

# Perioperative management of a patient with Gilberts syndrome and rheumatic heart disease

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## ABSTRACT

Anaesthetic management of patients with hepatic dysfunction can be quite challenging, as many anaesthetic agents are metabolized by liver. Heart disease on anti coagulation can pose additional challenge. Here we report a case of Gilbert's syndrome with rheumatic heart disease on anti coagulation posted for elective hernia repair.

**Key words:** *Anti coagulation, Gilbert's syndrome, hepatic dysfunction*

## INTRODUCTION

Gilbert's syndrome is a hereditary, mild, chronic, unconjugated hyperbilirubinemia occurring in the absence of overt hemolysis or any other evidence of liver disease. The hyperbilirubinemia is mild and, by definition, less than 6 mg/dL. However, most patients exhibit levels ranging from 3 to 8 mg/dL.<sup>[1]</sup> Gilbert's syndrome may be diagnosed by family history, duration of the disease, lack of other liver diseases justifying jaundice and jaundice triggered by predisposing factors such as fasting, menstruation, stress and exercise.<sup>[2]</sup> As majority of the anesthetic agents are metabolized in the liver, perioperative management in patients with Gilbert's syndrome can be quite challenging. Here, we report a case of Gilbert's syndrome and heart disease on anticoagulation posted for elective surgery.

## CASE REPORT

A 34-year-old male was scheduled for bilateral inguinal hernioplasty. His history revealed that he was a known

case of congenital hyperbilirubinaemia and rheumatic heart disease. The patient had undergone mitral valve replacement (MVR), right atrial reduction and tricuspid valve annuloplasty 1.5 years ago, and was put on oral medication of T. Warfarin, T. Aspirin, T. Digoxin, T. Furosamide Frusemide and Syrup Potassim Chloride (KCl).

On preanesthetic evaluation, the patient's pulse rate was found to be 70 beats per minute (bpm), in atrial fibrillation (AF). The blood pressure was 110/80 mmHg in the right arm in the supine position. Icterus was present. On examination of the cardiovascular system, a valvular click was heard. In the respiratory system, bilateral normal vesicular breath sounds with occasional rhonchi were heard. Abdominal examination did not reveal any abnormality.

Laboratory investigations revealed hemoglobin concentration (Hb): 10.3 gm%; platelets count: 1.5 lakhs/mm<sup>3</sup>; total bilirubin: 7.5 mg%, direct: 0.5 mg%; International Normalisation Ratio (INR): 1.5; secretory and synthetic functions of the liver were normal; urine was negative for urobilinogen, bile pigments and bile salts. Peripheral smear showed normochromic RBCs with moderate anisocytosis, spherocytosis, mild polychromasia and macrocytosis. ECG showed AF and left ventricular hypertrophy (LVH). Echocardiogram showed normal LV function, mild TR and a PASP of 35 mmHg.

The patient was advised to stop oral Warfarin and Aspirin 4 days prior to the surgery and was started on subcutaneous low molecular weight heparin (Enoxaparin 40 mg) once a

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day at 8 pm and stopped 12 h prior to surgery. INR done on the morning of surgery was 1.4. An intravenous injection of antibiotic Ampicillin 2 gm IV and Gentamicin 60 mg IV 0.5 h prior to the surgery was administered.

In our case, we kept the patient nil orally from 12 midnight and started glucose insulin potassium solution (500 mL of 10% glucose + 10 mEq of potassium + 10 units of insulin) at a rate of 75 mL/h. The same infusion was continued intraoperatively along with Ringer lactate to maintain mean blood pressure of more than 60 mmHg. Regional anesthesia was preferred for this patient because our goal was to provide adequate analgesia perioperatively and to avoid polypharmacy associated with general anesthesia.

Electro cardiogram, noninvasive blood pressure, pulse oximetry (SPO<sub>2</sub>), respiratory rate and urine output were monitored throughout the surgery. The baseline heart rate was 70 bpm and the BP was 110/60 mmHg, SPO<sub>2</sub> 100%. The patient was put in the left lateral position and, after infiltrating the skin with local anesthetic, an 18 G Tuohy's needle was inserted into the T12-L1 interspace and the epidural space was identified by loss of resistance technique. The epidural catheter was threaded through the needle and the test dose was given with 3 mL of 2% Lignocaine with Adrenaline. An initial dose of 16 mL 0.5% Bupivacaine was given and 5 mL of 0.5% Bupivacaine was given 15 min later. Analgesia was adequate. The surgery lasted 3 h and the intraoperative heart rate ranged from 60 to 100 bpm and BP from 90/60 to 110/70 mmHg. SPO<sub>2</sub> was 100%. Epidural top-ups with 0.5% Bupivacaine 5 mL were repeated three-times intraoperatively at 1 h 30 min and 2 h 30 min, to keep the level of blockade at T10, and at the end of surgery. Postoperatively, the patient was stable and was shifted to the recovery room. The immediate postoperative period was uneventful and the epidural infusion (0.0625% Bupivacaine + Fentanyl 2 mcg/mL) at a rate of 6 mL/h was started and continued for the next 24 h. The epidural catheter was removed after 12 h of the last low molecular weight heparin dose.

## DISCUSSION

Augustine Gilbert and Pierre Lereboullet first described the Gilbert syndrome,<sup>[3]</sup> the most common inherited cause of unconjugated hyperbilirubinemia, in 1901. This autosomal-recessive condition is characterized by intermittent jaundice in the absence of hemolysis or underlying liver disease. Unconjugated hyperbilirubinemia in Gilbert syndrome has long been recognized as due to underactivity of the conjugating enzyme system Bilirubin-Uridine Diphosphate Glucuronyl Transferase (Bilirubin-UGT). Bilirubin-UGT is responsible for

conjugating bilirubin into bilirubin monoglucuronides and diglucuronides, and is located primarily in the endoplasmic reticulum of the hepatocytes. Bilirubin-UGT is one of the several UGT enzyme isoforms responsible for the conjugation of a wide array of substrates, which include carcinogens, drugs, hormones and neurotransmitters.<sup>[2]</sup>

At least 30% of the patients are asymptomatic, although nonspecific symptoms, such as abdominal cramps, fatigue and malaise, are common. Mild jaundice is present intermittently in some individuals, but no other abnormal physical examination findings are evident.

Usually, the diagnosis of Gilbert's syndrome is that of exclusion. Most commonly performed laboratory studies include peripheral blood smear and lactate dehydrogenase (to rule out hemolysis) and liver function tests (with the exception of unconjugated hyperbilirubinemia), which are normal.

It is important for the anesthesiologist to understand conditions leading to decreased glucuronosyl transferase activity in Gilbert's syndrome patients to be submitted to anesthesia, to prevent intraoperative toxicity.<sup>[4]</sup> Perioperative goals in such patients are to (a) minimize fasting, start glucose infusion the night before surgery and perform the surgery in the morning session, preferably as the first case, (b) minimize stress by providing adequate analgesia during the intraoperative as well as during the postoperative periods, (c) avoid hepatotoxic drugs and drugs that are exclusively metabolized by the liver, (d) maintain hepatic blood flow by keeping the mean arterial pressure >60 mmHg and (e) avoid polypharmacy.

Epidural anesthesia was chosen in our patient primarily because of the potential deterioration in liver function and liver blood flow that may occur with general anesthesia. Other than this, we also had to deal with the unstable cardiac condition comprising of AF and increased pulmonary arterial hypertension in this patient. Studies have shown that controlled ventilation, inhalational anesthetics and surgical stress can decrease liver blood flow.<sup>[5-7]</sup> Regional anesthesia probably preserves liver blood flow as long as normotension is maintained.<sup>[8]</sup> Because the stress response during surgery is reduced with regional anesthesia, epidural anesthesia might be superior to general anesthesia as the stress associated with general anesthesia can lead to release of catecholamines, which can decrease liver blood flow. The rare potential hepatotoxicity associated with the inhalational anesthetics also makes regional anesthesia more attractive. Amide local anesthetics, which are the most commonly used, are metabolized primarily by microsomal P-450 enzymes in the liver (N-dealkylation and hydroxylation). The rate of liver metabolism among amides vary as follows:

Prilocaine > Lidocaine > Mepivacaine > Ropivacaine > Bupivacaine. Hence, Bupivacaine is the preferred agent for epidural anesthesia.

General anesthesia may also be considered for Gilbert's syndrome patients, but there are some caveats. Propofol and Remifentanyl should be preferred. Propofol has a higher clearance than liver blood flow, suggesting an extra-liver excretion pathway. Remifentanyl is an ester degraded by plasma and tissue esterases, unaffected by deranged liver function. Thiopental and ketamine affect liver function tests depending on the dose. Neuromuscular blocking agents of choice will be Atracurium and Cis-Atracurium, as these drugs undergo Hoffman's elimination and esterase metabolism.<sup>[9]</sup>

Among inhalational agents, halothane should be avoided during anesthesia because it is a halogenate with high liver metabolism (20%) and it has potential to cause postoperative jaundice. Sevoflurane undergoes 2% and Isoflurane has 0.2% liver metabolism. All volatile agents decrease total liver blood flow, and this decrease is maximum with Halothane and minimum with Isoflurane. For the above-mentioned reasons, Isoflurane is the most preferred volatile anesthetic agent in Gilbert's syndrome.<sup>[10]</sup>

To summarize, although Gilbert's syndrome is a benign condition with an indolent course, it poses a clinical challenge for anesthesiologists. The underactivity of bilirubin-UGT can lead to toxicity of most anesthetic agents, and this fact is of utmost importance to the anesthesiologists while choosing the type of anesthesia. It is prudent to use regional anesthesia whenever

possible and, if general anesthesia is required, it is better to use short-acting agents or those with extra hepatic metabolism.

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