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Association of Tetracycline with Hepatotoxicity: A Pharmacovigilance Study

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DESCRIPTION

Drug Induced Liver Injury (DILI), the most frequent cause of acute liver failure, has grown to be a critical public health issue that cannot be ignored. One of the main causes of DILI is antibiotic use. In 45.4% of DILI cases, according to the American DILI Network (DILIN), antibiotics were used. Tetracyclines are frequently prescribed antibacterial medications that have been widely utilised to treat a variety of infections. Due to drug resistance, some tetracyclines are no longer used in clinical practise, but others are still crucial. The medications with the highest antibacterial activity against tetracyclines are doxycycline and minocycline. Tetracyclines, however, can enter the primary and permanent dentitions and cause discolouration of the bone, cartilage, and teeth. As a result, patients over the age of 8 should only take the majority of tetracyclines.

Doxycycline has a low affinity to calcium and is safe for usage in children under the age of eight. The first glycylcycline antibiotic, tigecycline, is still effective in treating tetracycline-resistant microorganisms. Tetracyclines are typically regarded as safe, and the most frequent side effects are tooth discolouration, skin/subcutaneous tissue diseases, and gastrointestinal problems. Minocycline is one of the top 10 medications that could result in DILI in industrialised nations for liver damage. High intravenous tetracycline doses have been linked to fatty liver disease, which is more prevalent in pregnant women, according to earlier investigations. Other tetracyclines have been linked to hepatotoxicity, but this hasn't been established, according to studies.

Tetracyclines are becoming more and more necessary for clinicians as atypical pathogens and MDR pathogen infection rise. We must be aware of their detrimental effects on organ performance, particularly hepatotoxicity. The majority of tetracyclines are excreted through the liver and biliary tract, harming the hepatobiliary system, due to their high lipid solubility. Patients taking tetracyclines, particularly glycylcycline, were regularly shown to have liver damage in our clinical practise (tigecycline). It is challenging to determine whether liver

damage is caused by drugs or a disease, though. Finding a method to examine the relationship between tetracyclines and hepatic damage occurrences is crucial and relevant.

In order to track and reevaluate the safety of post-marketing medications, numerous nations and organisations have set up adverse event reporting systems. Due to its high data volume and open access policy, the FAERS database is widely used. To the best of our knowledge, this is the first big data pharmacovigilance investigation employing FAERS real-world data for tetracycline-associated DILI. Previous investigations have indicated that tetracycline and minocycline, particularly at high doses administered intravenously, are positively linked with liver damage. While minocycline is likely related to immunology, the mechanism of tetracycline-induced hepatotoxicity is likely related to mitochondrial injury caused by reduction of mitochondrial protein synthesis.

We discovered that doxycycline, tigecycline, and minocycline all demonstrated significant correlations with DILI in the current investigation. Additionally, tigecycline showed stronger signals in hepatocellular injury and cholestatic injury than did minocycline and doxycycline. Both tigecycline and minocycline were more risky than doxycycline for severe DILI. Additionally, liver failure may result from the usage of tigecycline and minocycline. Tetracycline and other medications did not demonstrate any significant effects, presumably because there were fewer cases reported for them. The three tetracycline medications that are most frequently used in clinical practise are tigecycline, minocycline, and doxycycline. Particularly for tigecycline, their link with DILI in empirical data is significant. Infections caused by MDR bacteria are treated with tigecycline, a glycylcycline antibiotic with broad-spectrum activity against practically all gram-negative, gram-positive, anaerobic, and atypical pathogens. Some investigations claimed that the association between tigecycline and liver damage was insignificant or that alanine aminotransferase and aspartate aminotransferase levels were only mildly elevated. By analysing the FAERS data, the current study concluded that severe DILI, hepatocellular injury, and cholestatic injury were strongly associated with tigecycline, minocycline, and doxycycline. Compared to minocycline and doxycycline, tigecycline had a stronger correlation with hepatocellular injury and cholestatic injury. More research is required to examine the dangers and features of tetracycline hepatotoxicity, particularly tigecycline.