OPEN ACCESS Freely available online

ISSN: 2167-0889
Journal of Liver

Commentary

Disruption of Triptolide Liver Injury and their Clinical Metabolism

Shiyuan Hua*

Department of Internal Medicine, Istanbul University, Istanbul, Turkey

DESCRIPTION

Triptolide (TRI) can cause metabolic disruption in the liver by interfering with various enzymes and transporters involved in bile acid synthesis and secretion, glucose metabolism, lipid metabolism, and xenobiotic metabolism. For example, TRI can inhibit the expression and activity of Bile Salt Export Pump (BSEP), Multidrug Resistance-Associated Protein 2 (MRP-2), and organic anion transporting polypeptide 1B-1/1B-3, leading to impaired bile acid efflux and accumulation in hepatocytes, which can trigger cholestatic liver injury and inflammation. TRI can also suppress the expression of Glycogen Synthase (GS) and Glucose-6-Phosphatase (G6Pase), resulting in decreased glycogen synthesis and increased gluconeogenesis, which can cause hypoglycemia and hepatic steatosis. Moreover, TRI can inhibit the activity of Cytochrome P450 (CYP) enzymes, such as CYP3A4 and CYP2C19, which are responsible for its biotransformation and detoxification. This can lead to increased systemic exposure and accumulation of TRI and its reactive metabolites in the liver, which can induce oxidative stress and cytotoxicity.

TRI can induce oxidative stress in the liver by increasing the production of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS), such as Superoxide Anion (O^{2-}), Hydrogen Peroxide (H_2O_2), Hydroxyl Radical (OH^-), Nitric Oxide (NO), and Peroxynitrite ($ONOO^-$), while decreasing the levels of antioxidant enzymes and molecules, such as Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GP_x), glutathione reductase (GR), Glutathione S-Transferase (GST), Glutathione (GSH), vitamin C, and vitamin E. The imbalance between ROS/RNS generation and scavenging can cause oxidative damage to cellular macromolecules, such as lipids, proteins, and DNA, leading to lipid peroxidation, protein carbonylation/nitration/oxidation, DNA strand breaks/adducts/mutations/oxidation.

TRI can induce different modes of cell death in the liver, such as apoptosis, necroptosis, and pyroptosis, which can contribute to liver injury and inflammation. Apoptosis is a form of programmed cell death that is characterized by cell shrinkage, chromatin condensation, DNA fragmentation, membrane blebbing, and formation of apoptotic bodies, which are phagocytized by macrophages without eliciting inflammation. Necroptosis is a form of regulated necrosis that is characterized by cell swelling, loss of membrane integrity, release of intracellular contents, and induction of inflammation. Pyroptosis is a form of inflammatory cell death that is characterized by caspase activation, gasdermin cleavage, pore formation, cytokine release, and cell lysis, which can trigger inflammation. However, TRI also has a narrow therapeutic window and a high risk of toxicity, especially hepatotoxicity, which is the main cause of its clinical limitation and withdrawal. TRI-Induced Liver Injury (TRILI) can manifest as elevated serum transaminases, jaundice, cholestasis, hepatic necrosis, fibrosis, or even Acute Liver Failure (ALF) in severe cases.

Moreover, TRI can induce the expression of Major Histocompatibility Complex (MHC) molecules and co-stimulatory molecules (such as CD80/CD86) on Antigen-Presenting Cells (APCs), such as Dendritic Cells (DCs) and KCs, which can enhance the antigen presentation and T cell activation. These immune alterations can lead to immune-mediated liver injury or hypersensitivity upon exposure to exogenous or endogenous antigens or stimuli (such as LPS).TRI-induced liver injury may also be influenced by genetic factors that affect the pharmacokinetics and pharmacodynamics of TRI in the liver. For example, polymorphisms in genes encoding CYP enzymes, transporters, receptors, cytokines, or inflammasomes may alter the metabolism, transport, binding, signaling, or response of TRI in the liver, which may modulate its toxicity or efficacy. Moreover, epigenetic modifications (such as DNA methylation or histone acetylation) may also affect the expression or function of these genes or their products in response to TRI.

CONCLUSION

Therefore, it is important to monitor the liver function and biomarkers of patients who are treated with TRI and adjust the dose or discontinue the treatment if necessary. Moreover, it is

Correspondence to: Shiyuan Hua, Department of Internal Medicine, Istanbul University, Istanbul, Turkey, E-mail: hua@shan.com

Received: 02-May-2023, Manuscript No. JLR-23-21821; **Editor assigned:** 05-May-2023, Pre QC No. JLR-23- 21821 (PQ); **Reviewed:** 19-May-2023, QC No JLR-23-21821; **Revised:** 26-May-2023, Manuscript No. JLR-23- 21821 (R); **Published:** 02-Jun-2023, DOI: 10.35248/2167-0889.23.12.181.

Citation: Hua S (2023) Disruption of Triptolide Liver Injury and their Clinical Metabolism. J Liver. 12:181.

essential to avoid the co-administration of TRI with other drugs or substances that may have hepatotoxic potential or interact with TRI. Therefore, genetic testing or screening may help to identify the individuals who are more susceptible or resistant to Triptolide-Induced Liver Injury (TRILI) and optimize the personalized therapy with TRI. The incidence of TRILI ranges from 2.6% to 28.6% in different studies, and the onset time varies from a few days to several months after TRI exposure. The mechanisms of TRILI are complex and multifactorial, involving metabolic disruption, oxidative stress, apoptosis/necroptosis/pyroptosis induction, immune dysregulation, and genetic susceptibility.