as an immune-toxin linked with biomarkers of autoimmunity, including the presence of antinuclear antibodies (ANA) and distinct cytokine profiles. A few studies have specifically examined the relationships among mercury, fish consumption, and autoimmune biomarkers in human populations. The findings of these studies are conflicting; this may be due to confounding exposures and opposing mechanisms of action. Additional studies are necessary to clarify the role of Hg through seafood consumption in autoimmunity.[10]

CONCLUSION

Pharmaceutical residues may extend themselves as major Environmental pollutants. The term Environmental / Eco Pharmacovigilance (EPV) is used with respect to the unforeseen consequences of the active residues or metabolites of a drug may cause once they enter the environment. Hence, EPV assesses Environmental risks through calculating Risk quotient and prepares Environmental Risk Management Plans (ERMPs) for safety of humans, animals, birds and aquatic organisms. Some acute toxic effects of product residues are well known and easily assessable, but still there is great need of developing techniques and strategies to understand & prevent chronic toxic effects and extinction of herbal as well as animal species.

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