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RESEARCH ARTICLE

HEPATIC RESECTION: A CHALLENGE TO ANAESTHESIOLOGIST!!!

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Abstract

Background: Hepatic resection is a surgery which is associated with high risk of patient's morbidity and mortality. Thereby requiring expert skills on anaesthesia front. With the advancement in medical science there has been reduction in morbidity of patient. Starting from the assessment of the patient preoperatively for preexisting parenchymal liver disease going through the intra op period in which haemodynamic alterations can take a toll to the postoperative part , all are very crucial.

Aims: 1. To study the anaesthethic strategies during perioperative period.

2. To assess the postoperative recovery phase.

Methodology: This was a retrospective analysis of 10 patients with established liver disorders excluding patients with alcoholic hepatitis planned for hepatic resection in age range of 40-50yrs, under ASA grade 3. After induction of patient under epidural and general anaesthesia, haemodynamic parameters, blood loss, central venous pressure(CVP) were observed. CVP was kept ≤5mmHg. Postoperative monitoring for vitals and complications was done.

Results: Out of the 10 patients,(Carcinoma GB, Hemangioma, Hydatid cyst). Two patients were not able to sustain low CVP, leading to acute transient renal failure in post operative period. Four (40%) patients needed blood transfusion. 20% patients had deranged coagulation profile which was managed by transfusion of fresh frozen plasma.

Conclusion: Improvement in surgical and anesthetic skills, use of risk reduction strategies, preoperative assessment, haemodynamic management can help in better patient outcome with reduction in mortality.

Background:-

Liver is a highly vascular organ with normal hepatic blood flow being 25% to 30% of the cardiac output. Liver has eight segments; each having its own blood supply by portal vein and hepatic artery. The segmental portal venous and hepatic arterial blood supply and biliary drainage help in resecting the contiguous segments without disrupting

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the vascular supply to neighboring tissue. There are few bloodless planes of dissection and divisions are invisible on the surface of the liver. Liver has an important role in the functioning of various body systems, such as activity of gastrointestinal tract, renal function, metabolic functions including the synthesis and degradation or detoxification of essential compounds; pharmacokinetics of anesthetic and anesthesia adjuncts; and hemostasis. Hepatectomy, an important surgery, done for benign and malignant diseases of liver is associated with high risk of patient's morbidity and mortality and thus demands expert skills on the anesthesia front. Larger the liver resection, more traumatic is the surgery, greater potential for blood loss, lengthy clamping time and more chances of ischemia reperfusion liver injury. Also, hemodynamic management is the main concern during the resection surgery. Blood loss during a liver resection is associated with increased post-operative morbidity rates.[1,2,3] Age, size of resection, elevated creatinine, bilirubin, albumin levels, deranged prothombin time, ascites and presence of heart disease are the pre operative risk factors associated with increased post operative mortality. With the advancement in medical sciences and vigilant perioperative care there has been reduction in morbidity of patient. Eighty percent of the liver can be removed, because of the hepatocytes; which are unipotent cells and have the capacity to develop or differentiate into only one type of cell but the risks of liver failure and other complications are high. Since the surgery is complex, the morbidity and mortality rates are high.

Methodology:-

A retrospective analysis of 10 patients with established liver disorders excluding patients with alcoholic hepatitis, ascites, cirrihosis and encephalopathy planned for hepatic resection in age range of 40-50yrs under ASA grade III was done. The study was done to observe the anesthetic strategies during peri-operative period and to assess the post operative recovery phase. After a detailed pre operative assessment, investigations like complete haemogram, liver function, renal function, serum electrolytes, prothrombin time/ INR, ECG, Chest X-ray were done and optimally corrected prior to surgery. Patients were kept nil by mouth overnight prior to day of surgery. On the day of surgery after well informed high risk consent, patients were taken into the operating theatre and multi-para monitors were attached. Intravenous access with two large bore (16G /14G) cannulae was done. They were pre medicated with glycopyrolate (0.004mg/kg), ondansetron (0.08mg/kg), midazolam (0.05mg/kg) and analgesia was given with fentanyl (1-2 µg/kg). An epidural catheter for intra and post operative analgesia was inserted at L1-2 with the tip of the catheter kept at T8/T9, bupivacaine and fentanyl in calculated dose were used. After pre oxygenation with 100% oxygen for 3 minutes induction was carried out with etomidate (0.3mg/kg) and intubation was facilitated by atracurium (0.5mg/kg). Maintenance of anesthesia was carried out with O_2, N_2O, isoflurane (1-2%) and atracurium infusion (0.1mg/kg/hr) under controlled ventilation. During resection PEEP was reduced to zero to reduce the intrathoracic pressure, thereby assisting in venous return and lack of back pressure on the hepatic veins. Post induction central venous catheter for central venous pressure monitoring and drug infusions was secured. Intra arterial blood pressure monitoring and gas analysis was carried out with arterial line access. Patients were monitored with ECG, SpO_2, NIBP, $EtCO_2$, CVP, IABP, temperature and urine output. Haemodynamic monitoring was the mainstay during the intraoperative period. CVP was recorded and kept below ≤5mmHg in view of reducing the amount of blood loss. Fluid balance was managed meticulously with crystalloids, colloids and blood products maintaining normovolumia. Packed red blood cells were transfused to compensate the blood loss. To maintain adequate perfusion pressure, infusion of dopamine (2-4 µg/kg) and noradrenaline (0.05µg/kg/min) were used. In postoperative phase, patient were reversed with neostigmine (0.05mg/kg) and glycopyrolate (0.1mg/kg) and started on CPAP to avoid lung atelectasis. Patients were shifted to post anesthesia care unit and were extubated once fully conscious and attaining the extubation criteria. Vital monitoring including ECG, SpO_2, blood pressure and temperature was done. Post operatively complete haemogram, blood sugar, electrolytes, blood gases, input-output charting and prothrombin time were assessed and corrected if required. Post operative analgesia was maintained with epidural dose of fentanyl and other IV analgesics.

Results:-

A total of ten patients were operated of which 50% had hemangioma, 30% had Carcinoma Gall bladder and 20% had recurrent multiple hydatid cysts (Fig 1). Degree of pre operative liver dysfunction and extent of liver resection are important for maintaining coagulation profile. Two patients had deranged coagulation profile post operatively managed with transfusion of FFP and vitamin K administration. Forty percent of patients required blood transfusion intra operatively as they had profuse bleeding needing transfusion with PCV and FFP in 1:1 ratio to overcome the loss. Two patients could not tolerate low CVP. In spite of adequate volume replacement two patients had post operative transient renal dysfunction (Table1).

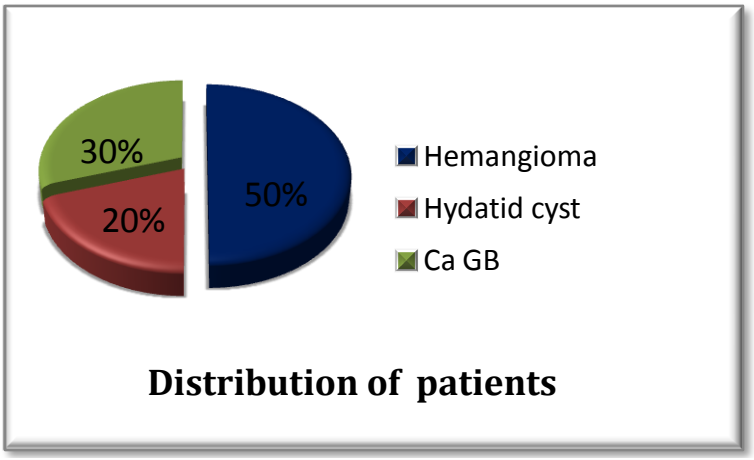

Fig 1:- A total of 10 patients: 5- Hemangioma; 3- Carcinoma Gall Bladder; 2- Hydatid cyst

Table 1:- Postoperative complications

TOTAL	10
BLOOD TRANSFUSION	04
ACUTE TRANSIENT RENAL FAILURE	02
DERANGED PROTHOMBIN TIME	02
ATELECTASIS	--
LIVER FAILURE	--
ASCITES	--
SEPTIC SHOCK	--
CARDIAC ARREST	--
MORTALITY	--

Discussion:-

Planning surgery for hepatic resection requires pre operative assessment and optimization of the physical and pathological condition of the patient. ASA grading assess the physical status, whereas Child Pugh Scoring is done for assessing the clinical status of the patient; which includes serum bilirubin, prothrombin time, presence of ascites, encephalopathy and nutritional impairment. Any pre existing liver pathology increases the risk of morbidity of the patient, thus strict perioperative monitoring and interventions are required during the procedure. Liver function tests are carried out to measure the hepatic dysfunction. Markedly increased aminotransferases reflect extensive hepatocellular injury, such as acute viral hepatitis, ischemic hepatitis and acute drug or toxin induced liver injury and hence they are contraindications to elective surgery. Raised alkaline phosphatase level indicates cholestasis due to calculi or tumors in the bile duct. Albumin, bilirubin, and prothombin time are laboratory parameters included in the Child-Pugh classification which are indicative of the biosynthetic functions and severity of cirrhosis. The MELD score (Model for End-stage Liver Disease score) is also an effective criteria for the assessment of chronic liver disease, its parameters being bilirubin, international normalized ratio (INR), creatinine and sodium levels. The coagulation profile is poor at predicting the risk of bleeding in individuals with liver disease because they reflect changes in procoagulant factors. Prolongation of the INR may reflect instability of the hemostatic balance, but not hypo or hyper coagulability in cirrhosis. Vitamin K (1mg/day) IV/ IM is administered for 3 consecutive days in patients with suspected deficiency (e.g, patients with poor nutrition, cirrhosis, cholestatic disease, with antibiotic use). Administration of antifibrinolytics such as tranexemic acid may reduce operative bleeding. As blood loss is suspected intra operatively; prior to surgery two large bore venous access is secured.

Patients with Child-Pugh scores of B or C should not undergo resection surgery because the risk of postoperative liver failure is very high. Similarly a MELD score of 10 to 15 confers increased perioperative risk, and patients with MELD scores >15 should not undergo surgery.

Alongwith anaesthesia its important to maintain organ perfusion, prevent air embolism, decrease blood loss using anaesthestic skills. Liver disease can affect the pharmacokinetics of anesthetic drugs by changing drug metabolism,

protein binding, and volume of distribution. Selection of drugs and dose adjustments depend on the severity of liver disease. Currently used volatile anesthetic agents (isoflurane, sevoflurane, desflurane) are not associated with hepatotoxicity as seen with halothane.[4] It is because of the risk of hepatotoxicity, and reduction in cardiac output and hepatic oxygen supply, halothane is not administered to patients with liver disease.[5] All volatile anesthetics decrease hepatic blood flow to a small extent. Isoflurane and sevoflurane result in little reduction and desflurane result in 30% reduction of hepatic blood flow. Isoflurane and desflurane, undergo less metabolism to trifluoroacetyl chloride (TFA) and sevoflurane does not undergo metabolism to TFA. There is an increase in elimination half life and free drug level of benzodiazepine leading to enhanced sedation. Metabolism is reduced in patients with liver disease, particularly for opioids like morphine and hydromorphone whereas, elimination of fentanyl is not appreciably altered in patients with liver disease, unless repeated doses are administered.[6] Elimination and recovery from remifentanil is unchanged by liver disease. Clearance, elimination, and duration of action of succinylchloine, rocuronium and vecuronium are prolonged in patients with liver disease and thus recovery time is delayed.[7] Metabolism of atracurium and cis-atracurium are unaffected by liver disease because it is broken down spontaneously by Hofmann degradation.[8] However, it is important to monitor the degree of relaxation because patients with liver disease show increased resistance to drug and shorter duration of action. Prolonged neuromuscular blockade can be reduced by decreasing the amount and frequency of neuromuscular blocking drugs. Drowsiness is related to opiates or other accumulating drugs. In case of liver failure,there is risk of hepatic encephalopathy and hypoglycemia. Hence, monitoring of ammonia and glucose levels is important.

It has also been observed that low CVP approach provides with good surgical field, decreased blood loss and requirement of transfusion. Liver has few bloodless planes of dissection therefore larger the resection more traumatic is the surgery. A study by Eid EA et al [9] (2005), also concluded that reduction in blood loss and blood transfusion is significantly reduced if CVP is maintained at or < 5mmHg. In 2014, meta-analysis of five randomized trials including 280 patients found that blood loss and transfusion were less with low CVP management for hepatectomy.[10] In another meta analysis of eight randomized trials (2015), low CVP was associated with less blood loss and lower risk of transfusion (odds ratio [OR] 0.65) than control patients with higher CVP.[11] Whereas retrospective reviews of living related donor hepatectomies have reported that CVP monitoring did not reduce blood loss, and that blood loss did not correlate with CVP level.[12,13,14] Reduced blood loss can be attributed to the fact that hepatic venous pressure is dependent on central venous pressure. Low CVP increases negative pressure gradient with respect to right atrium and increase in air embolism which can be detected by transechocardiography. There is a sudden fall in arterial oxygen and end tidal CO_2. Positioning patient in 15^0 Trendelenburg position can minimize incidence of air embolism.[15,16] Management requires infusing fluid rapidly, give 100% oxygen and aspiration of air from pulmonary artery floataion catheter in situ.

Blood loss plays an important role for predicting morbidity and mortality of the patient. Cardiac disease is ruled out as it may increase right side heart pressure, thereby increasing blood loss. In a study by Wong et al [17] (2003) stated that "maintaining a CVP < 5mmHg by volume restriction and intravenous infusion of nitroglycerine and a systolic blood pressure above 90 mmHg by intravenous infusion of dopamine (4–6µg/kg) had dramatically reduced bleeding and transfusion requirements." Epidural anesthesia does not lead to changes in intravascular volume, but only promotes redistribution of blood, decreasing both venous return and portal vein pressure, thus contributing to reduced hepatic congestion and surgical blood loss.[18] Blood loss is also reduced by clamping hepactic artery and portal vein called Pringel's manouver. Prolonged clamping leads to warm ischaemia. Clamping is not done for more than 15 mins and then released for 5 mins. The clamping of hepatic artery and portal vein increases the backflow through hepatic vein.

Positive end expiratory pressure (PEEP) is reduced to zero to reduce the intra-thoracic pressure, and to increase in venous return and thereby decreasing the back pressure on the hepatic veins. In case of blood loss more than expected, transfusion is required. All cases which are done under epidural anaesthesia are done after ruling out any coagulation abnormality and are observed in postop period for spinal haematoma. Patients with microvascular bleeding, or who are at risk of bleeding due to percutaneous procedures, platelets are transfused to achieve a platelet count ≥50,000/microL, and cryoprecipitate transfusion to maintain fibrinogen levels ≥200 mg/dL.[19,20] Ho AM et al [21] (2007) concluded that " the high prevalence of deranged haemostatic measurements after hepatectomy peak on day 2, because of the complex haemostatic changes related to both the cancer and the surgery and it could not be determined whether these changes were associated with an increased risk of epidural hematoma". Another study by Stamenkovic DM et al [22] (2011) noted that "there is no single reported case of epidural hematoma as a consequence of epidural catheter insertion or removal after elective hepatectomy".

Enhanced Recovery After Surgery (ERAS) protocols in postoperative period are being increasingly used which help in reducing the duration of hospital stay and morbidity rates. After the surgery is over patient is reversed back and extubated after full filling the extubation criteria. Prolonged intubation and sedationd may lead to retention of secretions in the basal lung leading to atelectasis. This can can be prevented by early application of Continous positive airway pressure (CPAP) after extubation. Postoperatively pain is managed with doses epidural and IV analgesics. Injection fentanyl 0.5- 1 µg/ kg in diluted form can be used for post operative analgesia through epidural catheter. IV analgesics like Nefopam which has no hepatic metabolism and can be used in combination with opiods.[23] Paracetamol infusion is used cautiously and for a short period. Coagulation profile (PT, aPTT, INR) is monitered as there is transient insufficieny of remnant liver to synthesize new factors. Coagulation disorder if present ,epidural cathter removal is delayed till coagulation profile is corrected. Intravenous fluids should be managed carefully to avoid ascites, edema, and/or heart failure.[24] Care is taken to prevent ascites, as incidence of exudative ascites is 50% in liver resection cases.[25] Ascites can occur because of cirrhosis, high portal pressure,exudation, splanchnic arteial vasodiltation. The management includes monitoring of fluid infusion and simultaneously taking measures to maintain renal perfusion and diuresis. The strategy includes plasma subtitutes, diuretics and vasoconstrictors. Hypovolumia is corrected which can predispose to decrease renal perfusion and GFR. Preventing renal impairment is another important consideration for the anesthesiologist. Renal auto-regulation ceases below a renal perfusion pressure of 70 to 75mmHg, below which, flow becomes pressure dependent. Renal failure can be corrected by hydration. Strict input output monitoring, BUN, serum creatinine are done to detect renal dysfunction. Patients with preoperative cirrhosis tolerate a reduction in renal perfusion pressure poorly and extra care must be taken to maintain perfusion pressure in order to preserve renal function.[26]Serum electrolytes are investigated and if hyponatremia needs to be corrected, it should be corrected and is done slowly to avoid central pontine myelinolysis. Hypokalemia and metabolic alkalosis can occur with liver disease, and may trigger or exacerbate hepatic encephalopathy. Hypothermia is taken care off with use of warming blankets, warm IV fluids and ambient room temperature. Early post operative nasojejunal feeding is important. It is usually started at the rate of 10ml/hr and is gradually increased . It helps to maintain gut function.

Conclusion: Improvement in surgical and anesthetic skills, use of risk reduction strategies, preoperative assessment, and hemodynamic management can help in better patient outcome with reduction in morbidity and mortality. Anesthetic vigilance along with thorough knowledge of surgical manipulations promotes team based health care in the operative room. Keeping in mind all the above discussed strategies and planning we were able to carry out the anesthesia with reduced post operative complications and any incidence of mortality.

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