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THE ANTAGONIST-TUBERCULOSIS DRUG WHICH INDUCES HEPATOTOXICITY IN A GERIATRIC PATIENT IN TERTIARY CARE HOSPITAL: A CASE REPORT

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ABSTRACT

Combination therapy is crucial for the short-term course of contrary-Tuberculosis treatment, It affirms the development the imperilling of Anti-TB drug-induced liver damage, Hepatocellular injury represented by a gradual increase in the aminotransferases in serum which precede elevations in total bilirubin levels and alkaline phosphatase levels. A 75yrs male subject to a tertiary care hospital with complaints of diminished appetite and generalized weakness for two days. History of type two diabetes mellitus for five years on insulin therapy and right pyopneumothorax with bronchopleural fistula, extensive pleural effusions, pulmonary Koch on Contrary-Tubercular Therapy (ATT) for one month. I formed a provisional conclusion as a contrary-tubercular drug (levofloxacin) induced hepatitis. Doctors should remain mindful that levofloxacin can cause hepatotoxicity in subtle incidents. it would be for physicians to remain conscious of the risk of levofloxacin-induced hepatotoxicity.

KEYWORDS: Anti-tuberculosis drugs, levofloxacin-induced hepatotoxicity.

BACKGROUND

The estimate of Drug-induced liver damage (DILD) correlated with contrary -TB treatment differed from 5% to 33% in early investigations, most first-line drugs to care for tuberculosis (TB), including isoniazid, rifampin, and pyrazinamide, are hepatotoxicity.[1] Although combination therapy is crucial for the short-term course of contrary-Tuberculosis treatment, It affirms the development the imperilling of Anti-TB drug-induced liver damage[1-3] the liver's function affects every separate organ system in the body, but there are no definite diagnostic investigations for Drug-induced liver disorder or a mechanism to individual out an accused drug. Therefore, it is noteworthy to recognize the varieties of Drug-related pathology to determine adverse reactions when they take place.

It is further essential to understand how and when to observe these reactions. Hepatocellular injury represented by a gradual increase in the aminotransferases in serum which precede elevations in total bilirubin levels and alkaline phosphatase levels.[4] Fluoroquinolones are not proposing as first-line therapy and maintain for therapy of DR-TB or as a replacement medicine for patients intolerant to first-line drugs.[5] The risk aspects of suffering include age, gender, irregular baseline transaminase levels, starvation and infection with HIV, hepatitis B infection or hepatitis C infection.[6-12] TB is one of the lead ten roots of death worldwide, TB caused about 1.3million deaths and 10.0million people gained the condition in 2017, According to global tuberculosis report 2018, India accounted 27% of world TB cases in 2017.[13]

CASE REPORT

A 75yrs male subject to a tertiary care hospital with complaints of diminished appetite and generalized weakness for two days. History of type two diabetes mellitus for five years on insulin therapy and right pyopneumothorax with bronchopleural fistula, extensive pleural effusions, pulmonary Koch on Contrary-Tubercular Therapy (ATT) for one month. I formed a provisional conclusion as a contrary-tubercular drug (levofloxacin) induced hepatitis. So, they stopped ATT. They performed liver function tests the investigation results are: Serum albumin-2.47g/dl, Serum globulin-3.57g/dl, Albumin/Globulin ratio-0.69, Serum direct bilirubin-1.29mg/dl, SGPT/ALT -97.82 u/l, Serum protein–6.04, The prescribed medicines have been mentioned, Those are Injection Streptomycin 750mg Intramuscular route once in a day, Injection levofloxacin 500mg, Intravenous route once in a day, Capsule Ethambutol 800mg Per-oral route Once in a day, Capsule Rifampicin 450 mg peroral route Once in a day, Injection pantoprazole intravenous route 40mg once in a day, Injection ondansetron 4mg intravenous route Tablet Ursodeoxycholic Acid 300mg twice in a day.

DISCUSSION

Anti-TB agents induced hepatotoxicity is a major complication, and it published that 2-28% of TB patients experienced drug-related hepatotoxicity during the

therapy.[14] Fluoroquinolones (levofloxacin) activity is inhibition of bacterial DNA gyrase, later to DNA strand breakage and resulting genomic damage, we have shown fluoroquinolones antibiotics to damage and deplete mitochondrial DNA (mtDNA) in natural cells.[15] Mechanism of levofloxacin-induced hepatotoxicity remains undiscovered, hepatic mitochondrial impairment in our subject because he becomes a geriatric patient[16], age factor also one of the causative agents in hepatic damage. A considerable ratio of adverse drug reactions in older individuals are dose-related, and it associates the rise of ageing with reduced drug clearance.[17] If do not support that older age is a general risk consideration.

In Spanish DILI registry, 46% of DILI patients were >60years old at the time of the episode and the US DILIN reported 16.6% of their subjects with DILI to be 65years or older.[18-19] It raises the DILI incidence rate with age, 15-29-year-olds had an incidence with increased age, whereby 15-19-year-olds had a prevalence estimate of 1 per 100,000 that raised to 41 per 100,000 for patients >70years old.[20]

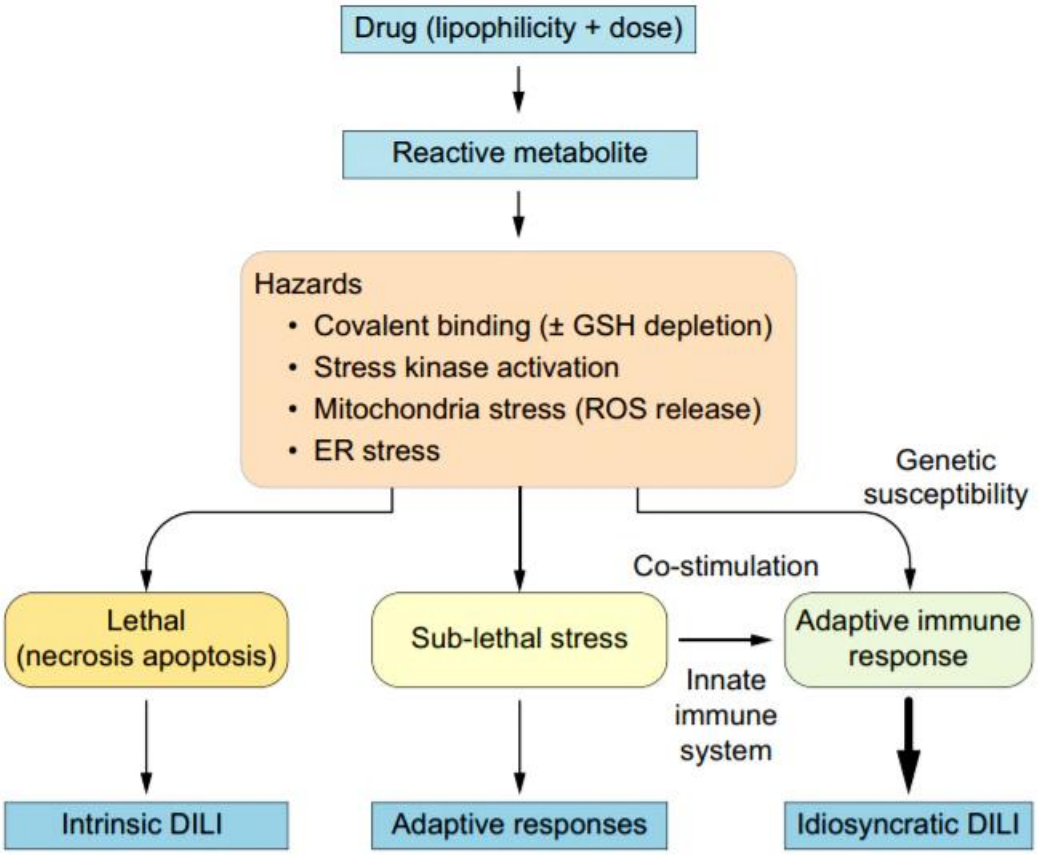

Fig. 1. Mechanistic relationship between intrinsic and idiosyncratic DILI. A common prerequisite for intrinsic toxicity and idiosyncratic DILI is the metabolism of lipophilic drugs in the liver, generating reactive metabolites which lead to initial consequences, such as covalent binding, oxidative stress, stress kinase signalling and organelle stress responses (mitochondria and ER) which either overwhelm defences and lead directly to necrosis or apoptosis or elicit an adaptive immune response to drug-adducts (haptens) in genetically susceptible individuals. DILI, drug-induced liver injury; ER, endoplasmic reticulum; GSH, glutathione; ROS, reactive oxygen species.

*European Association for the Study of the Liver clinical practice guidelines: Drug-induced liver injury Journal of Hepatology 2019 volume. 70 1222–1261.

The achiever of age on DILI incidence also parallel by the increase in drug usage, proposing that elder age patients have more prescriptions, we emphasize this point on the notices we consider the few essential

parameters while prescribing the medicines which includes BMI, IBW, Dosage form of the drug, Dose of the medicine, Co-morbidities of the subject condition.

CONCLUSION

Doctors should remain mindful that levofloxacin can cause hepatotoxicity in subtle incidents. Patients with previous liver damage might be unsafe, and levofloxacin may not be the clearest anti-microbial to suggest in unapt cases. Although rare, present proposals for levofloxacin mandate treatment stop if a subject develops symptoms and manifestations of hepatitis. Anti-TB drug-induced liver injury produces an opportunity for the investigation that will have a significant impact on large areas such as Drug discovery development process, primary and secondary care, it would be for physicians to remain conscious to the risk of levofloxacin-induced hepatotoxicity.

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Abbreviations:

ATT-antitubercular therapy
BMI- Body mass index
DR -TB-Drug resistance tuberculosis
DILI–Drug-induced liver injury
DILIN - Drug-induced liver injury
IDW- ideal body weight
mtDNA- Mitochondria DNA
SGPT-Serum glutamic pyruvic transaminase

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