CASE REPORT

ANAESTHETIC MANAGEMENT OF A DIAGNOSED CASE OF CRIGLER- NAJJAR SYNDROME POSTED FOR CAESAREAN SECTION

Mamta Khandelwal[1,*], Debojyoti Dutta[2], Samiksha Khanooja[3], Sunil Chauhan[4], Mohit Anand[5]

[1,4]Associate Professor, [3]Senior Resident, [2,5]Resident, Department of Anaesthesiology, SMS Medical College, Jaipur

*Corresponding Author
Email: drmamtakhandelwal@gmail.com

ABSTRACT

Crigler Najjar syndrome (CNS) is a rare disorder which affects the metabolism of bilirubin and clinically manifests as intense unconjugated hyperbilirubinemia without evidence of hemolysis. CNS-II in pregnant woman is a very rare condition and till now very little have been known about the maternal and foetal effect in this condition .We are presenting the anaesthetic management of a diagnosed case of Crigler – Najjar syndrome (CNS) 2 posted for emergency lower segment caesarean section (LSCS).

INTRODUCTION

Crigler-Najjar Syndrome (CNS) is an autosomal recessive genetic disorder characterised by persistent indirect hyperbilirubinemia due to defect in the bilirubin conjugation in the hepatocytes. There is the deficiency or defect in the enzyme UDP-glucoronyltransferase. It is of two types- type –I – there is total absence of the enzyme and in type-II – there is markedly reduced activity (0-10% of the normal activity) of the enzyme.[1] The enzyme UDP-glucoronyl transferase is encoded by the gene UGT1A1 which is located in the chromosome 2q37.In CNS-IA, majority of the patients , there is mutation in the common exon (2-5) of the UGT1 Gene complex leading to defect in the metabolism (glucoronidation) of bilbirubin and various other substrates including xenobiotics but in CNS-IB there is mutation in the bilirubin specific exon A1 , so there is only defect in the bilirubin conjugation. More than 77 genetic mutation have been found in the CNS-I & II but among them missense mutation is more common in CNS-II leading to production of a UDP-glucoronyl transferase of markedly reduced but detectable enzymatic activity [approx.10% of the normal UDPGT activity].[2,3]

The first case of CNS-I was reported by Crigler and Najjar in 1952 and which was characterised by hyperbilirubinemia that was resistant to phenobarbitone therapy and phototherapy and ultimately the child developed kernicterus and died.[4] The first case of CNS-II was reported by Arias in 1962 which was with mild hyperbilirubinemia and that responded to phenobarbitone therapy.[5] It is also known as Arias' syndrome and autosomal recessive in inheritance. The affected individuals usually have the total serum bilirubin level within 250–500μmol/L (15–30 mg/dL) and the total serum albumin of 550–650 μmol/L (3.6–4.4 g/dL). [6] These patients are mainly treated with enzyme induction therapy to enhance bilirubin excretion from the body by converting water soluble bilirubin molecule to water soluble form after conjugation. Among the drugs that induce glucuronosyl transferase activity phenobarbital and rifampicin are mostly used. [7]Phototherapy has recently been reported to be beneficial during pregnancy in a patient with Crigler-Najjar Type II syndrome by decreasing the maternal serum levels of bilirubin. [8]

As CNS-II in pregnant woman is very rare condition and till now very little have been known about the effect of this condition on the maternal and foetal outcome during pregnancy, we report a case of CNS-II in a pregnant woman, her pregnancy management and its outcome both maternal and foetal.

CASE REPORT

A 25yrs old pregnant woman gravida-2, abortion-1, presented to us at 37 weeks of gestation for emergency LSCS. She was a diagnosed case of Crigler–Najjar Syndrome type-II since her 13 yrs of age and was prescribed tab. phenobarbitone (60 mg) once daily to control serum bilirubin level but she never took the medication. She has jaundice from the 2nd day of her birth and there were several episodes of jaundice in the past but it never got cured. All developmental milestones were normal throughout the childhood and there has been no neurological deficit. In the family history, among the three brothers, one brother is normal and the other two brothers are also diagnosed as Crigler-Najjar Syndrome type-II and one of them has difficulty in speech and walking. In her current investigations, total serum bilirubin- 8.6mg/dL, (direct bilirubin-0.5 indirect bilirubin 8.1mg/dL) albumin- 3.5g/dL globulin 3.18g/dL A: G-1.1:1and
PT/INR(13.8(test),12.7(control)/1.1

The other routine blood investigation, USG abdomen and ECG were within normal limits and all the viral markers were non-reactive. Trial of vaginal delivery was given but it failed. Hence LSCS was planned and the patient was taken to the operation theatre with written informed consent. The patient had a cup of tea 1 hour back and hence was not fasting. Multipara monitor was attached to the patient. Preoperative vitals ECG- sinus rhythm ,SBP-131mmHg , DBP- 79mmHg , MAP - 93mmHg , Pulse – 107 / min and SPO2- 100 % in room air were recorded. IV line was secured with18G cannula and inj.ringer Lactate was started. inj.ranitidine (50mg) + inj.metoclopramide (10mg) iv given for aspiration prophylaxis .The patient was kept in sitting position. Sub-arachanoid block was given with Inj.Lignocaine 5% heavy (1.2 ml) in between L3-L4 space under full aseptic precaution. Then the patient was made supine with a slight head down tilt and surgery was started after complete sensory block up to T6 level and complete motor blockade (Modified Bromage-3) had achieved.

Intraoperatively 5min after the SAB, pulse rate dropped to 45 beats per min along with blood pressure of 76/60 mmHg. inj. atropine (0.6mg) and inj. mephenteramine (6mg) was given iv. The next reading of blood pressure was 80/60 and heart rate was 80/min hence a second dose of inj mephenteramine 6mg was given iv and inj. HES (hydroxyl ethyl starch)6% was started as second iv fluid. Vital parameters became stable. The blood pressure was 102/72mmHg, pulse rate 74/min and spo2 of 100%. After the delivery of the baby, inj.oxytocin (5 IU) diluted in 10ml normal saline was given through the iv cannula .Vitals remained within normal range for the rest of the procedure. Total iv fluid given was 1500 ml and urine output was 250 ml. Surgery lasted for 30 min. Her blood pressure was 114/70mmHg, pulse rate-70/min and Spo2-100% on room air when she was shifted to recovery room.

The baby was healthy, cried immediately after birth, weight- 2.8kg, APGAR score- 8, 9 at1 min, 5 min, cord was having yellowish tinge. The baby showed yellowish discolouration and icterus at the time of birth. After the delivery, maternal bilirubin level at 2nd postoperative day was 8.5mg/dl; albumin level was 3.1gm/dl. The baby became anicteric gradually within 1st week of birth. On the 7th postoperative day the mother was discharged from the hospital with a healthy baby.

DISCUSSION

As acute or chronic liver disease reduces the human fertility and increases the likelihood of abortion and foetal abnormalities[9,10],unconjugated hyperbilirubinemia can also pose detrimental effect to the foetus. The lipid soluble, unconjugated bilirubin can cross the placental barrier and also the foetal blood brain barrier (as it is not mature enough) and leads to foetal hyperbilirubinemia and kernicterus .[11] In CNS type II we as anaesthesiologists should be aware of the conditions which can lead to the rise of serum free bilirubin .Our goals being to1) avoid the drugs that displacebilirubin from albumin, 2) minimize the surgical stress as it rises the serum bilirubin: albumin ratio 3) avoid hepatotoxic drugs 4) maintain hepatic blood flow by keeping the mean arterial pressure >60mm Hg. Highly protein-bound drugs displace

bilirubin from albumin. As the drugs used in anaesthesia displace bilirubin from albumin hence a meticulous choice and administration of anaesthetic agents in appropriate dosage is must. Though certain anaesthetic drugs like benzodiazepines, sodium thiopental, etomidate are known to bound to the albumin but limited data is available whether these drugs displace bilirubin from albumin or not.[7] On the other hand, propofol displaces bilirubin from albumin by it's fatty acid components [7] and also inhalational anaesthetics like sevoflurane , isoflurane are known cause hyperbilirubinemia without altering protein binding efficacy of bilirubin.[12,13]

Albumin and alpha1-acid glycoprotein are the main binding sites for local anaesthetics. The binding affinity to alpha1-acid glycoprotein is greater than albumin. The high affinity and low capacity binding characteristics to the AAG makes it easily saturable and renders the rest of the LA to bind to the albumin. On the contrary, the concentration of the LA drugs can bind to the albumin is hugely greater than the clinically achieved concentration in the plasma. [14] Among the local anaesthetics, bupivacaine (85-90%), ropivacaine (94%) have higher protein binding affinity than lignocaine (55-65%).[15] Hence we used lignocaine for spinal anaesthesia to maintain or have minimal effect on serum bilirubin: albumin ratio.

Some case reports have been published in which general anaesthesia was administered for the surgeries to the patients who were the diagnosed case of Crigler-Najjar syndrome or other disorders of unconjugated hyperbilirubinemia. Robards et al [7] reported a patient with Crigler najjar 2 syndrome scheduled for mandibular reconstruction surgery. The patient was given general anaesthesia with sevoflurane 4%, inj.fentanyl 150µg and endotracheal intubation was done with inj.succinylscholine 120mg. One week after the surgery serum bilirubin level increased but rest of the liver function test and renal function test remain normal.

Namasivayam et al [16] reported the anaesthetic management of a patient who underwent laproscopic adhesiolysis and had an inherited unconjugated hyperbilirubinemia. Till now no studies or reports had been published to the effect of regional anaesthesia in pregnant woman with Crigler-Najjar syndrome type -2 and her foetal outcome. In this case we chose spinal anaesthesia over general anaesthesia. Spinal anaesthesia avoids the airway manipulation hence, less chance of aspiration in pregnant patients and it also has better neonatal outcome than general anaesthesia .[17] The use of lignocaine was also in favour of maintenance of serum bilirubin: albumin ration than local anaesthetics and to avoid chance of hyperbilirubinemia caused by the general anaesthetic drugs in crigler-najjar syndrome.

In conclusion, we came to a notion that regional anaesthesia could be safer and better alternative to general anaesthesia to the pregnant women with Crigler-Najjar syndrome type -2 with respect to maternal and foetal outcome.

REFERNCES

1. Chowdhury N, Chowdhury J. Crigler-Najjar syndrome.UptoDate.[cited 2014March 13] Available from:http://www.uptodate.com/contents/crigler-najjar-syndrome.html..
2. Wolkoff AW. The Hyperbilirubinemias. In: Fauci AS. Harrison's Principles of Internal Medicine.17th ed. McGraw Hill education;2008.p.1927-31.
3. Sampietro M, Iolascon A. Molecular pathology of Crigler-Najjar type I and II and Gilbert's syndromes. Haematologica 1999; 84:150-157.
4. Crigler JF Jr, Najjar VA: Congenital familial nonhemolytic jaundice with kernicterus; a new clinical entity. AMA Am J Dis Child 1952; 83: 259–260.
5. Arias M: Chronic unconjugated hyperbilirubinemia without overt signs of hemolysis in adolescents and adults. J Clin Invest (NY) 1962; 41: 2233–2245.
6. Robards C, Brull SJ. The anesthetic implications of Crigler-Najjar syndrome. Anesth Analg. 2007;104(2):435-6.
7. Prager MC, Johnson KL, Ascher NL, Roberts JP. Anesthetic care of patients with Crigler Najjar syndrome. Anesth Analg 1992;74:162– 4.

8. Holstein A, Plaschke A, Lohse P, Egberts EH. Successful photo and phenobarbital therapy during pregnancy in a woman with Crigler-Najjar syndrome Type II. Scand J Gastroenterol 2005;40:1124–6.
9. Furhoff AK (1974) Fate of children born to women with jaundice in pregnancy. Arch Gynäk 217:165–172.
10. Roszkowski I, Pizarek-Miedzinska D (1968) Jaundice in pregnancy. II. Clinical course of pregnancy and delivery and condition of neonate. Am J Obstet Gynecol 101:500–503.
11. Wilson JH, Sinaasappel M, Lotgering FK, Langendonk JG. Recommendations for pregnancies in patients with crigler-najjar syndrome. JIMD Rep. 2013;7:59-62.
12. Bito H, Ikeda K. Renal and hepatic function in surgical patients after low-flow sevoflurane or isoflurane anesthesia. Anesth Analg 1996;82:173– 6.
13. Obata R, Bito H, Ohmura M, et al. The effects of prolonged low-flow sevoflurane anesthesia on renal and hepatic function. Anesth Analg 2000;91:1262– 8.
14. Gadsden J.Local Anesthetics:Clinical Pharmacology and Rational Selection.The NYSORA.[cited 2013 Oct.14]. Available   from: http://www.nysora.com/regionalanesthesia/foundationsofra/3492localanestheticsclinicalpharmacologyan drationalselection.html
15. Dalens BJ. Regional anesthesia in children. In: Miller RD, ed. Miller's anesthesia. 6th ed. Philadelphia: Elsevier-Churchill Livingstone, 2005:1719–62.
16. Namasivayam SP, Saranya J, Ashiq MM, Kalaiselvi VS. A case of Inherited Unconjugated Hyperbilirubinemia for an incidental surgery: Anesthetic management and Review.IOSR-JDMS 2013;11(1): 17-20.
17. Mancuso A, De Vivo A, Giacobbe A et al.General versus spinal anaesthesia for elective caesarean sections: effects on neonatal short-term outcome. A prospective randomised study. J Matern Fetal Neonatal Med 2010; 23(10) :1114-8.