

Anesthetic management of a case of Gilbert's syndrome for mitral and aortic valve replacement: Role of transesophageal echocardiography

ABSTRACT

Gilbert's syndrome (GS) is an autosomal inherited disorder characterized by relative deficiency of glucuronyl transferase and poor uptake of unconjugated bilirubin by hepatocytes. Cardiac surgery on cardiopulmonary bypass (CPB) in these patients triggers further hepatic dysfunction. Transesophageal echocardiography (TEE) and Doppler assessment of hepatic vein help in assessing hepatic blood flow (HBF) during cardiac surgery. Here, we discuss anesthetic management and role of TEE in maintaining HBF perioperatively in a 25-year-old male patient with GS undergoing double valve replacement with tricuspid valve plasty. TEE-guided HBF monitoring and management of hepatic perfusion by modifying anesthetic and CPB protocol resulted in the favorable outcome.

Key words: Bilirubin, general anesthesia, Gilbert syndrome, transesophageal echocardiography

Introduction

Gilbert's syndrome (GS) is an autosomal hereditary disorder characterized by unconjugated hyperbilirubinemia with an incidence of 3–10%.^[1,2] It occurs due to an abnormal conjugation of bilirubin caused by deficiency of bilirubin uridine diphosphate glucuronyl transferase enzyme.^[3] Majority of GS patients present with mild jaundice (<6 mg/dl) but when exposed to triggering factors such as stress, infection, fasting, and exercise will result in exacerbation of the disease process.^[4] General anesthesia (GA), cardiac surgery and cardiopulmonary bypass (CPB) can act as precipitating factors which may

worsen the already compromised hepatic function. There are various techniques to monitor hepatic blood flow (HBF) intraoperatively which are invasive and not feasible.^[5] Transesophageal echocardiography (TEE) and Doppler assessment of hepatic vein help in assessing HBF during cardiac surgery. Here, we report the role of TEE in maintaining HBF perioperatively by modified anesthetic and CPB management in a 25-year-old male patient with GS undergoing double valve replacement (DVR) with tricuspid valve (TV) plasty.

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P. S. NAGARAJA, NAVEEN G. SINGH, S. SUBASH, N. MANJUNATHA, C. G. PRABHUSHANKAR, N. SATHISH

Department of Cardiac Anaesthesiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India

Address for correspondence: Dr. Naveen G. Singh, Department of Cardiac Anaesthesiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Jayanagara 9th Block, Bengaluru - 560 069, Karnataka, India. E-mail: drnaveengsingh@gmail.com

Case Report

A 25-year-old male presented with symptoms of dyspnea (New York Heart Association 2), palpitations and fatigue since 8 months who was diagnosed as GS 10 years ago. On examination pulse rate of 90/min, blood pressure (BP) 120/50 mm Hg, icterus positive, raised jugular venous pressure, early diastolic murmur at aortic area, pan systolic murmur heard both in mitral area and tricuspid area. Cardiomegaly was present in chest X-ray. Electrocardiogram (ECG) showed left ventricular hypertrophy and atrial fibrillation; trans-thoracic echocardiography revealed severe mitral regurgitation, severe aortic regurgitation with Grade 3 tricuspid regurgitation with pulmonary hypertension and biventricular dysfunction with ejection fraction of 36%. Preoperative blood investigation is shown in Table 1. The patient was scheduled for DVR with TV plasty under hypothermic CPB. The patient was kept nil per oral for 8 h but was allowed to have clear fluids 2 h before surgery. Intravenous 5% dextrose was started on the morning of surgery. The patient was premedicated with 2 mg of oral lorazepam, 2 h before surgery. ECG, invasive BP, central venous pressure, pulse oximetry, temperature, urine output, bispectral index (BIS), endtidal-CO₂ and TEE were monitored throughout the surgery. GA was induced with injection midazolam 0.02 mg/kg, injection fentanyl 4 mcg/kg, titrated dose of injection propofol and trachea was intubated with 8.5 cuffed endotracheal tube after adequate relaxation with 1 mg/kg of injection atracurium. The patient was mechanically ventilated with an oxygen-air mixture of 50:50 and anesthesia was maintained with fentanyl 0.5 mcg/kg/h, atracurium 0.5 mg/kg/h, isoflurane, and propofol infusion titrated to BIS value 50–60. Injection tranexamic acid 10 mg/kg was administered after induction, and 10 mg/kg was added to the CPB pump prime. 350 ml of autologous blood was extracted postinduction. A 5 MHz Biplane TEE probe (Philips EnVisor CHD, Bothell, Washington, USA 98041) was inserted after induction of anesthesia. Hepatic vein was

visualized using TEE as previously reported^[5] and HBF was calculated using the formulae: $\pi (d/2)^2 \times VTI \times HR$ during off pump and $\pi (d/2)^2 \times Vm \times 60$ during CPB (d = diameter, HR = heart rate, Vm = mean velocity, VTI = velocity time integral) [Figure 1].

After adequate heparinization to achieve ACT > 480 s CPB was initiated. A high flow rate of 2.2–2.5 L/min/m² maintaining a mean arterial pressure of 70–80 mmHg with temperature between 28°C and 30°C constituted CPB protocol for better hepatic perfusion. Anesthesia during CPB was maintained with propofol infusion and isoflurane titrated to BIS. Injection sodium nitroprusside (SNP) infusion was started to accommodate higher pump flow rate. Patient was weaned from CPB with injection dopamine 5 mcg/kg/min, adrenaline 0.05 mcg/kg/min, and SNP 0.5 mcg/kg/min. Modified ultrafiltration was performed after weaning from CPB. Heparin was neutralized with a corresponding dose of protamine sulfate. Aortic cross-clamp time was 118 min, total CPB time was 146 min, and total duration of surgery was 270 min.

The estimated average HBF using TEE was 390 ml/min after induction of anesthesia, 366 ml/min on CPB and 412 ml/min 1 h post-CPB [Figure 1].

The patient was shifted to postoperative Intensive Care Unit (ICU) for further management and was extubated 8 h postsurgery. Postoperative laboratory investigations are shown in Table 1. The patient was discharged after 7 days of surgery which included 3 days of ICU admission. One year follow-up of the patient showed no further deterioration in hepatic function.

Discussion

Augustine Gilberte and Pierre Leteboullet first described the Gilbert syndrome, the most common inherited cause of unconjugated hyperbilirubinemia. Previous case reports on GS undergoing noncardiac surgeries have documented better outcome.^[3,6] However, there is limited literature on the use of TEE for monitoring hepatic perfusion in GS patients undergoing cardiac surgery. GS is characterized by unconjugated hyperbilirubinemia with the absence of hemolysis or underlying liver disease. The present case was classified under Class B of modified Child-Pugh score. Previous articles have reported mortality ranging from 18% to 80% who were classified under Class B modified Child-Pugh score undergoing cardiac surgery.^[7,8] Preoperatively, patient had liver dysfunction both due to GS and right ventricular (RV) dysfunction. Anesthetic and CPB management goals were aimed at preventing further hepatic dysfunction [Tables 2a and b].

Table 1: Laboratory investigations

Parameters	Normal values	Preoperative	First POD	Second POD	Tenth POD	1 year
HB (g/dl)	14-16	12.3	11.4	8.8	10.2	11.6
Platelet count (L/mm ³)	1.5-4.5	1.89	1.24	1.04	1.35	1.7
INR		1.2	1.63	2.8	2.8	3.2
Serum bilirubin (mg/dl)	<1	9.5	8.9	8.0	3.5	4.7
SGOT (U/L)	4-40	78	139	100	16	37
SGPT (U/L)	2-40	69	88	61	10	44
Albumin (g/dl)	3-5	4.5	3.6	3.0	2.9	3.2
ALP (IU/L)	40-130	72	51	50	68	77

SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamate pyruvate transaminase; ALP: Alkaline phosphatase; POD: Postoperative day; HB: Hemoglobin

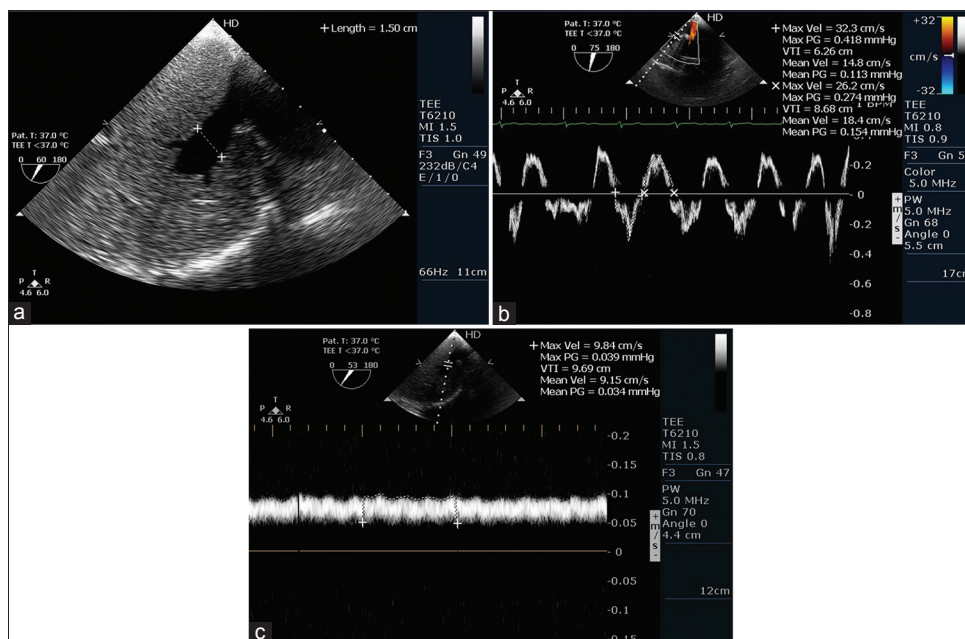


Figure 1: Transesophageal echocardiography estimation of hepatic blood flow. (a) Hepatic vein diameter, (b) pulse wave Doppler of hepatic blood flow off cardiopulmonary bypass, (c) pulse wave Doppler of hepatic blood flow on cardiopulmonary bypass

Table 2a: Anesthetic management

Anaesthetic management	Rationale for modification
Modified fasting guidelines: allowed clear liquids 2 h prior to surgery	Minimize fasting as it exacerbates GS ^[3,6]
Avoid hepatotoxic drugs	Lorazepam: Least hepatic metabolism ^[3] Propofol: Extrahepatic metabolism ^[3,6] Fentanyl: Redistribution to muscle and fat ^[3,6] Atracurium: Plasma esterase metabolism ^[3,6] Isoflurane: 0.2% hepatic metabolism and best maintains HBF as compared to other volatiles ^[3,6]
BIS monitoring for adequate depth and to titrate drugs	Stress due to surgery and CPB precipitates GS ^[3,6] Fast tracking
MAP > 70 mmHg	To maintain hepatic perfusion
Rationalize blood transfusions	Precipitates GS

CPB: Cardiopulmonary bypass; HBF: Hepatic blood flow; GS: Gilbert's syndrome; MAP: Mean arterial pressure; BIS: Bispectral index

The intra-operative monitoring of hepatic perfusion is ideal to guide the effectiveness of anesthetic goals. Various techniques have been used to record hepatic venous velocities, which are not feasible intraoperatively.^[5] TEE is routinely used in cardiac surgery for monitoring of valvular and ventricular function. Previous studies have demonstrated HBF using TEE in noncardiac surgery.^[9] CPB causes a decrease in hepatic perfusion. Previous studies have demonstrated a 19% drop in HBF during CPB using galactose clearance technique in patients with normal hepatic function.^[8,10] However, the present case had a total bilirubin level of 9 mg/dl, but in GS the bilirubin levels does not exceed 6 mg/dl, and high levels of bilirubinemia

Table 2b: Cardiopulmonary bypass management

CPB	Rationale for modification
Higher pump flow	To maintain HBF
MAP > 70 mmHg	
SNP infusion	To accommodate high pump flow rates and maintain hepatic perfusion
Mild hypothermia	Reduced hepatic perfusion due to vasoconstriction
Complete unobstructed venous drainage	Back pressure leading to hepatic congestion
Use of ultrafiltration and restricted blood transfusion	To reduce inflammation

HBF: Hepatic blood flow; MAP: Mean arterial pressure; SNP: Sodium nitroprusside; CPB: Cardiopulmonary bypass

could be explained by an added impact of RV dysfunction. Modified anesthetic and CPB strategies [Tables 2a and b] were aimed at maintaining HBF guided by TEE and was never allowed to drop more than 19%. In the present case, TEE demonstrated a drop of 6% in HBF during CPB as compared to the baseline value.

Conclusion

Understanding the pathophysiology of GS with associated RV dysfunction allowing modification of anesthetic, CPB management accordingly with TEE-guided HBF monitoring and management of hepatic perfusion resulted in the favorable outcome.

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Conflicts of interest

There are no conflicts of interest.

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