Research Paper

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Anaesthetic Management of a Patient With Gilbert's Syndrome Posted for Laparoscopic Cholecystectomy

Medical Science

KEYWORDS : Gilbert's syndrome, Laparoscopic cholecystectomy, Anaesthetic management

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ABSTRACT

Gilbert'sSyndrome, a common cause of congenital hyperbilirubinemia, is caused by deficiency of glucuronyl transferase enzyme in the liver. It is important for anaesthesiologist to understand the pathophysiology of the disease as well as conditions leading to decreased glucuronyl transferase activity. We report anaesthetic management of a case of Gilbert's syndrome posted for laparoscopic cholecystectomy under general anaesthesia.

Introduction

Gilbert's syndrome is an inherited disorder of hepatic bilirubin metabolism caused by relative deficiency of glucuronyl transferase and poor uptake of unconjugated bilirubin by hepatocytes[2]. It is characterized by increased indirect bilirubin but other liver function tests are normal. Although Serum bilirubin level is mostly < 3 mg/dl; higher and lower values are also common. Higher values are associated with stress, exercise, alcohol use, fasting, concomitant illness, menstruation[3].

Syndrome may be diagnosed by family history, duration of the disease, lack of other liver diseases justifying jaundice. Diagnosis may be confirmed by jaundice improvement after phenobarbital and worsening after intravenous nicotinic acid[4].

Case Report

An 18-year-old female weighing 50 kg was posted for elective laparoscopic cholecystectomy. She had repeated episodes of jaundice and abdominal pain exacerbated by infection since birth for which she was given symptomatic treatment only. She was diagnosed with Gilbert's syndrome 8 years ago. Since last 2 year she had developed gall bladder calculus leading to cholecystitis which was diagnosed on ultrasonography of abdomen. Her liver function tests preoperatively revealed total bilirubin 2.87 mg/dl of which unconjugated part was 2.54 mg/dl. Aspartate aminotransferase and alanine aminotransferase were 23 IU/L and 16 IU/L respectively. Alkaline phosphatase was 66 IU/L. Serum albumin and total protein were normal. PT, APTT were also normal with INR 1.051. She was pre medicated with tab. alprazolam 0.25 mg and tab. ranitidine 150 mg on night before and on the morning of surgery at 6 am. She was scheduled first on the list at 9 am. A dextrose 5% was started at 7 am on the morning of the surgery and in the operation room it was converted to a normal saline drip at the start of surgery. Standard monitoring with five lead electrocardiograph, oxygen saturation, non-invasive blood pressure monitoring and end-tidal CO_2 were established. After giving injection(Inj) Glycopyrolate 0.2 mg and Inj ondansetron 4 mg IV, anaesthesia was induced with Inj fentanyl 100 μg, Inj propofol 100 mg, Inj atracurium 25mg. Trachea was intubated with 7mm cuffed portex endotracheal tube. Mechanical ventilation was established using Drager Fabius plus and maintained throughout the procedure Anaesthesia was maintained with oxygen, nitrous oxide and isoflurane and Inj atracurium. Intraoperative period was uneventful. Surgery lasted for 90 minutes. At the end of surgery instillation of gall bladder fossa with 30ml of 0.25% bupivacaine and infiltration of wound margin with 10ml of 0.125 % bupivacaine was done to minimize postoperative pain. Reversal of neuromuscular blockade was done with 0.4 mg inj glycopyrrolate and inj neostigmine 2.5 mg. Patient was extubated after she was fully awake and responding to verbal commands.

Postoperative analgesia was provided with intramuscular inj diclofenac sodium and intravenous inj tramadol twice a day. Bilirubin and other liver function tests were repeated on 3rd postoperative day which were normal and patient was discharged.

Discussion

Gilbert's syndrome is a form of hereditary non-haemolytic jaundice. It is transmitted by autosomal dominant pattern[5]. It causes a mild chronic unconjugated hyperbilirubinemia in otherwise healthy person. Screening for liver disease or haemolysis reveals no pathological finding but hepatic glucuronidation capacity is reduced by 70% [6]. For safe administration of anaesthesia knowledge of precipitating factor is must. Surgery and anaesthesia are stressful events, thus there is a possibility that bilirubin may increase postoperatively[6].

Many drugs are metabolized by glucuronyl transferase enzyme in the liver. Gilbert's syndrome can potentially cause such drugs to accumulate and lead to adverse outcome. Women taking oral contraceptive pills do not have symptoms as sex hormones induce this enzyme[7]. For the same reason pregnancy seems to have protective effect. This might explain the male preponderance.

For Gilbert's syndrome patients it is desirable that surgery be performed first in the morning to minimize fasting and waiting stress, glucose infusion before surgery, to avoid surgery during active menstrual cycle bleeding, to assure satisfactory postoperative analgesia[6]

To overcome stress on the night before surgery alprazolam was prescribed. Although lorazepam clearances have been reported to be 20-40% lower in Gilbert patients when compared with controls[8] there is no evidence of any adverse effect of single-dose alprazolam premedication. 5% dextrose was infused before surgery to prevent jaundice triggering-factor, and was not maintained during surgery since it is well known that surgery represents major stress with increased glycaemia as neuroendocrine-metabolic response.

Thiopental and ketamine change liver function tests depending on the dose [9]and may impair postoperative investigation of jaundice. Etomidate may lead to adrenal failure by 17 alpha-hydroxilase and 11 beta-hydroxilase enzymes inhibition[10]. These drugs should be avoided. Propofol has a higher clearance than liver blood flow suggesting an extra-liver excretion pathway thus it should be preffered[10].

Fentanyl was 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[11]. Remifentanil is a safer alternative due to its ultra-short duration of action and its metabolism by blood and tissue esterase.. Atracurium was preferred due to its Hofmann degradation and ester hydrolysis. Mivacurium and Cisatracurium could have been the other safer alternatives due to its similar metabolic pathway. There is no evidence about prolongation of other muscle relaxants[12].

All volatile agents decrease total liver blood flow and this decrease is maximum with halothane and minimum with isoflurane[13]. Metabolism of Isoflurane in liver is < 0.2% therefore it is the most adequate volatile anesthetic agent for patients with liver dysfunction[9].

Diclofenac sodium and tramadol were used for postoperative analgesia. Paracetamol and morphine were specifically avoided. Paracetamol is metabolized by enzyme other than glucuronyl transferase, which may be also deficient in some cases of Gilbert's syndrome[14] leading to potential risk of paracetamol toxicity. Morphine is metabolized in the liver by glucuronyl transferase so its effect is prolonged in Gilbert's syndrome[15].

Conclusion

Gilbert's syndrome patients may be safely submitted to general anesthesia without toxicity, provided factors leading to decrease glucuronyl transferase activity are avoided. To prevent adverse outcome, we should avoid perioperative stress and ensure adequate hydration.

REFERENCE

1. Chapman RW, Collier JD, Hayes PC. Liver and biliary tract disease. In: Boon NA, Colledge NR, Walker BR, editors. Davidson's Principles and Practice of Medicine. 20th ed. Philadelphia, USA: Churchill Livingstone Elsevier 2008. pp. 925–6. | 2. Strassburg CP. Hyperbilirubinemia syndromes (Gilbert-Meulengracht, Crigler-Najjar, Dubin-Johnson, and Rotor syndrome) Best Pract Res Clin Gastroenterol 2010;24:555–71. | 3. Wolkoff AW. The hyperbilirubinemias. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, LOscalzo J, editors. Harrison's Principles of Internal Medicine. 17th edition. New York: Mcgraw-Hill 2008:1929. | 4. Radu P, Atsmon J - Gilbert's syndrome - clinical and pharmacological implications. Isr Med Assoc J 2001;3:593-598. | 5. Borlak J, Thum T, Landt O, Erb K, Hermann R. Molecular diagnosis of a familial non hemolytic hyperbilirubinemia (Gilbert's syndrome) in healthy subjects. Hepatology2000;32:792–5. | 6. Taylor S. Gilbert's syndrome as a cause of postoperative jaundice. | Anaesthesia 1984;39:1222–4. | 7. Powell LW, Hemingway E, Billing BH, Sherlock S. Idiopathic unconjugated hyperbilirubinemia (Gilbert's syndrome): A study of 42 families. N Engl J Med 1967;277:1108–12. | 8. Tukey RH, Strassburg CP. Human UDP-glucuronosyltransferases: Metabolism, expression, and disease.Annu Rev Pharmacol Toxicol2000;40:581–616. | 9. Savaris N, Freitas JCM - Complicações em Anestesia, em: Manica JT - Anestesiologia Princípios e Técnicas, 2ª Ed, Porto Alegre, Artes Médicas 1997;780-806. | 10.White PF, Gonzáles JM, Hemelrijck JV - Farmacologia dos Anestésicos Intravenosos, em: Rogers MC, Tinker JH, Covino BG et al - Princípios e Prática de Anestesiologia, 1ª Ed, Rio de Janeiro, Guanabara Koogan 1996;837-853. | 11. Mather LE. Clinical pharmacokinetics of fentanyl and its newer derivatives. Clin Pharmacokinet1983;8:422–46. | 12. Bosma PJ, Chowdhury JR, Bakker C, Gantla S, de Boer A, Oostra BA, et al. The genetic basis of the reduced expression of bilirubin UDP-glucuronosyltransferase 1 in Gilbert's syndrome. N Engl J Med1995;333:1171–5. | 13. Morgan Jr GE, Mikhail MS - Fisiologia Hepática e Anestesia, em: Morgan Jr GE, Mikhail MS. Anestesiologia Clínica, 2ª Ed, Rio de Janeiro, Revinter 2003;587-99. | 14. Rauchschwalbe SK, Zühlsdorf MT, Wensing G, Kuhlmann J. Glucuronidation of acetaminophen is independent of UGT1A1 promotor genotype. Int J Clin Pharmacol Ther 2004;42:73–7. | 15. Nishimura TG, Jackson SH, Cpohen SN. Prolongation of morphine anaesthesia in a patient with Gilbert's disease: Report of a case. Can Anaesth Soc J 1973;20:709–12.