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# PHENYTOIN INDUCED JAUNDICE IN SEIZURES: A CASE REPORT IN PAEDIATRIC DEPARTMENT

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## ABSTRACT
Phenytoin is a highly effective and widely prescribing anticonvulsant agent, but it can be associated with dose-related side effects like liver damage, jaundice, hepatocellular degeneration, megaloblastic anaemia. We found a case of phenytoin-induced jaundice in a 10-year-old male patient who had yellowish discoloration of eyes, an increase in bilirubin levels 9.5mg/dl, SGOT-1800 IU/lt, SGPT-1890 IU/lt, alkaline phosphate 373 IU/lt associated with vomitings for 3 days, abdominal distension for 1 day.15 days back patient had diagnosed as epileptic and prescribed with phenytoin 100 mg OD., but on evaluation we found that he took 100mg BID. So, this may be the reason for developing jaundice and the suspected ADR was Probable ADR (Naranjo's scale). T. hepamerz 250mg BD is used to treat jaundice.

**KEYWORDS:** SGPT (serum glutamic pyruvic transaminase), SGOT (serum glutamic oxaloacetic transaminase), LFT (liver function test), CBP (complete blood picture), Hb (hemoglobin), ALF (Acute liver failure).

## INTRODUCTION
Drug-induced hepatitis involves inflammation of the liver, caused by medication. Drug-induced hepatitis is similar to acute viral hepatitis but parenchymal destruction tends to be more extensive.[1] Based on the criteria established by the council for international organizations of medical sciences [CIOMS] liver injury is classified as Hepatocellular, Cholestatic, or Mixed.[2]

Drug induced liver injury associated with anti-epileptic drugs is well recognized. The frequency of the most common antiepileptic drugs is rare but the consequences can be very serious leading to death or liver transplantation due to acute liver failure induced by these drugs.[3] Drug induced liver injury [DILI] is responsible for 5% of all hospital admissions and 50% of all Acute liver failure [ALF].[4] Phenytoin hepatotoxicity is a serious idiosyncratic reaction that occurs in less than one percent of patients. The phenytion hepatotoxicity can elevate the level of aminotransferases, lactic dehydrogenase, alkaline phosphatase, bilirubin and prothrombin time in serum.[5] Drugs are an important cause of liver injury. More than 900 drugs, toxins and herbs have been reported to cause liver injury.[6] Although the exact mechanism of phenytoin hepatotoxicity is unknown; the majority of literature supports a hypersensitivity mechanism.[5] Factors influencing drug induced hepatotoxicity are Age, Ethnicity, Race, Gender, Nutritional status, Underlying liver disease, Renal function, Pregnancy, Duration and dosage of drug, Enzyme induction, Drug-drug interaction.[4] Phenytoin is an anti-seizure medication. It is useful for the prevention of convulsions and tonic-clonic seizures, partial seizures, but not absence seizures. Historically, phenytoin has been used as an antidysrhythmic agent, especially in the treatment of dysrhythmias due to digoxin toxicity.[9]

## CASE REPORT
A 10 years old male patient was admitted in paediatric ICU ward with the chief complaints of yellowish discoloration of eyes, vomiting 2 episodes, since 3days and abdominal distension from 1 day.

On examination, he had decreased Sleep and appetite, Bowel and bladder- normal. His past history revealed that he was not a known Hypertensive, diabetic and hepatitis patient but he had a seizure attack 15days back and on under treatment of T. Phenytoin 100mg OD.

On the day of admission he was advised for Liver function profile, Complete blood picture, Hb, HBsAg

and he was treated with Inj. Ceftriaxone 500mg IV BD, Inj. Ondansetron 2mgIV BD, T. Paracetamol 250mg BD, 3 Sporolacsachets and 3 ORS sachets. Lab investigations reports shown that bilirubin 9.5mgs/dl (normal upto1mgs/dl); direct4.2mgs/dl (normal 0.2mgs/dl); indirect 5.3mgs/dl (normal 0.2 to 0.8mgs/dl); proteins4.7gm/dl (normal 6.4 to 7.8gm/dl); albumin 3.4gm/dl (normal 3.5 to 5.0gm/dl); globulin 1.3gm/dl (normal 1.8 to 3.6gm/dl); SGOT 1800IU/L(normal 8 to 40IU/L); SGPT 1890IU/L (normal 5 to 35IU/L); Alkalinephosphate 373IU/L(normal 12 to 115IU/L); RBS 92mgs/dl(normal 80 to 120mgs/dl); ESR 20mm/hr, WBC 7900cumm(normal 4000 to 11000cumm); Hb-8gm/dl(normal 14 to 16gm/dl) and no abnormalities found in urine analysis and renal function test.

Based on this examination he was diagnosed as **"Jaundice"** and he was treated with Inj. Ceftriaxone 500mg IV BD, IV fluids DNS 500ml at 40ml/hr, T. BC 67.5mg, T.Hepamerz 250mg BD, advise to take fluids and glucose. On 3rd day patient had complaints of cough, yellowish discoloration of urine and same treatment was continued and he was advised to take USG Abdomen. Ultra sound abdomen reveals that appearance of fatty liver & he was treated with same medication and he was advised to LFT. Lab investigations reports reveals that bilirubin 8.9 mgs/dl (normal upto1mgs/dl); direct4.0mgs/dl (normal 0.2mgs/dl); indirect4.9mgs/dl (normal 0.2to0.8mgs/dl); SGOT 1700IU/L (normal 8 to 40IU/L); SGPT 1790IU/L (normal 5 to 35IU/L); Alkaline phosphate 346IU/L (normal 12 to 115IU/L). He was treated with same medication. On 5th day he was discharged with following medication T.Hepamerz 250mg, T.Vitamin $B_{12}$ 500mcg OD, T. Ascorbic acid 500mg OD, T. Iron folic acid 325mg OD.

**Analysis of ADR**

Patient past history revealed that he had a seizures attack 15 days back and on T. phenytoin 100 mg OD, up to 13 days, but last two days he took twice in a day, accidentally. So, the symptoms of hepatic disease may aggravate. So, it is suspected as drug induced hepatic disease, here suspected drug is PHENYTOIN.

The suspected ADR was analyzed by using Naranjo's and WHO scale, the ADR was found to be "Probable" and the Severity of the suspected ADR was analyzed by using Modified Hartwig and Siegel scale and the ADR was "Severe (level-5)". Preventability of an ADR was analyzed by using Schumock and Thornton scale the ADR was "Definitely probable".

## DISCUSSION

It is the case of drug induced hepatic disease. In this case the suspected drug is phenytoin. Generally Hepatic toxicity of antiepileptic drugs has been well recognized for many years. Phenytoin hepatotoxicity is a serious idiosyncratic reaction and can elevate the level of alkaline phosphatase, bilirubin and prothrombin time in serum. Lab investigations reports showed that increased levels of bilirubin, indirect bilirubin, direct bilirubin, SGPT, SGOT and alkalinephosphate. We had provided patient counseling regarding disease, medication and life style modifications. Drug induced liver injury occurs as several different clinical presentations such as Idiosyncratic reactions, Allergic hepatitis, Toxic hepatitis, Chronic active toxic hepatitis, Toxic cirrhosis, Liver vascular disorders.[8] Since 1965 with phenytoin hepatoxicity six fatal cases have been reported.[5] Mechanisms of Injury: It is mediated by two chief mechanisms-1. Intrinsic and 2. Idiosyncratic hepatotoxicity Intrinsic hepatotoxins cause hepatocellular damage in a predictable dose-dependent manner directly by the drug or indirectly by its metabolite. The majority of the drugs lead o idiosyncratic liver injury and can be classified into metabolic and immunological categories. In general, Intrinsic hepatotoxicity manifests with Hepatocellular necrosis with little inflammation, while idiosyncratic drug reactions often show inflammation-dominant hepatic injury.[2] With phenytoin, the onset of symptoms occurs easily in therapy, usually within the 1st six weeks. Presenting symptoms often include fever, rash, lymphadenopathy, hepatomegaly, anorexia, myalagias or arthralgia's.[5] Common side effects include nausea, stomach pain, loss of appetite, poor coordination, increased hair growth and enlargement of the gums. Potentially serious side effects include sleepiness, self-harm, liver problems, bone marrow suppression, low blood pressure and toxic epidermal necrolysis.[10] Over dosage of phenytoin intake leads to symptoms of coma, confusion, convulsions, dizziness, fever, low blood pressure, rigidity, sleepiness, nystagmus, slurred speech, swollen gums, tremor and unsteadiness.[9] The assessment of possible liver injury due to drugs should include what is known in the literature, the timing involved, the clinical course and always on exploration for preexisting conditions that may have encouraged the lesions development.[8]

## CONCLUSION

Patient had taken phenytoin at normal dose for some days by that hepatic disease occurred and also while increasing the dose the symptoms of the disease got aggravated. When prescribing the antiepileptic drugs, patients should be monitored closely for LFT and it also helps in early detection of hepatic diseases. There are a large category of drugs used for different therapeutic indications which are toxic to the liver one of the drug is phenytoin and thus should be cautiously administered; particularly when given at normal doses, high doses or used for chronic or long term administration liver disorders can occur easily. Hepatic toxicity of antiepileptic drugs has been well recognized for many years. So, the increasing awareness of chronic toxicity of antiepileptic drugs is necessary.

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