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Case Report

Terlipressin Induced Headache- An Uncommon Phenomenon

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ABSTRACT
Introduction: Terlipressin is used in treatment of variceal bleed and hepatorenal syndrome in cirrhotic patients. It may cause neurological or cardiac problems like cardiac ischemia, cerebrovascular ischemia, peripheral ischemia, or mesenteric ischemia. It may also cause confusion, constipation, diarrhea, headache, itching skin, numbness and tingling of the face, fingers, or toes, pain in the arms, legs, or lower back, especially pain in the calves and/or heels upon exertion, pain or discomfort in the arms, jaw, back or neck, pale, bluish-coloured, or cold hands or feet.
Case Report: We report a fifty-two-year-old male, a known case of alcoholic liver disease for last two years who presented with haematemesis and malena for last two days. On clinical examination, he was thin with average stature. He was looking pale with hypotension and reflex tachycardia. He had mild anemia, ascites and bilateral pedal edema. Rest of general physical and systemic examination was normal. On biochemical evaluation complete hemogram revealed pancytopenia, liver function test was deranged i.e. there was mild hyper bilirubinaemia, transaminitis, hypoproteinaemia and hypoalbunemia. The complete lipid profile was in below normal range but renal function test, serum electrolytes and blood sugar level were in normal range. The ultrasonogram abdomen showed altered echotexture with moderate ascites. The upper gastro-intestinal endoscopy revealed grade two oesophageal varices with stigmata of recent bleed, hence endoscopic variceal ligation was done. The AFP level was normal. His viral screen, autoimmune, wilson's profile was negative. He was started on injection Terlipressin, vitamin K, broad spectrum antibiotic, proton - pump inhibitor and other supportive therapy. After first dose of injection Terlipressin, he developed severe headache which warranted even need of injectable analgesics. There was no documented hypertension at this point of time, to which headache could have been attributed. Immediately, injection Terlipressin was stopped and patient headache subsided after few hours. After, a gap of one day, again injection Terlipressin was re-started on trial basis but again patient developed severe headache which again needed injectable analgesics. Again, injection Terlipressin was stopped and patient became headache free after few hours. Patient was switched to tablet carvedilol which he tolerated well and he was discharged under haemodynamically stable condition.
Conclusion: Terlipressin is commonly used for treatment of variceal bleed and hepatorenal syndrome. The most common side-effects noted are pain abdomen, diarrhoea, cardiac ischemia but headache is not frequently seen. The awareness regarding the same can lead to timely intervention and substitution with other oral alternative drugs.

Keywords: Chronic Liver Disease, **T**erlipressin**,** Headache, Variceal Bleed, Hepatorenal Syndrome.

INTRODUCTION

Terlipressin is widely used in the treatment of bleeding esophageal varices in patients with cirrhosis. It is found to decrease the mortality by reducing splanchnic blood flow and portal pressures and the need for emergency procedures required to stop rebleeding [1]. Ischemic adverse events are uncommonly observed with terlipressin of which cutaneous complications are among the rarest [2,3]. Acute variceal bleed (AVB) is a potentially life-threatening complication of cirrhosis. Mortality has decreased substantially over the last three decades due to advancements in medical and endoscopic therapies. Current guidelines advocate combined endoscopic and pharmacological therapy in patients with AVB due to improved outcomes as compared to either modality alone [4]. Pharmacotherapy in AVB includes vasoconstrictors like terlipressin, somatostatin, and octreotide. Where available, terlipressin is usually the preferred vasoconstrictor as it has been shown to have a survival benefit [4]. It acts on V1 receptors in vascular smooth muscle cells leading to splanchnic vasoconstriction and reduction of portal venous pressures. Apart from AVB, terlipressin is also used in the management of

hepatorenal syndrome (HRS) in cirrhosis and has been recently approved by the US FDA based on the phase 3CONFIRM trial [4]. Adverse events with terlipressin are infrequent. The most concerning adverse effects are related to respiratory failure, myocardial ischemia, arrhythmias, brady -cardia, and fluid overload. Other commonly reported adverse events include abdominal pain, nausea, and dyspnoeal [5]. Headache has been reported in some studies as a side effect in 2-10% of patients on terlipressin but in majority of studies highlighting side effects, headache is not frequently reported [5].

CASE REPORT

We report a fifty-two-year-old male, a known case of alcoholic liver disease for last two years who presented with haematemesis and malena for last two days. On clinical examination, he was thin with average stature. He was looking pale with hypotension and reflex tachycardia. He had mild anemia, ascites and bilateral pedal edema. Rest of general physical and systemic examination was normal. On biochemical evaluation complete hemogram revealed pancytopenia, liver function test was deranged i.e. there was mild hyper bilirubinaemia, transaminitis, hypoproteinaemia and hypoalbunemia. The complete lipid profile was in below normal range but renal function test, serum electrolytes and blood sugar level were in normal range. The ultrasonogram abdomen showed altered echotexture with moderate ascites. The upper gastro-intestinal endoscopy revealed grade two oesophageal varices with stigmata of recent bleed, hence endoscopic variceal ligation was done. The AFP level was normal. His viral screen, autoimmune, wilson's profile was negative. He was started on injection Terlipressin, vitamin K, broad spectrum antibiotic, proton -pump inhibitor and other supportive therapy. After first dose of injection Terlipressin, he developed severe headache which warranted even need of injectable analgesics. There was no documented hypertension at this point of time, to which headache could have been attributed. Immediately, injection Terlipressin was stopped and patient headache subsided after few hours. After, a gap of one day, again injection Terlipressin was re-started on trial basis but again patient developed severe headache which again needed injectable analgesics. Again, injection Terlipressin was stopped and patient became headache free after few hours. Patient was switched to tablet carvedilol which he tolerated well and he was discharged under haemodynamically stable condition.

DISCUSSION

Cirrhosis causes significant morbidity and mortality and with time its incidence and prevalence is increasing. One of the common complications are variceal bleed and hepatorenal syndrome for which terlipressin is main treatment. We have used it for last fifteen years in thousands of patients in dosage of 1 mg QID. The most common side effects seen at this dose was pain abdomen and diarrhoea. This is our first case where we encountered headache which even occurred at normotensive level, meaning by hypertension was not cause of headache. Terlipressin was cause of this severe headache was verified by restarting of it and same pattern of headache occurred. As per our inference, headache can occur with terlipressin but it is not as common as reported in some studies which have shown its prevalence to 2%-10%.

CONCLUSION

Terlipressin is commonly used for treatment of variceal bleed and hepatorenal syndrome. The most common side-effects noted are pain abdomen, diarrhoea, cardiac ischemia but headache is not frequently seen. The awareness regarding the same can lead to timely intervention and substitution with other oral alternative drugs.

Conflict of Interest

The authors declare that there was no conflict of interest or any kind of funding was taken for publishing this case report.

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