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ANESTHETIC MANAGEMENT OF LIVER RESECTION IN PEDIATRIC HEPATOBLASTOMA PATIENTS

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ABSTRACT **Background –** Children who present for liver resection are a challenge to anesthesiologists. They require adequate preoperative assessment and planning to improve their postoperative outcomes. A balanced technique providing organ protective anesthesia and hemodynamic stability ensures optimal surgical results. **Result:** Anaesthesia for hepatic resection has seen great changes with improvements in surgical technique and a better understanding of the underlying physiology. Good communication and interdisciplinary strategization between the pediatric oncologist, surgeon and the anesthesiologist also facilitate a good outcome. A retrospective review was performed on 20 cases of pediatric hepatoblastoma planned for partial hepatectomy in a pediatric tertiary care center in South India, over a 3-year period. **Conclusion:** In this study, general anesthesia with epidural analgesia and goal directed fluid management with monitoring of central venous pressure and mean blood pressure during liver resection was found to be acceptable for pediatric liver resection without any significant complications

KEYWORDS : pediatric hepatectomy, hepatoblastoma, anesthesia

INTRODUCTION:

Hepatic tumors in children represent 1% of all pediatric malignancy and 5% of all extra-cranial solid tumors. Hepatoblastoma is the most common primary liver tumor in children and is diagnosed generally by 3 years of age[1]. Most cases manifest within the first 18 months of life. Its occurrence can be sporadic or associated with genetic abnormalities and syndromes like Beckwith- Wiedemann syndrome, familial adenomatous polyposis and hemiatrophy[2, 3]. The incidence of hepatoblastoma is more common in premature or low birth weight babies.

The presenting symptom is with abdominal distension, palpable abdominal mass or both. Tumor growth may also compress or obstruct the normal hepatic architecture causing ascites due to portal and hepatic vein occlusion. Icterus and pruritus can occur from biliary tree obstruction. Other symptoms include anemia, thrombocytopenia, leukocytosis, fever, weight loss and anorexia.

The most useful diagnostic modality is CT or MRI. Ultrasonography and Doppler imaging are used to localize the tumor and also to assess the patency of inferior vena cava, hepatic vein and portal vein. Alpha fetoprotein is the tumor marker whose levels are elevated in around 50-70% of these children[4]. Routine biochemical tests including a full blood count, urea and electrolytes, liver enzymes and liver synthetic function tests are included in the preoperative work up of these patients.

These patients are subjected to chemotherapeutic agents like Adriamycin, vincristine and anthracycline. These agents are associated with dose dependent, irreversible cardiomyopathy. Pulmonary function can also be impaired due to presence of shunts or due to diaphragmatic splinting caused by ascites or hepatomegaly. In addition to these issues, resection of hepatoblastoma tumors pose a challenge to anesthesiologists with regard to coagulation defects, impaired liver function tests and massive blood loss. Hence, we undertake this study with the aim of understanding the conduct of anesthesia for pediatric hepatoblastoma resection in 20 cases with an institute-based protocol for anesthesia management.

MATERIALS AND METHODS:

We evaluated the data of children who were operated for hepatoblastoma at Indira Gandhi institute of child health, Bangalore. The diagnosis of hepatoblastoma was confirmed histopathologically and radiologically.

We reviewed the anesthetic details and clinical records of all 20 children. Pre anesthetic details including age of presentation, weight of the child, gender, preoperative investigations and other relevant data were collected. Anesthetic records mentioning the anesthetic technique, medications used, hemodynamic parameters, central venous pressure, blood loss and blood transfusion data were noted. Postoperative outcome with regard to the need for mechanical ventilation and inotropic support was also noted.

ANAESTHETIC MANAGEMENT:

All the patients underwent a pre anesthetic checkup 1 week prior to the surgery. 11 patients in our study group had received chemotherapy prior to surgery. Adriamycin, anthracycline and cisplatin were the chemotherapeutic agents used and these were associated with dose dependent, irreversible cardiomyopathy. Hence to assess cardio toxicity and cardiac reserve, ECG and echocardiography were done apart from routine biochemistry.

Preoperatively, on the day of surgery, fasting orders for 6 hours to solid food in view of ascites, was issued with arrangement for postoperative PICU and availability of adequate, compatible blood components. According to the protocol, all patients received general anesthesia with tracheal intubation and mechanical ventilation with epidural analgesia. All the patients were secured with a 22G IV cannula in the ward and were premedicated with injection Midazolam 0.1 mg/kg. In the operating room, standard monitoring devices (ECG, NIBP, pulse oximetry) were attached to the patients. Induction was facilitated with injection Thiopentone 5mg/kg and injection Fentanyl 2 mcg/kg. Once mask ventilation was confirmed, injection Atracurium besylate 0.5mg/kg was given for tracheal intubation. All patients routinely received injection Ondansetron 0.15mg/kg and injection dexamethasone 0.1mg/kg as postoperative nausea and vomiting prophylaxis. Antibiotic prophylaxis was given according to institutional protocol. In addition to the standard noninvasive monitoring devices, oropharyngeal temperature monitoring, end tidal CO2, intra-arterial blood pressure monitoring and central venous pressure monitoring was performed in all the cases.

All patients received thoracic epidural analgesia at T7- T8 level using loss of resistance technique to saline for identifying the epidural space. Epidural bolus of 0.125% bupivacaine 0.5 ml/kg was given to all the patients after induction of anesthesia. Controlled mechanical ventilation with oxygen, air and isoflurane was delivered to all patients. Nitrous oxide was avoided due to probability of gut distension and risk of air embolism. Neuromuscular blockade was maintained with atracurium infusion at 0.3 mg/kg/hr. Analgesic supplementation was done with bolus of intravenous fentanyl 1 mcg/kg, injection paracetamol 10 mg/kg and intermittent epidural boluses. Plasmalyte solution was used as the crystalloid of choice. Packed red blood cells and fresh frozen plasma were administered when the loss exceeded maximal allowable blood loss. Intraoperative epidural top ups were given on an hourly basis according to hemodynamic parameters. Single inotropic support with dopamine at 5mcg/kg/hr or noradrenaline at 0.05mcg/kg/hr was started as required during the resection phase.

Surgical technique that ensured the removal of the diseased part of the liver with adequate oncological clearance, minimal blood loss and preservation of enough healthy liver tends to avoid liver failure and allow for liver regeneration. The initial step involved dividing the ligamentous attachments of the liver to mobilize it. If the liver was exteriorized to achieve this, it was associated with a fall in cardiac

output and CVP. Subsequent step involved isolation of the blood vessels from the segments being resected.

During the liver resection period, clamping time of the IVC and hepatic vein was noted. Intraoperative CVP was adjusted to be maintained within 5 cm of H_2O. Mean blood pressure and blood loss was noted and replacement was done with PRBC and FFP at 10 to 15 ml/kg. A balance between low CVP an euvolemia was achieved by ensuring goal directed fluid therapy. This was achieved by using basic hemodynamic variables as target. Normothermia and normoglycemia was maintained for all patients. Intraoperative coagulopathy was closely monitored. Recovery and extubation was planned with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg, provided the patient was hemodynamically stable with minimal inotropic support. All patients were shifted to PICU for further management. Epidural analgesia was continued postoperatively keeping in mind the hemodynamic parameters and coagulation profile.

RESULTS:

This retrospective study was conducted at Indira Gandhi institute of child health. 20 children with hepatoblastoma were included in the study. Out of the 20 patients, 9 were female (45%) and 11 were male patients (55%). The median age of the children was 13 (IQR=14.5) months with a range of 2 months to 10 years. The median weight of the patients was 9 kgs (IQR=5.3). Presentation during admission involved abdominal distension in all patients with loss of appetite and weight loss. 11 out of the 20 patients (55%) underwent chemotherapy with carboplatin, Adriamycin and vincristine. The mean preoperative hemoglobin levels were 10.3 g/dl (SD=1.3). The average duration of liver resection period was 30.25 minutes. The mean CVP intra-operatively was maintained at 4 cm of H_2O. The average mean blood pressure was 59 mm Hg. The average intra-operative blood loss was 255 ml. 19 patients (95%) received PRBC transfusion of which 13 (65%) also received FFP. Only 1 (5%) patient received FFP transfusion alone. 15 patients (75%) required intra-operative inotropic support with noradrenaline or dopamine. 10 of the operated patients were extubated while 10 of them required postoperative ventilatory support. Recovery of all the patients postoperatively was successful and was managed in the PICU.

Table 1: Demographic variables

Variable	Median	IQR
Age (Months)	13.0	14.5
Weight (Kilograms)	9	5.3

Table 2: Hemodynamic parameters, transfusion requirements

Variable	Mean	Std. Dev
Hb (g/dl)	10.2	1.3
MBP (mm Hg)	59.1	7.7
CVP (cm H2O)	4.0	1.4
Resection Time (minutes)	30.3	16.2
Blood Loss (ml)	255	122.6
PRBC (ml)	201.6	124.7
FFP (ml)	168.6	84.0

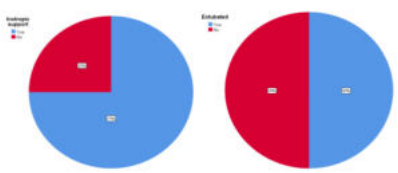

Figure 1: Requirement of inotropic support
Figure 2: Patients extubated

DISCUSSION:

Management of hepatoblastoma has significantly improved in the last few years. The presence of effective chemotherapeutic drugs, better understanding of the liver anatomy, improved anesthetic and postoperative care and reliable surgical techniques have played a role in such improvement. Hepatoblastoma is the 3rd most common malignant tumor in children under 3 years of age. Its prevalence in children is 1.5/1000000[5]. Being a chemo-sensitive tumor, cisplatin is a commonly used chemotherapeutic agent[6]. Chemotherapy helps in eliminating distant metastases, reduces mass volume[7, 8]. Liver transplant is an option available for patients not eligible for surgery. Trans-arterial chemo embolization is an alternative mode of treatment. Anesthetic management of a patient with hepatoblastoma presenting for hepatic resection presents several unique challenges. It involves planning for intravenous access, arterial access, intra-operative fluid management, intra-operative and postoperative pain management and maintaining hemodynamic balance. Biochemical tests include a full CBC, LFT with AFP, urea and electrolytes, coagulation profile. AFP is the most important tumor marker with 50- 70% children showing an elevated level. Radiological investigations include USG, MRI and CT to delineate the extent and multiplicity of the lesions and to detect vascular involvement and metastases. The aim of the resection is to excise the diseased part with minimal blood loss and to preserve enough healthy liver to prevent failure and allow regeneration. The most critical part of the surgery is ligation of the hepatic vein as avulsion or injury to the hepatic vein can result in massive haemorrhage[4]. Most of the patients present for surgery after receiving neo-adjuvant chemotherapy which can have multiple side effects.

General anesthesia with tracheal intubation and mechanical ventilation with epidural analgesia is the anesthetic technique of choice. The anesthetic goal is to maintain hemodynamic balance, ensure intra-operative CVP is within 5 cm H_2O and to restrict intra-operative fluids during resection time to 10 ml/kg/hr[9]. Modified RSI is preferred for patients for patients with ascites. Cisatracurium and atracurium are preferred due to their non liver dependent metabolism. Volatile agents commonly used are O2/ air mixture with sevoflurane/ isoflurane/ desflurane. Invasive arterial and CVP allows for monitoring hemodynamic parameters and regular blood samplings. A low CVP of 2- 5 cm H2O reduces bleeding. This can be ensured by limitation of IV fluids while maintaining adequate tissue perfusion, ensuring diuresis and usage of vasodilating agents as needed. However adequate perfusion of vital organs with euvolemia should be ensured. Hypoglycemia is also a concern during hepatic vascular occlusion. Serial blood glucose monitoring to ensure normoglycemia is necessary.

Inflow vascular occlusion has been associated with increase in SVR up to 40%, 10% reduction in cardiac output and increase in MAP by 15% in adults[10]. Following unclamping, return of the baseline parameters occurs. Total vascular exclusion combines portal vessel clamping with occlusion of supra and infra hepatic IVC with significant hemodynamic consequences. Cross clamping of IVC and portal vein results in 40-60% reduction in venous return and cardiac output with compensatory 80% increase in SVR and 50% increase in heart rate[10,11]. Cardiac index reduces by half. Following unclamping, an increase in cardiac index with decrease in SVR occurs[10, 11]. Pringle maneuver, a surgical maneuver is also used to control bleeding from the liver. A large atraumatic hemostat is used to clamp the hepatoduodenal ligament, thus interrupting the flow of blood through the hepatic artery and portal vein.

Anesthesia management is dictated by the surgical approach and patient's health status. Maintenance of a low CVP of 2 to 5 mm Hg while maintaining the volume status is achieved by limiting IV fluids, ensuring adequate dieresis and usage of vasoactive agents. Goal directed fluid therapy has been used in many clinical trials conducted for major surgery in enhancing postoperative recovery of patients.[12] It refers to optimization of flow related parameters such as CO and SV. Numerous hemodynamic variables are also used as target such as HR, BP, CVP, SV and CO/CI. Perioperative goal directed therapy includes variables reflecting blood flow and this can be tailored to the individual needs of the patient.

Factors predisposing to air embolism during liver resection include surgical technique, size and site of tumor, blood loss and low CVP techniques. Hypoglycemia and hypothermia should be prevented. Postoperative analgesia is multimodal with parenteral narcotics and epidural analgesia. Use of caudal and epidural analgesia is effective but coexisting coagulopathies must be kept in mind. USG abdominal wall blocks and truncal blocks can also be considered.

CONCLUSION:

Management of pediatric hepatoblastoma requires a multidisciplinary involvement. Good communication between the pediatric oncologist, surgeon and anesthetist is essential for a smooth peri-operative experience. Balance between organ protection and hemodynamic stability ensure optimal surgical results with a successful postoperative recovery.

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