PP16 ACETAMINOPHEN USE IN PATIENTS WITH GILBERT'S SYNDROME, CAUSES DETERIORATION OF THE CLINICAL PRESENTATION: CASE REPORT

Lichoska-Josifovikj F., Trajkovska M., Nikolovska E., Joksimovikj N.

University Clinic for Gastroenterohepatology, Skopje, Macedonia

BACKGROUND: Gilbert Syndrome is a benign often familial condition characterized by recurrent mild unconjugated hyperbilirubinaemia in the absence of haemolysis or underlying liver diseases. Augustine Gilbert and Pierre Lerebullet first described Gilbert syndrome in 1901. Gilbert Syndrome is a common genetic liver disorder found in 3-12% of the population.

CASE REPORT: We present a single case of 24 years old man with history of Gilbert's syndrome (2008), treated with Phenobarbital therapy during one year, interrupted self-initiatively afterwards. That same year he was made the cholecystectomy. Currently, he had appeared in the ambulance of the University Clinic for Gastroenterohepatology, because he had noticed more intensive yellowing, fatigue, darker urine. He notified that, due to cold with fever, fifteen days earlier, he had been using Paracetamol tablets (500mg), 4 times a day, a total of 5 days. Initial laboratory results were: total Bilirubin-222μmol/L, indirect bilirubin -212 μmol/L, direct bilirubin – 9.8 μmol/L, AST – 60 U/L, ALT-68 U/L. Analysis made by MANU: UGTA1A 28/7/7 genotype, consulted hematologist (excluded hematological diseases, including genetic testing for thalassemia). He had been given advice for resting and use of vitamins, including therapy with Phenobarbital tablets. Control, conducted 2 weeks later, showed a decline of the total Bilirubin - 89 μmol/L, the indirect Bilirubin - 81 μmol/L and direct Bilirubin - 8.8 μmol/L, with normalisation of the transaminase activity. The Bilirubin status was normalising one month later.

DISCUSION: While paracetamol (acetaminophen) is not metabolized by UGT1A1, it is metabolized by one of the other enzymes also deficient in some people with GS. A subset of people with GS may have an increased risk of paracetamol toxicity. Gilbert's syndrome is a genetic cause of chronic unconjugated hyperbilirubinemia. Although no articles in the literature suggest hepatotoxicity with recommended dosing, certain studies have shown a potential for people with Gilbert's syndrome to be more prone to complications with normal/supra-therapeutic doses of acetaminophen. There is no clear suggestion in that therapeutic doses of paracetamol (acetaminophen) are associated with increased risk for hepatic or systemic toxicity in subjects with GS. This may be explained by the fact that UGT1A6 (and to a lesser extent UGT1A9) are the isoenzymes that are primarily involved in paracetamol metabolism, rather than UGT1A1. Patients with Gilbert's syndrome need to be educated about possible complications. These may include exacerbations of jaundice, especially when the patient is using acetaminophen and/or alcohol.However, Harrison's goes on to say that it has been reported that there may be abnormal metabolism of menthol, estradiol benzoate, acetaminophen, tolbutamide, and rifamycin. If the jaundice becomes severe and/or the appearance is bothering the patient, a reduction in the serum bilirubin can be temporarily achieved with phenobarbital tablets. Until a more research based opinion is available, clinicians must educate Gilbert's syndrome patients of the potential hazards of using acetaminophen and alcohol separately or together.

KEYWORDS: Gilbert's syndrome, acetaminophen.