Anesthesia for Pregnancy Induced Liver Disease

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1.1 Introduction

Pregnancy induced liver diseases according to the frequency of reported incidence are hyperemesis gravidarum (HG), intrahepatic cholestasis of pregnancy (IHCP), hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome, and acute fatty liver of pregnancy (AFLP). The IHCP, HELLP, and AFLP are very challenging for the anesthesiologists in case of need for urgent delivery, while HG which occurs in the first trimester is challenging for mostly obstetricians [1–4]. Therefore, in this chapter, after brief overview of the physiologic changes and alterations related to liver during pregnancy, anesthetic management and specific considerations in pregnant women undergoing either non-obstetric surgery or delivery are addressed based on the current literature.

The physiologic changes and/or abnormalities associated with pregnancy induced liver diseases are summarized.

Physiologic changes and markers of liver dysfunction during pregnancy are indicated below [3, 5]:

- Maternal plasma volume increases approximately 50% by the end of 34 weeks gestation resulting in a physiologic anemia because red blood cell volume increases more than plasma volume.
- Leukocyte count increases progressively but platelet count decreases or does not change.
- Cardiac output rises by 35–40% above baseline towards the end of first trimester.

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- Alkaline Phosphatase (AP) which is found in biliary tract cells normally increases due to placental and fetal production but an elevated level of gamma glutamyl transferase (GGT) is suggestive of liver disease.
- Due to hepatocyte injury, release of alanine and aspartate aminotransferases (ALT and AST) increase which is called transaminitis.
- Coagulation factors I, VII, VIII, IX, X, and XII increase resulting in a physiologic hypercoagulable state, prothrombin time (PT) is unchanged and antithrombin III concentrations decreases whereas fibrinopeptide A, plasminogen, and fibrin degradation products (FDP) increase. Thus, increased PT/INR and/or PTT are indicators of liver disease.
- Progesterone inhibits contractility of gastrointestinal smooth muscle leading to gallbladder hypomotility and biliary stasis. Resulting increased bile secretion and cholesterol may increase the risk of gallstones during pregnancy.
- Albumin and total serum protein levels decrease.

However, there are no physiologic changes in the liver size, morphology, and blood flow in otherwise healthy parturients. Therefore, determining any hepatomegaly and/or increased serum bilirubin or bile acid levels are abnormal during pregnancy and regarded as supportive evidences for a pregnancy induced liver disease. Regarding aminotransferases, ALT is more specific than AST in liver diseases because ALT does not elevate due to tissue injury like AST [6].

1.2 Intrahepatic Cholestasis of Pregnancy

1.2.1 Incidence and Risk Factors

The incidence of IHCP is between 0.1% and 1.5% in Central Western Europe and North America but it may rise up to 4% in Chile and Bolivia [7]. The common risk factors are advanced maternal age, multiparity, family history, preexisting liver disease, or history of cholestasis while taking oral contraceptives [8, 9]. Pregnancy induced liver diseases except HG usually manifest either in the second or third trimester and reported incidences of these disorders are presented in Table 1.1.

Table 1.1 Incidences of unique liver diseases during pregnancy

	Incidence	Trimester
HG	<2%	First
IHCP	0.1–1.5%	Second or third
HELLP syndrome	0.1–0.6%	Third
AFLP	1:7000–1:16000	Third

HG hyperemesis gravidarum, *IHCP* intrahepatic cholestasis of pregnancy, *HELLP* hemolysis, elevated liver enzymes and low platelets, *AFLP* acute fatty liver of pregnancy

1.2.2 Diagnosis

The diagnosis is made by clinical signs and laboratory tests. Most of the parturients suffer from unbearable pruritis depending on the severity of the disease. Jaundice may develop in 50% of the patients. Elevated bilirubin (up to 6 mg/dL), transaminase (approximately 20 times than normal values), and serum bile acid levels (higher than 10 μmol/L) are the hallmark laboratory findings. However, the most sensitive diagnostic biomarker is the elevation in the fasting serum bile acid level, which is used to classify the disease as mild, moderate, or severe (mild: 10–39 μmol/mL, moderate: 40–99 μmol/mL and severe: ≥100 μmol/mL) [7].

1.2.3 Obstetric Management

Obstetric management of IHCP might affect the outcomes of the mother and the baby [10–16]. Medical treatment of pruritis during the perinatal period includes ursodeoxycholic acid, which is an FDA class B drug during pregnancy. Delivery of the baby at the fetal maturity is planned. In mild cases, delivery can be performed at term. However, in moderate or severe cases, early delivery at 36 weeks gestation should be considered due to the increased risk of preterm labor and/or birth, meconium staining of amniotic fluid, fetal loss, and abnormal fetal heart rate changes [2–4, 7].

1.2.4 Anesthetic Management

Choice of anesthesia for delivery seems to be controversial in IHCP. Due to the physiologic decrease in gallbladder contractility resulting in cholestasis, pregnant women tend to have a malabsorption of vitamin K, which is a cofactor responsible for synthesis of coagulation factors II, VII, IX, and X [11–15]. Because of the theoretical concern, studies have been conducted to elucidate whether alterations in coagulation status might be problematic in parturients with IHCP for the anesthesiologists [10, 16].

In a retrospective study (n = 319), estimated blood loss and the incidence of coagulopathy in IHCP parturients with (n = 223) or without (n = 96) preoperative coagulation tests (PT, PTT and platelets) were compared. No significant differences in estimated blood loss were found between them and no neuraxial hematoma was observed in subjects who received neuraxial analgesia and anesthesia. The incidence of postpartum hemorrhage (PPH) was reported to be 2.4% and 6.3% after vaginal and cesarean delivery, respectively. Of note, no abnormal coagulation studies were encountered postpartum even in the presence of preoperative increased liver enzymes in 13 subjects [16]. These authors reported that the presence of coagulopathy in parturients with isolated IHCP was very low and they concluded that use of neuraxial analgesia and/or anesthesia may not necessarily be delayed. Although preoperative coagulation test is not routine for performing neuraxial analgesia and/or anesthesia in isolated IHCP, it is recommended particularly in case of

coexisting preeclampsia with IHCP [16]. In a recent retrospective study, maternal, fetal, and neonatal outcomes of parturients according to the severity of IHCP who delivered in 1 year at Gazi University were documented. The incidence of IHCP in Gazi University was 2% [10].

Delivery modes and anesthesia types in studies with IHCP patients were comparatively presented in Table 1.2 [7, 10, 16]. Severity of IHCP especially bile acid levels higher than 40 μmol/L may affect pregnancy outcomes. Parturients with severe IHCP delivered were preterm, whereas mild and moderate groups delivered at term [7, 10]. The CS rates were 14%, 73%, and 65.5% [7, 10, 16].

The rates of mild, moderate, and severe IHCP in Gazi University were 65%, 21%, and 14%, respectively. Twenty-seven percent of the cases had normal spontaneous vaginal delivery whereas the rest of the parturients (73%) underwent cesarean section (CS), 18.5% being not elective. The rates of neuraxial and general anesthesia for CSs were 85% and 15%, respectively. The most common neuraxial anesthesia type was spinal anesthesia (96%) [10].

1.2.5 Prognosis

There is no increased risk in maternal death rate and maternal outcomes are good because the disease disappears rapidly after delivery and it rarely progresses to cirrhosis [3]. According to the latest records, coagulation tests including PT, PTT, INR, and platelet counts did not differ between the preoperative and postoperative periods. But increased preoperative transaminases and AP in parturients with IHCP significantly returned to almost normal clinical laboratory limits on the 3rd postoperative day [10].

1.2.6 Maternal, Fetal, and Neonatal Outcomes

Comparison of maternal, fetal, and neonatal outcomes in three studies was summarized in Table 1.2. In general, documented adverse fetal and neonatal outcomes were comparable among the studies [7, 10, 16].

1.3 HELLP Syndrome

1.3.1 Definition and Incidence

The acronym for HELLP comes from hemolysis, elevated liver enzymes, and low platelet count. HELLP syndrome, either alone or associated with severe preeclampsia was first described by Weinstein in 1982 [17]. HELLP has an incidence of 0.1–0.6% that develops usually in the third trimester (Table 1.1). The rate of HELLP patients with severe preeclampsia varies between 4% and 12%,

Table 1.2 Delivery modes, anesthesia types and maternal, fetal, and neonatal outcomes

	J Clin Anesth 2014 [16] (n = 319)		Am J Obstet Gynecol 2015 [7] (n = 215)			Turk J Med Sci 2017 [10] (n = 37)		
Severity of IHCP (n)	Not documented clearly		Mild (n = 108)	Moderate (n = 86)	Severe (n = 21)	Mild (n = 24)	Moderate (n = 8)	Severe (n = 5)
Gestational age (week)	37.2 (36.8–38.1)		Term	Term	Preterm	Term	Term	Preterm
Preoperative coagulation tests (PT, PTT, platelet count)	Yes (n = 96)	No (n = 223)	Not documented			Yes (n = 37)		
Postoperative coagulation tests (PT, PTT, platelet count)	Yes (n = 319)		Not documented			Yes (n = 37)		
Preoperative liver enzymes and bilirubin levels	Not documented clearly		Highest data throughout the pregnancy were documented (n = 215)			Documented (n = 37) Elevated transaminases and AP Normal GGT, LDH, and bilirubin		
Postoperative liver enzymes and bilirubin levels	Not documented clearly					Documented (n = 37) Transamniases, AP, GGT, LDH, and bilirubin are normal		
VD (n (percent))	111 (34.5%)		185 (86%)			10 (27%)		
CS (n (percent))	208 (65.5%)		30 (14%)			27 (73%)		
Neuraxial analgesia for labor (n)	Not documented clearly		Not documented clearly			CSE: 1		
Anesthesia type for CS (n)	Not documented clearly		Not documented clearly			Spinal: 22 General: 4 CSE:1		
Adverse fetal and neonatal outcome (n)	Not documented clearly		74 (preterm birth, perinatal death, meconium stained fluid, and asphyxia)			7 (preterm labor and birth, perinatal death, newborn hepatitis)		
Adverse maternal outcome (PPH)	Overall rate 3.4% (6.3% after CS)		Overall rate 7.4%			0%		

CS cesarean section, *VD* vaginal delivery, *PPH* postpartum hemorrhage

while 70% of patients with HELLP syndrome present before delivery, 30% of them develop postpartum mostly in the first 48 h [1, 18–21].

1.3.2 Pathophysiology

Approximately 20% of preeclamptic women with severe features develop HELLP. Mechanism of preeclampsia might be explained because of failed remodeling of spiral arteries by the cytotrophoblasts leading to hypoperfusion and ischemia of the placenta. The fetal consequence is intrauterine growth retardation. On the maternal side ischemic placenta releases several factors that provoke a generalized endothelial dysfunction which in turn is responsible for maternal symptoms and complications. Pathophysiology of HELLP with or without preeclampsia includes endothelial injury with fibrin deposits that causes microangiopathic hemolytic anemia and platelet activation-consumption leading to thrombocytopenia [17–20].

1.3.3 Diagnosis and Classification

Accurate diagnosis is made mainly by laboratory tests. Low platelet count (<100,000/μL), increased AST or ALT (≥70 IU/L) and LDH levels (≥600 IU/L) are required for complete diagnosis but if only one or two of these abnormalities are present it becomes partial HELLP syndrome. However, 50% patients with HELLP syndrome might be free of all diagnostic criteria [20, 22].

The severity of HELLP syndrome is basically classified depending on the platelet count [22]. According to the Mississippi classification, elevated AST and LDH associated with platelet count ≤50,000/μL are in class 1, platelet count between 50,000–10,0000/μL in class 2, and platelet count between 100,000–150,000/μL in class 3. However, in Tennessee classification, diagnosis is either complete or partial (severe preeclampsia + one or more of the hallmark laboratory findings) [22].

In the guidelines of Antwerp University, anesthetic technique can be chosen according to the platelet count. If platelet count is >90,000/μL, any anesthetic technique (either regional or general) can be chosen, if platelet count is between 60,000 and 90,000/μL some prefer single shot spinal anesthesia and as for platelet count <60,000/μL commonly general anesthesia is performed [23].

1.3.4 Obstetric Management

HELLP syndrome often progresses and may eventually compromise maternal and fetal outcomes. Therefore, obstetric management includes delivery at ≥34 weeks' gestation. Vaginal delivery may be proceeded in active labor, if there is no fetal distress or risk of disseminated intravascular coagulopathy (DIC). However, in the presence of coexisting multi-organ dysfunction, renal

failure, or abruption, immediate cesarean delivery should be performed and induction of labor is avoided [1, 15, 24].

1.3.5 Medical Treatment

Basically, three drug groups (corticosteroids, antihypertensives, and anticonvulsants) are used for perinatal and expectant management of HELLP. Benefit of using IV corticosteroids before 34 weeks' gestation is recommended for fetal lung maturation in standard dose (betamethasone 6 mg twice a day). High doses may be preferred in patients with extremely low platelets, high liver enzymes, and low urine output. As an antihypertensive medication, labetalol is one of the first line drugs used to lower high blood pressure and monitoring blood pressure at least postpartum 24 h is required. Even if the HELLP diagnosis is not complete, hypertension crisis should be controlled by either hydralazine or labetalol within the first 1 h urgently. Intravenous magnesium sulphate 4–6 gram (g) of loading dose in 20 min followed by 1–2 g/h infusion should be administered for seizure prophylaxis in mild or severe preeclampsia complicated with HELLP and for treatment of ongoing seizures during labor until postpartum 24 h at least. Recommended therapeutic magnesium concentration is kept between 4–7 mg/dL by checking serum magnesium levels every 4 h along with monitoring urine output, respiratory rate, SpO_2, and patellar reflexes [24].

1.3.6 Preoperative Transfusion

Platelet transfusion is generally required in patients with HELLP when preoperative platelet count is <20,000/μL or <50,000/μL and cesarean delivery is mandatory. It is advisable to keep platelet count above 50,000/μL to avoid risk of bleeding. Of note, there is no need to transfuse platelet more than once, since thrombocytopenia improves usually 24 h after delivery [25]. Plasmapheresis might be a supportive therapeutic option in refractory patients [24].

1.3.7 Choice of Anesthesia

General anesthesia for CS has been the safest and most commonly preferred technique in HELLP syndrome. However, high rate of use of regional anesthesia for CS has been documented in 102 cases with preterm HELLP syndrome (antepartum $n = 95$, postpartum $n = 7$). Mean gestational age was 30.6 ± 2.7 weeks. Most of the parturients underwent regional anesthesia ($n = 65$). Cases having mean preoperative platelet count of 113,000/μL ($n = 53$) underwent CS under CSE, while patients ($n = 12$) with mean preoperative platelet count of 95,000/μL underwent spinal anesthesia. Interestingly, two patients with platelet count <50,000/μL underwent CS with CSE. Only one of them received platelet transfusion

immediately before CSE. No epidural hematoma has been reported in that retrospective study [23].

1.3.8 Prognosis

HELLP syndrome is associated with increased risk of maternal and fetal morbidity and mortality. Rate of maternal death is approximately 1%. According to the latest revision in Mississippi classification related to composite major maternal morbidity (CMMM), patients with class 1 HELLP have higher CMMM [26]. Noteworthy maternal complications include pulmonary edema, acute renal failure, DIC, abruptio placenta, liver hemorrhage or failure, ARDS, retinal detachment, stroke, adverse events due to blood transfusion and neuraxial hematoma. The rate of perinatal death varies between 7.4% and 20.4%, depending on the gestational age and concurrent factors related to the pregnancy. The highest morbidity and mortality rates are observed <28 weeks' gestation. Most perinatal morbidity is due to prematurity that may cause respiratory distress syndrome, bronchopulmonary dysplasia, intracerebral hemorrhage, or necrotizing enterocolitis [1, 27–29].

1.3.9 Complications

A subarachnoid hematoma after CS under spinal anesthesia in a 39-year-old severe preeclamptic parturient associated with HELLP syndrome was reported. Complete recovery of motor block occurred 5 h after spinal block. Although preoperative platelet count was 91,000/μL, it declined progressively to 30,000/μL on the second postoperative day and patient started to suffer from sensory and motor deficit in the lower extremity, urinary retention, and flaccid paraparesis. Magnetic resonance imaging (MRI) revealed spinal subarachnoid hematoma compressing cauda equina. Three months after conservative medical treatment (Vit B12, PG E1, oral neostigmine + bladder exercise, flurbiprofen and rehabilitation), complete recovery with hematoma regression on the MRI was observed [29]. Another severe complication is massive hepatic infarction requiring surgical intervention 24 h after emergency CS which has been reported in a severe preeclamptic parturient with HELLP [30].

1.3.10 Follow-Up

Despite careful perioperative fluid therapy, patients should be monitored to avoid pulmonary edema for at least 48 h postpartum. Laboratory abnormalities usually regress 24 h postpartum and complete recovery occurs 48 h postpartum [1].

1.4 Acute Fatty Liver of Pregnancy

1.4.1 Definition and Incidence

Acute fatty liver of pregnancy was described as yellow atrophy of the liver in early 1950s. AFLP is an idiopathic fatal disease with a 10–85% mortality rate. The incidence is between 1/7000–1/16000 or 1:10,000–15,000 pregnancies. It often develops between 27 and 40 weeks' gestation, but may be undiagnosed until the postpartum period [1, 31].

1.4.2 Risk Factors

Advanced maternal age, primiparity, multiple pregnancies, preeclampsia, male fetus, being underweight, the use of non-steroidal anti-inflammatory drugs and previous AFLP are considered to be some of the risk factors [1, 32].

1.4.3 Pathophysiology

The incidence of AFLP is high in women with a genetic mutation. Basically, mitochondrial fatty acid oxidation pathway is affected. Fetus has a long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency [31].

1.4.4 Clinical Features and Laboratory Findings

Patient is presented with fatigue, vomiting, headache, hypoglycemia, lactic acidosis. Prolonged prothrombin time, depressed antithrombin III, elevated liver enzymes, persistent DIC, elevated direct bilirubin, creatinine, AP and leukocytosis are observed in almost all cases. Profound hypoglycemia might occur due to impaired glycogenolysis [33, 34].

1.4.5 Prognosis

Decision to make immediate delivery is extremely important because of high maternal (23%) and fetal (18%) mortality rate. If early diagnosis is made and properly treated, AFLP is a reversible peripartum liver failure. Most of the patients recover within 48–72 h after delivery with improved aminotransferase levels [35].

1.4.6 Diagnosis

Currently, there are no uniform diagnostic criteria for AFLP [36–39]. However, markedly elevated levels of serum transaminases (>200 U/L) and direct bilirubin

(60 μmol/L) should be considered in the accurate diagnosis because perinatal death was linked to elevated levels of direct bilirubin [38].

1.4.7 Obstetric Management

Early diagnosis, prompt delivery, and intensive supportive treatment by close monitoring are essential, since recovery before delivery is not possible. For severe cases, plasmapheresis and liver transplantation may be considered [33–35, 40].

1.4.8 Anesthetic Management

General anesthesia is usually required in patients with coagulopathy because of the concern for regional anesthesia related hematoma risk. Perioperative anesthesia care includes establishing adequate intravenous accesses readily available for cross matched blood and blood products against increased risk of PPH [1, 11].

1.4.9 Postoperative Care

Patients with coagulopathy, encephalopathy, or hypoglycemia may require admission to intensive care unit [33–38, 40].

Remarkable clinical and laboratory findings, anesthesia types, maternal, fetal, and neonatal outcomes from retrospective AFLP studies were summarized in Table 1.3 [36–39].

1.5 Hyperemesis Gravidarum

HG is characterized by severe and persistent form of nausea and vomiting resulting in dehydration, malnutrition, and weight loss [3]. It is always managed by the obstetricians, since planned anesthetic support is not needed for the disease during early pregnancy. Sometimes differential diagnosis may be required to rule out any gastrointestinal pathology (e.g., Helicobacter pylori infection) in serious cases refractory to treatment. Such a particular case was referred to outpatient anesthesia clinic after first unsuccessful awake endoscopy attempt without sedation. For the 2nd endoscopic procedure, propofol, which is a safe intravenous anesthetic agent in liver disease, was used under monitored anesthesia care [41]. Dose adjustment is made due to 10% decrease in propofol requirement in the first trimester [5].

Table 1.3 Anesthesia types and outcomes as potential predictors

Retrospective AFLP studies	Anesthesia types and outcomes
Zhou et al. [36] Retrospective analysis of AFLP 28 cases from Shanghai Public Health Center over 5 years. Gynecol Obstet Invest 2013	2 maternal deaths (7.1%) without fetal deaths CS under neuraxial (n = 16) and general anesthesia with RSI (n = 12)
Cheng et al. [37] AFLP: A retrospective study of 32 cases in South China J Matern Fetal Neonatal Med 2014	18 parturients recovered due to rapid diagnosis, early termination of pregnancy and supportive treatments Newborn male sex and vaginal delivery were risk factors of fetal outcome
Zang et al. [38] A retrospective analysis of 56 cases Chinese Med J 2016	PT/INR are risk factors for fatal complications – Perinatal mortality is linked to FDP
Qu Y et al. [39] Retrospective analysis of anesthetic and perioperative management in patients of AFLP in Peking University Zhonghua Yi Xue Za Zhi. 2017	12 cases were identified (91.7% primigravid, 50% twin pregnancies and 1 with concomitant preeclampsia) CS under neuraxial (n = 1) and general anesthesia with RSI (n = 9) 1 patient admitted after delivery died postpartum 6 out of the 18 fetuses were transferred to the pediatric department due to preterm, low birth weight, intrauterine restriction or asphyxia and they all survived

RSI rapid sequence induction

1.6 General Considerations for Anesthesia Management

1.6.1 Anesthesia Technique

During liver dysfunction and/or failure, metabolism of general anesthetic drugs is delayed. Therefore, regional anesthesia, either a neuraxial or peripheral block, is considered in the absence of coagulopathy whenever possible. Regional anesthesia is superior to general anesthesia in patients with particularly advanced liver disease because of the less systemic effects of the neuraxial and locally administered drugs. Additionally, regional anesthesia blunts hemodynamic effects of stress hormones in the circulation better than general anesthesia [1, 11, 15].

1.6.2 Local Anesthetics

Anesthetists must consider the altered pharmacokinetics in liver disease. Total drug dose used for a peripheral block should be cautiously calculated and possible side effects should be closely monitored. Regarding local anesthetic drugs, lidocaine has

the longest $t_{1/2elim}$. Meanwhile, increased volume of distribution (Vd) of lidocaine may offer some protection against it. Toxicity is mostly dependent on the free fraction of the local anesthetic drug. Fortunately, α1 acid glycoprotein (GP), which is the main plasma protein that binds local anesthetics, is synthesized even in end stage liver disease. Noteworthy, clearance of ropivacaine is less in the end stage liver disease than normal. For metabolism of ester type local anesthetic drugs, though pseudocholinesterase enzyme production in the liver may decrease in disease state, overall clearance of chloroprocaine is unclear [15].

1.6.3 Intravenous and Inhalation Anesthetics

The elimination half-life of propofol is unaffected although its clearance may be higher. As for thiopental, the elimination half-life is 2.5 times longer than normal, which is explained by the marked increase in Vd despite increased clearance [5]. Considering inhalation anesthetics, when sevoflurane or desflurane was compared with isoflurane, sevoflurane seems to be advantageous without significant differences. Nitrous oxide is no more commonly preferred to provide perioperative analgesia [1, 15]. However, liver cell injury with xenon anesthesia has been shown to be impossible which might be a promising alternative agent if available [42, 43].

Since minimum alveolar concentration (MAC) of volatile anesthetics is decreased up to 40% in pregnancy, despite bispectral index (BIS) monitorization is not a standard tool it might be helpful in adjusting inhaled anesthetic requirements [3, 5].

1.6.4 Muscle Relaxants

Either atracurium or cisatracurium is a reasonable option due to its independent liver metabolism. Despite reduced pseudocholinesterase activity, suxamethonium is used for rapid sequence induction (RSI) since it does not result in clinically relevant prolongation in liver dysfunction and during pregnancy [1, 3, 5]. Although aminosteroid type muscle relaxants have enhanced sensitivity in liver disease, rocuronium induced prolonged neuromuscular block could be completely antagonized by sugammadex. Therefore, muscle relaxants are used by neuromuscular block monitoring [15, 44].

1.6.5 Practice of General Anesthesia

General anesthesia induction and maintenance are provided with possibly safe IV and inhalation anesthetic drugs under standard monitorization including heart rate, ECG, non-invasive blood pressure, peripheral oxygen saturation, and end tidal carbon dioxide pressure measurement. Among intravenous anesthetic agents for induction of anesthesia, propofol is the most favorable because of its rapid metabolism even in cirrhosis. Isoflurane, desflurane, or sevoflurane with or without small doses

of fentanyl seems to be reasonable for maintenance of anesthesia. Fentanyl, if used in relatively moderate doses, is a good choice without affecting oxygen supply. Long acting narcotics and benzodiazepines should be avoided in cirrhotic patients [1, 3, 5, 15]. Total intravenous anesthesia (TIVA) with RSI using target controlled infusion (TCI) of propofol and remifentanil was reported. Rocuronium 1.2 mg/kg was used to facilitate endotracheal intubation. For induction of anesthesia, TCI propofol (4 ng/mL) and remifentanil (3 ng/mL) were used and maintenance of anesthesia was provided with 3 ng/mL of propofol and remifentanil. Recently, an emergency CS was performed with total intravenous anesthesia in a severe preeclamptic parturient associated with HELLP and renal insufficiency [45]. In another case report using TIVA, anesthesia induction with remifentanil and propofol with RSI using succinylcholine followed by propofol and remifentanil infusion [46].

Fetal heart rate monitoring is mandatory by a qualified obstetrician during expectant management of the parturient when necessary. However, invasive monitoring (intraarterial or central venous pressure) is not a must for anesthesia practice. Continuous invasive monitoring of intraarterial blood pressure is indicated only in patients with poorly controlled high blood pressure, rapid need for lowering blood pressure and frequent use of blood gases. Central venous pressure monitoring is only indicated in case of assessment of renal oliguria and response to fluid administration. Thus, careful fluid administration is required because of the increased risk of pulmonary edema particularly with which is one of the leading causes of morbidity in preeclamptic HELLP patients. According to the most recent meta-analysis investigating the incidence of pulmonary edema associated with colloid versus crystalloid administration in preeclampsia, no significant differences were found between them. The authors recommended an individually tailored fluid management with the aid of non-invasive modalities of hemodynamic measurement such as lung ultrasound, transthoracic echocardiography, or pulse waveform monitors if available [47].

1.6.6 Postoperative Care

Even though delayed clearance is a concern in severe liver disease, intravenous or neuraxial opioids can be administered to provide postoperative analgesia. Since advanced liver disease has an increased risk of hepatic encephalopathy, residual effects of anesthetics or analgesics may result in neurologic deterioration in the postoperative period. Therefore, neurologic and liver function monitoring is essential [1, 3, 15, 23].

Conclusion

Recent evidences about the anesthetic management in parturients with pregnancy induced liver diseases are not clear regarding the best approach. General anesthesia technique with RSI is the preferred choice in case of coagulopathy. Regardless of the selection of any anesthesia technique, hepatic blood flow and oxygenation should be maintained and hemodynamic alterations and sympathetic stimulation should be avoided at all times. Management of anesthesia in

this particular group needs special attention and care with rational choice of available local and general anesthetic drugs that provide greater stability both for general and regional anesthesia under continuous careful monitoring.

Key Learning Points

- Isolated IHCP may be managed in the same manner like a healthy parturient. Coagulopathy should be excluded or corrected before regional anesthesia if possible. Since presence of coagulopathy in parturients with isolated IHCP is very low, neuraxial analgesia and/or anesthesia may not necessarily be delayed. Preoperative coagulation tests are recommended in case of coexisting preeclampsia with IHCP.
- General anesthesia with RSI is the safest choice in class I and II HELLP patients scheduled to undergo CS. Total intravenous anesthesia with propofol and remifentanil was reported in a severe preeclamptic parturient associated with HELLP and renal insufficiency for emergency CS. Spinal anesthesia may be selected if there is no progressive thrombocytopenia. Close patient monitoring is a must against hemorrhagic complications, DIC or eclampsia at all times.
- Anesthesia selection should be individualized in patients with AFLP. General anesthesia with RSI is recommended in case of severe coagulopathy. Perioperative anesthetic care includes establishing adequate IV access with readily available cross matched blood and blood products against anticipated PPH.
- Despite its rarity, when anesthesia support is needed in a patient with severe HG, anesthesia is provided with safe IV drugs under monitored anesthesia care.

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