e-ISSN: 2322-0139
p-ISSN: 2322-0120

RESEARCH AND REVIEWS: JOURNAL OF PHARMACOLOGY AND TOXICOLOGICAL STUDIES

Drug Induced Liver Injury

Usha Sangana*

Aditya Institute of Pharmaceutical sciences and research, Surampalem, Andhra Pradesh, India.

Commentary

Received: 23/05/2015

Accepted: 28/05/2015

Published:06/06/2015

***For Correspondence**

Aditya Institute of Pharmaceutical sciences and research, Surampalem, Andhra Pradesh, India.

Keywords: Hepatotoxicity, Drug induced liver injury, Adverse reaction

INTRODUCTION

Liver is a most important organ of our body which plays a vital role in several body functions from protein production and blood clotting to cholesterol, glucose and iron metabolism [1]. Liver failure is nothing but the inability of the liver to perform its normal and metabolic functions as a part of physiology. Liver injury is also called as Hepatotoxicity.

Two types of liver injury acute and chronic [2]
Acute Liver injury: Acute liver failure is most uncommon in which damage liver function results coagulopathy. Acute liver failure mostly affects youngster and carries a very high mortality [3].

Diagnosis: physical examination, Examination of liver tissue, Imaging tests, Blood tests, measurement of prothrombin time (PT)

Symptoms [4]:

- Weakness and fatigue
- Encephalopathy
- Ascites
- Abdominal swelling
- Nausea
- Vomiting
- A general sense of feeling unwell (malaise)

e-ISSN: 2322-0139
p-ISSN: 2322-0120

- Disorientation or confusion [5]
- Sleepiness
- Yellow discoloration of the skin (jaundice)

Chronic liver disease: It is a gradual and regeneration of the liver tissue leading to fibrosis and cirrhosis [6].

Diagnosis: It was diagnosed by many laboratory tests which include Liver function tests, Liver biopsy, Cholangiography, CT scan, and Ultrasound [7-9]

Symptoms:

- Abnormal nerve function
- Ascites (fluid buildup in the abdominal cavity)
- Breast enlargement in men
- Vomiting blood
- Curling of fingers (Dupuytren's contracture of the palms)
- Jaundice (yellowing of the skin and eyes)
- Kidney failure
- Liver encephalopathy
- Muscle loss
- Poor appetite

Drug induced Liver injury (DILI)

Drug-induced liver injury (DILI) may be a major reason behind Liver failure, and is also the foremost common reason behind failure of medicine throughout each preclinical or clinical development [10]. Good type of medicine may end up in liver injury, as well as antibiotics, system medicine and non-steroidal medicine. Most commonly drug induced liver injury is classified into predictable and unpredictable. In predictable it is a dose related and occurs with short latency where as unpredictable is with low incidence and may or may not be dose related.

Many of the drugs cause liver injury infrequently. These reactions are considered idiosyncratic. Idiosyncratic reactions are characterized within 5 to 90 days from intake of drug, and sometime causes drug if it is continued once the reaction has stated [11-15]. In contrast, with some of drugs like such as isoniazid, mild injury may disappear despite continued use.

Adverse events caused by medicine are often thought-about to be either certain (high incidence) or unpredictable (low incidence). Some drugs commonly causes certain liver injury, like like paracetamol, non-steroidal anti-inflammatory drugs, statins,isoniazids, antimicrobials etc. Sometimes they directly results in liver toxicity of the parent drug or its metabolites [16]. Unpredictable events manifest as bald or symptomatic malady and might occur with intermediate (1–8 weeks) or long (1 year) periods of latency.

Two classes of Drug-induced liver injury are designated: intrinsic and individual. Tylenol (APAP) drug may be a well-studied example of intrinsic hepatotoxicity, which ends up from metabolism of APAP to the electrophilic N-acetylp- benzoquinoneimine which might covalently bind to cellular proteins. Individual DILI is determined in barely a tiny low proportion of treated patients, however overall, accounts for over 100% of all cases of acute liver failure [17-20]. The manifestation of DILI is kind of heterogeneous, and includes a clinical spectrum from a rise in liver enzymes to acute liver failure. As a result of this, DILI may betroublesome to diagnose, and there's a scarcity of ordinary diagnostic tests and biomarkers [21-24]. With so many drugs rechallange can be typically met irrespectively whether the reaction was mild or severe.

Drug-induced liver injury may end up within the termination of compounds in presymptomatic development, similarly as withdrawal of marketed medication. Identification of the sign pathways and proteins concerned in injury is a crucial step towards establishing assays that might be used to spot potential hepatotoxicants early within the drug discovery method [25-27]. During this study we tend to used high turnout quantitative mass qualitative analysis genetic science involving Stable atom Labeling with Amino acids in Cell culture (SILAC) leveraged by a recently developed systems biology approach (Causal Reasoning Engine, CRE) to analyze the results of toxic compounds on the cellular protein of HepG2 cells [28]. Cells were treated with numerous concentrations of nefazadone, nimesulide, nomifensine, or glafenine, all of that cause hepatotoxicity in humans [29-34]. Deciding whether or not the disease was caused by a drug needs the exclusion of alternative plausible causes and therefore explores for a clinical drug signature. The drug signature consists of the pattern of liver check abnormality, the length of latency to symptomatic presentation, the presence or absence of immune-mediated hypersensitivity and therefore the response to ending [35,36].

The Causative agents for drug induced liver injury in kids and in adults vary, and that they dissent supported the indication that the medications are prescribed. Age could confer a condition which is susceptible to drug induced liver injury during a drug-specific manner. An example, medicine that acts on the central system and antimicrobials are the common causes of drug induced liver injury in kids. Infants and kids seem at risk of liver injury caused by valproate associate degreed are at an increased risk of Reye's syndrome caused by salicylate [37].

Some drugs completely or preponderantly induce Cholestasis. Many of those, such assulindac and chlorpromazine, are related to hypersensitivity-type reactions. The precise immunologic targets of those hypersensitivity-type adverse reactions are poorly understood. However, as long as the predominant microscopic anatomy options are portal inflammation and biliary injury, they're possible to be associated with the bile duct. It's potential that deadly metabolites endureing duct excretion reacts with macromolecules within the duct cells or undergo any metabolism at intervals these cells, leading to ductal injury [38]. Drug-induced immune-mediated injury, therefore, is associate adverse immunologic response against the liver and/or epithelial duct that ends up in a sickness with clinical options that are viscus, cholestatic, or a combination, the mechanisms of that aren't clearly understood. Some pathological symptoms are the reactions that are similar to the symptoms of acute hepatitis. The latency period can be short, medium or long.

Few drugs presently in clinical use are related to inevitable dose-related liver toxicity; example is Tylenol. Most instances of drug-induced disease are not predictable, and symptoms can occur either with medium or long periods of latency before on set [39-40]. Low-frequency, unpredictable reactions, either immune-mediated hypersensitivity or individual, typically occur on a background of the next incidence of gentle, symptomless, and frequently transient liver injury.

Prevention

Avoiding the intake of drugs, that is more than recommended dose of over the counter drugs. Prevention of drug hepatotoxicity before the drug entering into the market which includes increased vigilance during pre-clinical drug development and clinical trials [41].

Acknowledgement

I would like to acknowledge the support of my colleagues Rakesh M, Sateesh V in assisting with proper guidance. This content is reviewed and approved by Murali M.

References:

1. http://en.wikipedia.org/wiki/Liver_injury
2. http://emedicine.medscape.com/article/177354-overview
3. http://www.mayoclinic.org/diseases-conditions/liver-failure/basics/definition/con-20030966
4. Naseemuddin R and Singal AK. Liver Transplantation for Alcoholic Hepatitis: Light at the End of Tunnel. J Liver. 2015; 4: e110.
5. Ibrahim AA, et al. Dietary Patterns in Egyptian Patients with Chronic Hepatitis C Related Liver Disease: A Cross-Sectional Study. J Liver. 2015; 4:176.
6. Sato M, et al. Smad3 Deficiency Counteracts Hepatocyte Apoptosis and Portal Fibrogenesis Induced By Bile Duct Ligation. J Liver. 2014; 3: 145.
7. Yang X. Use Circulating microRNAs as Biomarkers of Drug- Induced Liver Injury. J Vaccines Vaccin 2012; 3: e105.
8. Salminen WF, et al. Using microRNA as Biomarkers of Drug-Induced Liver Injury. J Mol Biomark Diagn. 2011; 2: 119.
9. Friedman RC, et al. Most mammalian mRNAs are conserved targets of microRNAs. Genome Res. 2009; 19: 92-105.
10. Wang K, et al. Circulating microRNAs, potential biomarkers for drug-induced liver injury. Proc Natl Acad Sci USA; 2009; 106: 4402 - 4407.
11. Chitturi S and George J. Hepatotoxicity of commonly used drugs: nonsteroidal anti-inflammatory drugs, antihypertensives, antidiabetic agents, anticonvulsants, lipid-lowering agents, psychotropic drugs. Semin Liver Dis. 2002; 22: 169-183.
12. Russmann S, et al. Current concepts of mechanisms in drug-induced hepatotoxicity. Curr Med Chem. 2009; 16: 3041-3053.
13. McGill MR and Jaeschke H. Metabolism and disposition of acetaminophen: recent advances in relation to hepatotoxicity and diagnosis. Pharm Res. 2013; 30: 2174-2187.

14. Hussaini SH and Farrington EA. Idiosyncratic drug-induced liver injury: an update on the 2007 overview. Expert Opin Drug Saf. 2014; 13: 67-81.
15. Adejo GO, et al. Anti-Peroxidative, Protective and Ameliorative Properties of Methanol Extract of All Parts of Morinda Lucida Benth in CCl_4-Induced Liver Injury. Nat Prod Chem Res. 2014; S1:003.
16. Enayetallah A, et al. Assessing Hepatoxicants based on High-throughput Quantitative SILAC Proteomics and Causal Biological Networks. J Proteomics Bioinform. 2015; 8:049-059.
17. Kloosterman WP and Plasterk RH. The diverse functions of microRNAs in animal development and disease. Dev Cell. 2006; 11: 441-450.
18. Davis BN and Hata A. microRNA in Cancer---The involvement of aberrant microRNA biogenesis regulatory pathways. Genes Cancer; 2012; 1: 1100-1114.
19. Mitchell PS, et al. Circulating microRNAs as stable blood-based markers for cancer detection. Proc Natl Acad Sci U S A. 2008; 105: 10513-10518.
20. Baraniskin A, et al. Identification of microRNAs in the cerebrospinal fluid as marker for primary diffuse large B-cell lymphoma of the central nervous system. Blood.2011; 117: 3140- 3146.
21. Wei J, Xie L, et al. Epigenetic alterations of tumor marker microRNAs: towards new cancer therapies. Drug News Perspect. 2010; 23: 655-661.
22. Hayback J, et al. The parallel universe: microRNAs and their role in chronic hepatitis, liver tissue damage and hepatocarcinogenesis. Swiss Med Wkly. 2011; 141: w13287.
23. Chen T, et al. MicroRNA expression profiles distinguish the carcinogenic effects of riddelliine in rat liver. Mutagenesis. 2011.
24. Barry CT, et al. Micro RNA Expression Profiles as Adjunctive Data to Assess the Risk of Hepatocellular Carcinoma Recurrence After Liver Transplantation. Am J Transplant. 2011.
25. Taylor DD and Gercel-Taylor C. MicroRNA signatures of tumor-derived exosomes as diagnostic biomarkers of ovarian cancer. Gynecol Oncol 2008; 110: 13-21.
26. Reid G, et al. Circulating microRNAs: Association with disease and potential use as biomarkers. Crit Rev Oncol Hematol. 2011; 80: 193-208.
27. Dwivedi V, et al. Efficacy Study of Livartho against Paracetamol Induced Hepatotoxicity in Adult Sprague Dawley Rats. J Drug Metab Toxicol. 2015; 5: 175.
28. Al-Amoudi W. Ameliorative Role and Antioxidant Effect of Propolis against Hepatotoxicity of Fenvalerate in Albino Rats. J Cytol Histol. 2015; 6: 303.
29. Mathieu Vinken's Work on the Role of Connexin-related in Hepatic Homeostasis and its Relevance for Liver-based In vitro Modelling. Pharm Anal Acta. 2011; 2:101e.
30. Periasamy J, et al. Nimesulide and Celecoxib Inhibits Multiple Oncogenic Pathways in Gastric Cancer Cells. J Cancer Sci Ther. 2013; 5:126-136.
31. Essawy AE, et al. Hepatotoxicity Induced by Antifungal Drug Fluconazole in the Toads (Bufo Regularis). J Drug Metab Toxicol. 2010; 1: 106.
32. El Mesbahi O and El M'rabet FZ. Reversible Hepatic Cytolysis Secondary to Sunitinib in Metastatic Renal Carcinoma. J Cancer Sci Ther. 2011; 3: 047-049.
33. Gomez AMG, et al. Clinical Functioning in a Cohort of Patients with Severe Mental Disorder, before and after Joining a Workplace Reintegration Program. Brain Disord Ther.2015; 4:159.

34. Trad MA. Perspectives on Delivering Healthcare in the Nuba Mountains-Sudan: A Personal Experience. J Anc Dis Prev Rem. 20154; 3: 120.
35. Macpherson D, et al. The Biotransformation and Pharmacokinetics of 14C-Nimesulide in Humans Following a Single Dose Oral Administration. J Drug Metab Toxicol. 2013; 4:140.
36. Altamimi A, et al. Successful Outcome Following a Loading Dose of NAcetylcysteine to Treat Hepatotoxicity after Repeated Therapeutic Doses of Paracetamol. J Clin Toxicol. 2015; 5: 245.
37. Abdel Ghany SM, et al. Emerging Prognostic Biomarkers in Non Small Cell Lung Cancer Patients: Impact of Treatment with Nimesulide (COX-2 Inhibitor) Combined with Chemotherapy. J Pulmonar Respirat Med S2011; 5: 003.
38. Hashem HE. Light and Electron Microscopic Study of the Possible Protective Effect of Nigella Sativa on Metalaxyl Induced Hepatotoxicity in Adult Albino Rats. J Cell Sci Ther. 2012; 3:118.
39. Arroyo VS, et al. Liver and Cadmium Toxicity. J Drug Metabol Toxicol S. 2012; 5: 001.
40. Waer HF, et al. Ameliorated Effects of Verapamil on Hepatotoxicity Induced by Ethanol and Carbon Tetrachloride. J Cytol Histol. 2012; 3:142.
41. Laarman ARC, et al. Pain Treatment of Newborns: Paracetamol Rectal Versus Intravenous Administration, A Randomised Open Clinical Trial. J Neonatal Biol. 2015; 4: 172.