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Case of Tigecycline Induced Liver Injury: A Cautionary Tale

Jeeva Elizabeth Thomas[1], Dr. M Manish Mohan[2], Dr. Rinku Elsa Reji[3]

[1]Pharm D Intern, Nazareth College Of Pharmacy, Othera, Thiruvalla, Kerala, India

[2]Department Of Pharmacology, Believers Church Medical College Hospital, Thiruvalla, Kerala, India

[3]Department Of Clinical Pharmacy, Believers Church Medical College Hospital, Thiruvalla, Kerala, India

ABSTRACT

Tigecycline, the inaugural glycylcycline antibiotic in clinical use, is experiencing rising global utilization owing to its effectiveness against multidrug-resistant (MDR) bacteria. Although gastrointestinal side effects like nausea and vomiting are more prevalent, it is important to recognize that tigecycline can also lead to liver injury. The manufacturer has issued a warning regarding tigecycline's potential to elevate total bilirubin (TB) and transaminase levels. [1] We present the case of a 74-year-old female with a history of multiple comorbidities who developed severe hepatotoxicity following tigecycline therapy for a complicated intra-abdominal infection. The patient shows an abnormal liver function test with hyperbilirubinemia. Later on she developed jaundice. This case underscores the importance of considering TILI in patients receiving tigecycline, particularly those with preexisting liver disease or receiving other potentially hepatotoxic medications.

KEYWORDS: Tigecycline, adverse reaction, hyperbilirubinemia, jaundice

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INTRODUCTION

Tigecycline, a member of the glycylcycline class of antibiotics, was introduced into clinical practice as a promising agent against multidrug-resistant (MDR) pathogens. Its unique mechanism of action, which includes binding to the bacterial 30S ribosomal subunit, has made it a valuable tool in the treatment of complicated skin and soft tissue infections, intra-abdominal infections, and community-acquired bacterial pneumonia. The increasing prevalence of MDR bacteria has led to the expanded use of tigecycline globally. However, along with its efficacy, tigecycline use has been associated with a range of adverse effects, including gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Despite these known gastrointestinal side effects, tigecycline-induced liver injury (TILI) remains an underrecognized and potentially severe complication.[2]

Drug-induced liver injury (DILI) is a frequent adverse reaction evidenced by abnormal liver function tests. Among all drug classes, antibiotics, including tigecycline, are prominent contributors to DILI incidents. Although tigecycline therapy can lead to minor increases in aminotransferase levels, liver injury during treatment may also stem from sepsis or multiorgan failure rather than direct drug toxicity.[3] The exact mechanism of TILI is not fully understood but is believed to involve immune-mediated responses or direct toxic effects on hepatocytes. Given the widespread use of tigecycline and the potentially severe consequences of TILI, it is important for clinicians to be aware of this complication and monitor patients accordingly.Dosage adjustment is unnecessary for tigecycline in patients with mild to moderate liver impairment. However, for patients with severe impairment (Child-Pugh C), the tigecycline dosage should be reduced to 25 mg every 12 hours. When drug-induced cholestasis is suspected, discontinuing the implicated drug is typically the initial action taken.[4]. Treatment options for tigecycline-induced liver injury typically involve discontinuing tigecycline to prevent further damage to the liver. Supportive care may be provided to manage symptoms such as nausea, abdominal pain, and fatigue. In more severe cases, medical interventions to address liver dysfunction, such as medications to support liver function or in extreme cases, liver transplantation, may be necessary. It's essential for healthcare providers to closely monitor the patient's liver function and overall condition

during and after treatment for tigecycline-induced liver injury.

CASE REPORT

A 74 year old female presented with complains of burst abdomen, no history of trauma. She was admitted earlier for intestinal perforation and underwent emergency exploratory laprotomy + Hartmann's procedure. She was a known case of Diabetes Mellitus, Hypertension, Chronic kidney disease. Patient underwent an exploratory laparotomy and multiple procedures, including adhesiolysis, resection of perforated ileum, and creation of a double-barrel ileostomy, under high-risk conditions. Post-operatively, she was managed in the ICU and treated with meropenem and noradrenaline support. Despite initial stabilization, the patient developed complications, including multi-drug-resistant infections. Tigecycline 100mg once daily was administered, leading to deranged liver function test with hyperbilirubinemia. Her total bilirubin was 2.61 mg/dl, direct bilirubin was 1.33 mg/dl , indirect bilirubin was 1.28 mg/dl, protein was 5.67 g/dl, albumin was 3.39 g/dl, alkaline phosphatase was 480 U/L. However, the patient experienced various challenges, including fungal infections, low platelets, and catheter-related issues, necessitating multidisciplinary care. Imaging studies were recommended for further evaluation. She underwent additional procedures, including cystoscopic suprapubic catheterization, to manage urological issues. Later on she developed jaundice .Her alkaline phosphatase levels were becoming elevated and cause a liver injury.

DISCUSSION

Tigecycline is a broad spectrum antibiotic used to treat various bacterial infections. Tigecycline induced liver injury refers to liver damage that can occur as a rare adverse effect of tigecycline therapy. This condition can manifest as elevated liver enzymes , jaundice or even more severe liver dysfunction. It has been reported that 2% to 5% of users of tigecycline have moderate, temporary rises in blood aminotransferase levels; these rates are comparable to those observed in patients using comparator antibiotics. Jaundice and a clinically evident liver damage must be quite uncommon. The tigecycline product labels discuss post marketing experiences of rare incidences of severe cholestasis, jaundice, and hepatic dysfunction. No information is provided regarding the latency, pattern, and duration of liver damage in tigecycline-induced hepatotoxicity patients. Rather than being the result of medication hepatotoxicity, the reports of jaundice and fatalities from hepatic dysfunction in sizable clinical trials of tigecycline most likely represented consequences of sepsis and multiorgan failure[4].Tigecycline-induced liver injury can occur through various mechanisms. One possible way is through direct toxicity to liver cells, leading to cellular damage and inflammation. Another potential mechanism is immune-mediated liver injury, where the body's immune system reacts to tigecycline or its metabolites, causing liver inflammation and injury. Additionally, tigecycline may disrupt normal liver function by affecting metabolic pathways or altering the balance of enzymes involved in liver detoxification processes. These combined effects can contribute to liver injury in some individuals treated with tigecycline[5]. In our patient after the administration of tigecycline, she developed hyperbilirubinemia and elevated alkaline phosphatase (ALP) which was similar to **Liang J**. *et. al*., which shows increased alkaline phosphatase and bilirubin after the administration of tigecycline[6].Extreme hyperbilirubinemia and jaundice are rare side effects of tigecycline which was seen in our patient was similar to **Althomali SA,** where in that case the patient has developed jaundice with elevated bilirubin levels[7].

Upon evaluation at our ADR monitoring centre, the causality was determined to be “probable” using the WHO-UMC causality assessment scale. The type of ADR was classified as “type c” according to the Rawlims-Thompson classification and was assessed as “level 7- severe” in terms of severity based on the modified Hatwig’s scale. As per who criteria, the seriousness of the reaction was categorized as “ hospitalization” and the outcome of the reaction was “ recovering”. Additionally, according to the Schumock and Thornton scale, the ADR was deemed “non preventable”. The assessment of causality and other attributes of the ADR was conducted using established scales and criteria to ensure comprehensive and standardized evaluation.

CONCLUSION

Tigecycline-induced liver injury (TILI) is an uncommon but potentially dangerous side effect of tigecycline therapy. Although early clinical trials indicated a low incidence of liver enzyme elevation, more recent retrospective studies have shown higher rates of tigecycline-associated drug-induced liver injury (DILI), especially in patients receiving longer treatment duration. Most cases have a cholestatic pattern and are mild, though severe cases have been documented. In our case, patient was found to have hyperbilirubinemia and jaundice after the administration of tigecycline. Physicians should be alert for liver injury symptoms in patients on tigecycline, especially in those with longer treatment regimens or underlying liver disease. Additional research is required to better understand the risk factors and mechanisms underlying TILI, enabling improved monitoring and management.

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LIST OF ABBREVIATIONS:

MDR: Multidrug Resistant

TB: Total Bilirubin
TILI: Tigecycline induced liver injury
DILI: Drug induced liver injury

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