ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS: Crigler-Najjar syndrome, Liver transplant, Isoflurane

ANAESTHETIC MANAGEMENT OF A PATIENT POSTED FOR LIVER TRANSPLANT WITH CRIGLERNAJJAR SYNDROME TYPE-1

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ABSTRACT

Introduction: Crigler-Najjar syndrome is a rare genetic disorder caused by lack of UDP- lucuronyltransferase enzyme. Type I-characterized by a nearly complete lack of enzyme activity and severe and It has to be immediately treated after birth by exchange transfusion followed by phototherapy. Orthotropic liver transplant is currently preferred type of Liver transplant which is performed at the age of 3-5 years. This syndrome can potentially affect the metabolism of these drugs leading to adverse outcomes.

Case report:A 6 year old male child withCriglerNajjar Syndrome Type-1 was posted for orthotopic liver transplantation. LFT showed total bilirubin 26.5 md/dl, Direct bilirubin 0.9 mg/dl,Indirect bilirubin 25.6 mg/dl. Premedication was with Inj. Glycopyrollate 0.1mg and Inj. Fentanyl 40ug. The patient was maintained intra-operatively with infusions of Atracurium and Noradrenaline. Inj midazolam was given in anhepatic phase. Patient was connected to circle system and maintained with N2O: O2 – 2: 1 and Isoflurane – 0.2% – 1%.The Patient was shifted to Post-Liver Transplant ICU as intubated and kept on SIMV-PC for 2hrsThe patient was then shifted to CPAP-PSV mode for 2hrs and finally extubated after 4hrs and shifted to Post-Liver Transplant ward.

Conclusion: Anaesthesiologists should be aware of the medicine decreased glucuronyltransferase activity to prevent intraoperative toxicity of anaesthetic drugs. The anaesthetic goal in caring for patients with Crigler-Najjar disease is prevention of increased free bilirubin in the serum. Halothane should be avoided during anaesthesia because of its high liver metabolism (20%). Isoflurane was the preferred volatile anaesthetic.Paracetamol and morphine were specifically avoided as they are metabolized by conjugation in the liver.Meticulous peri-operative management can result in giving a new life to a moribund patient.

INTRODUCTION:

Bilirubin is conjugated into a more soluble form by the enzyme UDP- lucuronyltransferase[1]. Crigler-Najjar syndrome is a rare genetic disorder caused by lack of this enzyme. It is characterized by an inability to convert and clear bilirubin from the body. The hallmark finding is a persistent yellowing of the skin, mucous membranes of the eyes. There are two forms of this disorder: Type I-characterized by a nearly complete lack of enzyme activity and severe and Type II-characterized by partial enzyme activity and milder symptoms. Both forms are inherited as autosomal recessive traits[2].CNS type 1 has to be immediatelytreated after birth by exchange transfusion followed by phototherapy. Orthotropic liver transplant is currently preferred type of Liver transplant which is performed at the age of 3-5 years[3]. Many anaesthetic drugs are metabolized in the liver via conjugation by the same enzyme. This syndrome can potentially affect the metabolism of these drugs leading to adverse outcomes. Despite this significance, reports on anaesthetic management of patients with CNS are few.

Case Report:

A 6 year old male child had history of yellowish discoloration of eyes and urine on and off since birth. Patient was evaluated during childhood for jaundice and diagnosed with CriglerNajjar Syndrome Type-1. He had taken symptomatic treatment for jaundice and daily phototherapy since birth. Patient was posted for orthotopic liver transplantation.

The pre operative investigations revealed normal complete blood count, renal function test and coagulation profile. LFT showed total bilirubin 26.5 md/dl, Direct bilirubin 0.9 mg/dl,Indirect bilirubin 25.6 mg/dl. Viral markers were negative.USG Abdomen showedno significant abnormality.

Preoperative vitals were within normal limits. Premedication was with Inj. Glycopyrollate 0.1mg and Inj. Fentanyl 40ug. The patient waspreoxygenated with 100 % O2. Intra-operatively the patient was monitored with Et CO2, pulse rate, 6 lead ECG, hourly urine output, blood loss and serial arterial blood analyse for acidosis, electrolyte imbalance, blood sugar levels and haematocrit. FLO TRAC was attached to measure IBP, CVP, PAP, C.O, SV, SVV and SVR.

The patient was maintained intra-operatively with infusions of Atracurium and Noradrenaline. Injmidazolam 1 mg was given in anhepatic phase. Patient was connected to circle system and maintained with N2O: O2 – 2: 1 and Isoflurane – 0.2% – 1%.Inj.calciumgluconate and Inj.soda bicarbonate were required during intra operatively. The patient was transfused with 250 ml PCV and 1.5 l crystalloid fluid. Blood loss was 350 ml and urine output was 260 ml.

The Patient was shifted to Post- Liver Transplant ICU as intubated and kept on SIMV-PC for 2hrs. Immediate Post-Operative ABG Analysis was done. Urine output and vitals were monitored and managed appropriately.The patient was then shifted to CPAP-PSV mode for2hrs and finally extubated after 4hrs.Immunosuppressive Therapy was started immediate post-operatively and on the 4th day,the patient was shifted to Post-Liver Transplant ward.

TABLE 1: Timing of intra operative event.

EVENT	TIME
Incision time	10:15 am
Portal clamp time	12:55 pm
Liver explanation time	12:57 pm
Anhepatic time	55 min
Coldischemia time	8 hrs

TABLE 2: Post-operative bilirubin profile

BILIRUBIN		TOTAL BILIRUBIN	DIRECT	INDIRECT
PREOP		26.5	0.9	25.6
POSTOP	Day 1	16.3	9.6	6.7
	Day 2	5.6	2.8	2.8
	Day 3	3.9	1.2	1.7
	Day 4	2	0.8	1.2
	After shifting to ward	0.6	0.2	0.4

CONCLUSION:

Unconjugated hyperbilirubinemia in child, not responding to phenobarbitone should be evaluated to rule out Crilgarnajjar syndrome. Liver transplantation is considered as definative therapy.Anaesthesiologists should be aware of the medicine decreased glucuronyltransferase activity to prevent intraoperative toxicity of anaesthetic drugs. The anaesthetic goal in caring for patients with Crigler-Najjar disease is prevention of increased free

bilirubin in the serum. Highly protein-bound drugs may displace bilirubin from albumin. Among inhalational agents, halothane should be avoided during anaesthesia because of its high liver metabolism (20%). This decrease is minimum with Isoflurane. Isoflurane was the preferred volatile anaesthetic4.Diclofenac sodium and pentazocine were used for postoperative analgesia. Paracetamol and morphine were specifically avoided as they are metabolized by conjugation in the liver5.Meticulous peri-operative management can result in giving a new life to a moribund patient.

ACKNOWLEDGEMENTS:
I express my sincere gratitude to Dr. Guru Prasad Bhosle, Professor to sharing her wisdom with us during the course of this research. Last but not the least I want to thank whole heartedly to patient without whom this report would has been impossible.

Abbreviation list:
CNS-Crigler-Najjar syndrome FFP- Fresh Frozen plasma
ICU – Intensive Care Unit
LFT – Liver Function Test
OLT- Orthotopic Liver Transplantation
PCV- Packed cell volume,

Disclosure: Noconflict of interest, financial, or otherwise are declared by authors

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