Case Report

# Voriconazole Induced Cholastatic Jaundice: A Case Report

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**ABSTRACT**

Voriconazole-induced cholestatic jaundice is a relatively rare but serious clinicopathologic symptoms. This drug is commonly used for invasive aspergillosis and other fungal infections. This report presents a case of voriconazole induced cholestatic jaundice. Hepatotoxicity is the most common adverse effect of voriconazole.

**Keywords:** Voriconazole, cholestatic jaundice, hepatotoxicity.

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## INTRODUCTION

Voriconazole is a triazole antifungal agent which inhibits ergosterol synthesis and it is a drug of choice for the treatment of invasive aspergillosis. Its metabolism occurs in the liver by P450 enzymes CYP2C9, CYP3A4 and CYP2C19 and metabolites are excreted through kidneys.[1] Voriconazole therapy is associated with transient, asymptomatic serum aminotransferase elevations and is a known cause of clinically apparent acute drug induced liver injury.[2]

Common Hepatic Adverse Effects of Voriconazole includes, Cholestasis (<5%), Hepatitis (<2%), Increase in bilirubin level (1.1%), Jaundice (<2%), abnormal liver function test (12.4%). Altered liver function test values are common in every hepatic abnormality. Among these jaundice, including the cholestatic one, is more common while hepatitis or hepatomegaly occurs less frequently. It rarely induces hepatic coma and liver failure. So the hepatic damage created by voriconazole is primarily due to cholestasis, and less often can be cytotoxic and mixed.[3]

## CASE HISTORY

A 58-year-old male patient had past history of right leg cellulitis, soft tissue abscess (fungal infection) and underwent surgical procedure incision and drainage and prescribed with Tablet Voriconazole 200mg BD for 1 month. After 7 days he came up with the complaints of wound over lower limb, giddiness and vomiting since 2 days and diagnosed with sepsis with septic shock, AKI with CKD, Urethral stricture, $T_2DM$, Anaemia due to chronic disease. As per the record patient was administered with Voriconazole for 7days, and advised to continue voriconazole along with other drugs such as pantoprazole-40mg-OD, Ondansetron-4mg-OD, Optineuron-2 ampoule-OD, Meropenam-500mg-BD, N-acetyl cysteine-3 ampoule BD and Carnitidine – 1gm- OD given through IV route. Haemup gems- OD, Acetaminophen 650mg- SOS and sodium bicarbonate 500 mg- BD given per oral and topical creams were prescribed.

### Laboratory Investigations

**Table 1:** Patient's Laboratory data

| | Day 2 | Day 5 | Day 10 | Day 12 | Day 14 | Day 17 |
|---|---|---|---|---|---|---|
| Total Bilirubin (mg/dl) | 5.1 | 4.2 | 6.1 | 6.4 | 4.1 | 2.9 |
| Direct Bilirubin (mg/dl) | 2.8 | 2.3 | 3.2 | 3.7 | 2.8 | 1.8 |
| SGOT/AST (U/L) | 215 | 137 | 128 | 229 | 158 | 126 |
| SGPT/ALT (U/L) | 81 | 51 | 28 | 45 | 40 | 32 |
| ALP (U/L) | 598 | 665 | 440 | 444 | 196 | 157 |

On day 2 of his admission, it was observed that patient has ictrus skin and sclera, upon his liver function data it showed increased levels of liver enzymes, but it was not ruled out the cause for that after 3 days also his liver function test was abnormal and then checked for the liver toxic drugs, we found out that voriconazole is having liver toxic effects.

After identifying the liver toxicity of voriconazole, it was stopped then later one-week liver function test values were found near to the normal values. And yellowish of skin and sclera was also reduced. (Figure 1 and Figure 2).

**Figure 1:** Patient with yellowish sclera

**Figure 2:** yellowish hands and skin

## DISCUSSION

We present a case of voriconazole induced CHOLASTATIC JAUNDICE. Although voriconazole-induced hepatotoxicity has been reported previously, the exact mechanism and direct cause-effect relationship remains to be established. The plasma level of this drug is the best predictor of its efficacy and toxicity. As voriconazole is mainly metabolized in the liver, hepatic failure leads to high plasma levels.[4] But it is a costly procedure and patient is economically backward we cannot assess TDM in this case.

Although yellowish of skin and sclera was decreased and become normal, liver function tests were above the normal values means it mayrequire much more time to reach normal values of liver function test. And also, he had other comorbid condition and other drug administration.

In a retrospective observational study conducted by Jan G. den Hollander, voriconazole treatment need to be discontinued in only 3 of the 46 patients because of its hepatotoxicity and increased. They concluded in their study that, for the treatment of invasive fungal infection with voriconazole, liver function tests(enzymes) were increased more frequently than previous report, there is a need for future randomized prospective clinical trails to confirm this observation.[5]

## CONCLUSION

The case report of voriconazole-induced hepatotoxicity is >5% common and the exact mechanism and direct cause-effect relationship remains to be established. We reported this case because clinicians must be aware of these ADRs to prevent and monitor acute liver toxicity. As a duty of clinical pharmacist, we identified the adverse drug reaction of voriconazole and immediately reported to doctor and then patient was monitored closely.

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