Journal of Anesthesia and Clinical Research

Mohanty, J Anesth Clin Res 2018, 9:7
DOI: 10.4172/2155-6148.1000845

Case Report Open Access

Anaesthetic Management in a Case of Wilson's Disease in Pregnancy

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Received date: June 21, 2018; **Accepted date:** July 13, 2018; **Published date:** July 18, 2018

Abstract

Wilson's disease (WD) is an inherited autosomal recessive disease results due to deficiency of ceruloplasmin leading to copper deposition mainly liver, brain and cornea. This accumulation can cause liver cirrhosis, ataxia and kayser Fleischer ring (KF) in cornea. I present a case of 21-year-old primigravida diagnosed WD 3 years back on treatment with Zinc was referred to our hospital for elective caesarean section (CS). She had thrombocytopenia, extrahepatic portal vein obstruction with hypersplenism and mild ascites. She has undergone CS under general anaesthesia (GA) with successful outcome. The anaesthetic management in presence of hepatic dysfunction and thrombocytopenia was challenging and there are only few case reports on WD patients undergoing CS under GA.

Keywords: Wilson's disease; Pregnancy; Caesarean section; Thrombocytopenia; General anaesthesia

Introduction

Wilson's disease (WD) or hepatolenticular degeneration is an autosomal recessive disorder characterized by a reduction in the synthesis of the copper transporter protein ceruloplasmin leading to the accumulation of copper in body tissues and consequent hepatic and neurological impairment. Excessive copper is teratogenic and has been associated with foetal intrauterine growth restriction and neurological sequel. There is also an increased risk of hypertensive disorders in Pregnancy, HELLP (haemolytic anaemia, elevated liver enzyme and low platelet count) and placental abruption associated with WD. The disease status at the time of presentation for surgery should determine the mode of anesthesia, intraoperative management and post-operative care. I present a 21-year-old female pregnant patient posted for elective CS, where surgery was successfully done under GA.

Case Report

A 21-year-old pregnant female who was diagnosed Wilson's disease (WD) 3 years back was admitted for safe confinement of pregnancy. She was diagnosed WD with extra hepatic portal venous obstruction, chronic liver disease with hypersplenism. She had history of one abortion at 12 weeks gestation in previous pregnancy. She had history of recurrent jaundice and platelet transfusion of 4 units 8 months back. Her investigations revealed Hb-10.3 gm%, Platelet- 40,000/cmm, BUN (blood urea nitrogen)-7.1 gm, Creatinine-0.6 mg. Bilirubin T/D (total/direct)-1.2/0.8, Serum aspartate aminotransferase (SGOT)-53, Serum alanine transaminase (SGPT)-33 I, alkaline phophatatse (ALP)-170 U/L, and serum electrolytes were within normal limits. Serum Copper-76 mg/dl, Urine copper-224 µg/min, prothrombin time (PT)-14.3/13, international normalized ratio (INR)-1.07, serum ceruloplasmin-13.7 mg/dl. Liver biopsy not done in view of pregnant status. Ophthalmology opinion revealed no KF (Kayser–Fleischer) ring. Ultrasonography of abdomen revealed mild ascites, liver parenchymal disease with massive splenomegaly. Hepato-portal Doppler showed dilated portal vein of 15 mm and splenic vein. She was on treatment with Zinc acetate 50 mg three times a day. The patient was of average built with weight 55 Kg. Pulse rate of 90/min, BP-130/80, RR-14/min. Her mallampati grading was II. Gastroenterology opinion was taken for medical management before surgery and clearance was obtained for surgery. She was advised to continue Zinc as before. She was posted for elective Caesarian section. Induction was conducted with Propofol 2 mg/kg, atracurium 0.5 mg/kg followed by securing of airway with 7.0 no cuffed endotracheal tube. Anesthesia was maintained with 66% N_2O with O_2 and 1% isoflurane. 4 units of Platelet concentrate was transfused at the time of induction. After delivery of baby patient was sedated with fentanyl 100 microgram. There was no hemodynamic instability perioperatively with a normal urine output of 150 ml. The approximate blood loss was 1200 ml. After surgery patient was reversed with neostigmine 2 mg and glycopyrrolate 0.3 mg and extubated successfully.

Transverse abdominis plane block was administered using 0.3 ml/kg of 0.25% isobaric bupivacaine both sides towards the end of closure. Post-operative analgesia was supplemented with oral paracetamol and diclofenac for initial 48 h. In terms of rescue analgesia, we have used intravenous tramadol 100 mg along with antiemetic intermittently (maximum upto 3 times) in the post-operative 48 h observation period.

Patient was transfused with one unit of fresh whole blood and 2 units of remaining platelet concentrate after shifting to post anesthesia recovery unit. Both mother and baby were discharged in a stable condition after 4 days with advice for follow up with the hepatology department.

Discussion

Wilson's disease (WD) is an autosomal recessive disorder with an estimated incidence of 1: 40,000 characterized by hepatic, ophthalmic, and neuropsychiatric symptoms from excess copper accumulation [1]. Due to involvement of liver and brain, pregnancy becomes high risk and is associated preeclampsia, thrombocytopenia and deranged coagulation. Pregnancy with Wilson's disease (WD) becomes high risk as it is associated with high incidence of abortions [2]. The mechanism

of abortion is same as that of copper containing contraceptive devices which exert their contraceptive actions due to deposition of copper ions in endometrium. My patient had a previous miscarriage before this pregnancy. Członkowska et al. reported a case where thrombocytopenia was a component of HELLP syndrome [3]. Thrombocytopenias as a single complication of Wilson's disease without preeclampsia are rare. Acharya et al. reported a case where the patient had only thrombocytopenia without preeclampsia [2]. In our case also patient had thrombocytopenia without any feature of preeclampsia.

Treatment of WD includes reducing dietary copper intake, antagonizing its absorption with zinc, or chelation with penicillamine, trientine or ammonium tetrathiomolybdate. Liver transplantation is indicated when all treatment measures failed [4,5]. Penicillamine, trientine and zinc are the approved drug by the US FDA in pregnancy. There is a report of chromosomal abnormality in a woman who took trientine during pregnancy. Brewer et al reported that use of zinc in 26 pregnancies with WD resulted in 24 healthy pregnancies, 1st baby was born with a heart defect requiring surgery at 6 month and a 2nd baby was born with microcephaly [5]. Our patient was on zinc therapy throughout the pregnancy without any complications and congenital abnormalities.

Successful spontaneous normal vaginal delivery in pregnancy with Wilsons disease has been reported in literature. Malik et al. reported a case series where 3 out 4 cases with WD have normal vaginal delivery, while one has to do emergency caesarean section due to non progress of labour [6]. In our case as the patient had history of previous abortion, elective caesarean section was planned for this precious pregnancy.

Although different anaesthesia technique has been used in WD patients undergoing different surgeries, the best anesthesia technique remains elusive. General, subarachnoid and epidural anesthesia have all been reported in patients with Wilson's disease [7]. Either general or regional anesthesia causes a moderate reduction in hepatic blood flow and hepatic oxygen uptake.

Regional anesthesia may be safe since peripheral nerve transmission is not altered in Wilson disease. Neuraxial anesthesia could be considered in the absence of significant coagulopathy or thrombocytopenia [8,9]. Kerem et al. has reported a case with cerebral manifestations of WD where spinal anesthesia was safely given to an 18-year-old girl for fixation of femur fracture [10]. Kousalya et al. reported a case where they have successfully managed a case of emergency caesarean section in a Wilson's disease patient with lower limb weakness with spinal anaesthesia [11,12]. However, in our case, patient was having thrombocytopenia which is a contraindication for regional anaesthesia, hence administered general anesthesia.

Successful general anaesthesia has been described by Baykal et al. in a 4-year-old child with Wilson's disease [13]. Nanjangud et al. reported a case where they have successfully managed abscess drainage in a 15-year-old girl with Wilson's disease having severe neuropsychiatric manifestation under general anaesthesia [14]. To our knowledge, this is the first case of pregnancy with Wilson's disease who was managed with general anaesthesia without any complications.

General anaesthesia usually causes hypotension and decreased liver blood flow, which can cause increased damage to an already compromised liver. Moreover, impaired hepatic function adversely affects the absorption, distribution, metabolism, and elimination of anaesthetic drugs. Hypnotic sedatives may have delayed or incomplete metabolism exacerbating postoperative neurological and psychiatric problems [7]. Fentanyl, which is a narcotic which is least affected by liver disease and isoflurane, an inhalational agent that can cause increased blood flow to liver are safer agents to use in this condition [12]. As our case had no previous neuropsychiatric manifestations before induction, we have successfully given opioids and also postoperatively patient was neurologically intact.

There is increased sensitivity to sedative and cardiorespiratory depressant effects of propofol; however, clearance is not significantly impaired by liver disease. The metabolism of suxamethonium may be slowed because of reduced pseudo cholinesterase. Patients may be more sensitive to neuromuscular relaxants from reduced muscle functioning secondary to the disease, elevated blood copper levels interfering with neuromuscular transmission, or the use of D-Penicillamine [7]. We have used atracurium, which is considered safe in liver disease due to its spontaneous degradation by Hoffmann elimination.

The pharmacokinetic parameters of paracetamol are altered in patients with severe liver disease, but the short-term use of this drug at reduced dose appears to be safe in patients with non-alcoholic liver disease [15]. In our case, because of mild deranged liver enzymes, we have used paracetamol for post op analgesia.

The main concern with NSAIDs in liver disease is the risk of precipitating renal impairment *via* constriction of afferent glomerular arterioles and hence reduced renal perfusion. Pre-existing renal dysfunction is quite common in liver disease [16]. In our case, the patient did not have feature of renal dysfunction apart from thrombocytopenia. There are evidences showing liver toxicity with use of diclofenac causing rise in transaminases and cholestatic hepatitis [17]. NSAIDS unlike aspirin reversibly inhibit cyclooxygenase and have very minimal effect on bleeding time [18]. But in our case diclofenac was used only for a short period upto initial 48 h.

Conclusion

Wilsons disease patient in pregnancy having thrombocytopenia and mild liver derangement can be safely administered general anaesthesia for caesarean section using agents which are least toxic to liver with meticulous monitoring during intraoperative and post-operative period. Regular follow up in subsequent days is indicated for better outcome and avoidance of post-operative complications. Further large studies are recommended in this area for better evidence.

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