Fracture Femur: A Case Report
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Abstract: Gilbert’s syndrome is a form of hereditary non-hemolytic jaundice transmitted by autosomal dominant pattern. Due to low glucuronyl transferase activity in the liver, there is a risk for toxicity towards various anaesthetic agents. It is important for the anesthesiologists to understand the pathophysiology of the disease and the conditions leading to decreased glucuronyl transferase activity. Here we report anaesthetic management of a case of Gilbert’s syndrome with chronic malunited supracondylar fracture femur with fracture upper end of tibia, the principles of management in intraoperative and postoperative period. Minimal administration of intravenous drugs, maintaining the organ perfusion and postoperative pain relief using epidural anesthesia offers a safe conduct of anesthesia which can be considered as an alternative to general anesthesia and can avoid potential toxic effects of the agents metabolised by the liver.

Keywords: Gilbert’s syndrome, general anesthesia, glucuronyl transferase.

INTRODUCTION
Gilbert’s syndrome is a hereditary (autosomal recessive) chronic unconjugated hyperbilirubinemia occurring in the absence of any symptoms of liver disease or in the absence of significant hemolysis. The hyperbilirubinemia, by definition is mild and less than 6 mg/dl [1]. The most significant feature of the hyperbilirubinemia is its aggravation with stress, fasting, infection, exercise and there may be a family history suggesting its inheritance pattern[2]. The perioperative anaesthetic management in a case of Gilbert’s syndrome can be challenging as most of the anaesthetic agents are metabolized in liver. Here we report anaesthetic management in a patient with Gilbert’s syndrome for fracture femur and fracture upper end tibia for illizarov’s fixation. Patient was on treatment with tab. Metoprolol and amlodipine for hypertension and tab metformin for diabetes.

CASE REPORT
A 52 year old male patient was scheduled for Illizarov’s external fixation for chronic malunited supracondylar fracture femur with fracture upper end of tibia. He was diagnosed with Gilbert’s syndrome 10 years back with yellowish discolouration of skin & sclera during period of stress and used to resolve spontaneously without any medical intervention. Patient was also on treatment with tab. Metoprolol and amlodipine for hypertension and tab metformin for diabetes. Laboratory Investigations showed 11.3 gm% Hb, Platelet counts 3.90 lacs/cumm, total bilirubin 7.3 mg% with direct bilirubin 0.6 mg%. Coagulation profile was normal. Liver enzymes were within normal limits except of raised serum alkaline phosphatase. Fasting and postprandial blood sugar was mildly elevated with normal serum glycosylated hemoglobin. Urine was negative for urobilinogen, bile pigments and bile salts. Peripheral smear showed normocytic norchromic RBCs with mild anisocytosis. Electrocardiograph was normal.

The patient was shifted on inj. Human Insulin as per sliding scale preoperatively with advice to withhold the drug in the morning of the surgery. Pt was adequately premedicated with T. Alprazolam 0.5 mg on the night prior to surgery and was kept 8 hr fasting for surgery with advice to take antihypertensive medications with sips of water on the morning of the surgery.

On the day of surgery, patient was taken for surgery yearly in the morning to avoid fasting for long duration. standard monitoring (pulse oximetry, NIBP, ECG) applied, oxygen was delivered via facemask at the rate of 5 lit/min and two wide bore intravenous access was instituted. Capillary blood sugar level was found to be 176 mg/dl and a neutralizing drip with 500 ml 5% dextrose, 10 meq potassium and 8 U Insulin was started at the rate of 100 ml/h. After that, infusion with normal...
saline and ringer lactate was continued intraoperatively as per hourly blood sugar monitoring.

Patient was given right lateral position and with all aseptic precaution, combined spinal-epidural (CSE) was given with inj Bupivacaine 0.5% (Hyperbaric) 3.5 cc as spinal drug. Patient was now given supine position. Adequate sensory level was achieved.

The surgery lasted for 8 hours. Epidural test dose was given after 1 hr of surgery and epidural infusion was started with 0.25% Bupivacaine at the rate of 6 ml/hour after giving an initial bolus dose with 0.5% bupivacaine 4 ml to keep the level of blockade at T10. There was profuse blood loss (around 2.5 litres) which was supplemented with colloids, 4 units of packed cell and 6 units of FFP. Intraoperatively, vitals, blood sugar level and urine output were maintained within normal range.

Postoperatively, the patient was started on LMW Heparin as DVT prophylaxis due to immobilisation 12 hrs after the surgery. Epidural Catheter was left in situ and epidural top ups with inj Bupivacaine 0.125% and Inj Fentanyl 25 mcg was given three times a day till 48 hrs. No other analgesic was required by the patient. There was a minimal rise in the bilirubin level on the second post operative day with total bilirubin of 8.1 mg/dl and indirect bilirubin of 7.4 mg/dl, with no significant changes in the enzyme levels. Epidural catheter was removed 12 hrs after last dose of LMW Heparin and the next dose was given after 6 hours of epidural catheter removal. On the subsequent days the bilirubin levels came down to 4.8 mg/dl and 4.2 mg/dl. His follow up after one week and at one month was uneventful.

**DISCUSSION**

Augustine Gilbert and Pierre Lereboullet first described the Gilbert syndrome, the most common inherited cause of unconjugated hyperbilirubinemia, in 1901[3]. 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[2]. Diagnosis is confirmed by giving phenobarbital which relieves the jaundice and IV nicotinic acid which aggravates it[4]. 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 individual.

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 to understand conditions leading to decreased glucuronosyltransferase activity in Gilbert’s syndrome patients to be induced, to prevent intraoperative toxicity [5]. Perioperative goals in such patients are to (a) minimize fasting 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 metabolized by the liver, (d) maintain hepatic blood flow by keeping the mean arterial pressure >60 mmHg and (e) avoid administration of multiple drugs.

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 worsen jaundice by causing stress response with sympathatic stimulation and decrease liver blood flow [6-8]. In our case, we decided to go for epidural anesthesia for better control of hemodynamics, attenuation of surgical stress response, effective pain relief, reduction in postoperative thrombo-embolic and cardio-respiratory complications. The rare potential hepatotoxicity associated with the inhalational anesthetics also makes regional anesthesia more attractive. The blood levels of local anesthetics are determined by the rate of uptake, tissue redistribution, metabolism and excretion. 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 varies as follows: Prilocaine>Lidocaine>Mepivacaine>Ropivacaine> Bupivacaine. Bupivacaine is cleared more slowly due to its decreased rate of hepatic degradation [9]. The aminooamide local anesthetics should be used cautiously used as decreased hepatic blood flow or impaired hepatic enzyme function can produce substantially elevated levels [10]. Moreover, it has been suggested that, for bilateral total knee arthroplasty, neuraxial anaesthesia decreases the rate of blood transfusion [11], which is applicable for major surgeries also as in this case.

When General anesthesia is required for patients with Gilbert’s syndrome, Propofol and Remifentanil should be preferred. Propofol has a higher
clearance than liver blood flow, suggesting an extra-liver excretion pathway via renal and lung metabolism. Remifentanil 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[12].

Among inhalational agents, halothane should be avoided because of it being a halogenated compound with high liver metabolism (20%) and having 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. Isoflurane, hence, is the most preferred volatile anesthetic agent in Gilbert’s syndrome [13].

Fentanyl is considered safe as its effect after a single bolus dose is terminated by redistribution to muscle and fat; subsequent metabolism is primarily by N-dealkylation to norfentanyl and its hydroxylation along with norfentanyl [14]. Although in a case report, general anesthesia was safely given with fentanyl, propofol, atracurium and maintained with isoflurane, oxygen and nitrous oxide [15], remarkable perioperative complications have also been reported after general anesthesia. Alarming levels of bilirubin in the postoperative period requiring plasmapheresis for 4 days have been reported [16]. Paracetamol was avoided as analgesic agent as the enzyme, metabolizing paracetamol, can be defective in Gilbert’s Syndrome.

TENS has also been applied in the postoperative period for pain relief. It has been proven by Chandra et al [17], that TENS can be used as an adjunct to epidural analgesia for acute postoperative pain without causing any squeals in addition to stabilizing the hemodynamics. The mechanism by which TENS produces analgesia is unclear and may be related to the modulation of nociceptive impulses in the spinal cord, release of endogenous endorphins and enkephalins or a combination of these and other mechanisms [18].

CONCLUSION
Although Gilbert’s syndrome is a benign condition, it poses a clinical challenge for anesthesiologists. The underactivity of bilirubin-UGT can lead to toxicity of most anesthetics, and this fact is of utmost importance while choosing the type of anesthesia. It is superior 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 or those that reduces hepatic blood flow least.

REFERENCES
17. Chandra A, Banavaliker JN, Das PK, Hasti S. Use pf TENS as an adjunctive to epidural analgesia in

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