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Review Article

Neuroanesthesia and pregnancy: Uncharted waters

Shalendra Singh^{a,*}, Navdeep Sethi^b^a Assistant Professor, Department of Anaesthesiology & Critical Care, Armed Forces Medical College, Pune 411040, India^b Commandant, Command Hospital (Southern Command), Pune 411040, India

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ABSTRACT

An incidence of 30–40 deaths per triennium in pregnant patients is reported because of brain pathology. Over the last two decades, the obstetric cause of mortality in the pregnant patient has declined, but the trend is rising for non-obstetric cause of mortality. Pregnancy is associated with a host of anatomical and physiological alterations that complicate the conduct of anesthesia. The brain is one of the vital organs of the body, and physiological changes during pregnancy alter the anesthesia management if associated with brain pathology. Malignant brain tumors and trauma remain a leading cause of indirect maternal mortality. Review of literature revealed paucity of evidence-based neuroanesthesia management for such patients. Navigating these uncharted waters remains a challenging exercise. With the lack of guidelines, the management is based largely on few case reports or case series.

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Introduction

A pregnant lady requiring non-obstetric surgery during pregnancy is rare.¹ An incidence of 30–40 deaths per triennium in pregnant patients is reported because of brain pathology.² Over the last two decades, the obstetric cause of mortality in the pregnant patient has declined, but the trend is rising for non-obstetric cause of mortality.² Pregnancy is associated with a host of anatomical and physiological alterations that complicate the conduct of anesthesia. The brain is one of the vital organs of the body, and physiological changes during pregnancy alter the anesthesia management if associated with brain pathology. Malignant brain tumors and trauma remain a leading cause of indirect maternal mortality. Review of literature revealed paucity of evidence-

based neuroanesthesia management for such patients. Navigating these uncharted waters remains a challenging exercise. With the lack of guidelines, management is based largely on few case reports or case series. The following neurological conditions would merit special consideration during pregnancy.

Subarachnoid hemorrhage

Bleeding due to arteriovenous malformation (AVM) and intracranial aneurysm are the most common causes of subarachnoid hemorrhage (SAH) during pregnancy. SAH may be up to five times common during pregnancy compared with non-pregnant states.³ Hypertensive bleed, vasculitis, and traumatic bleed are other possible causes. The risk of bleeding

* Corresponding author.

E-mail address: drsinghafmc@gmail.com (S. Singh).<https://doi.org/10.1016/j.mjafi.2018.10.001>

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is higher during pregnancy because of the increased intravascular volume and cardiac output along with the effects of hormones on the vessel wall. The risk of rupture of an aneurysm increases with each trimester, with the greatest risk around the time of child birth.

Aneurysmal subarachnoid hemorrhage (aSAH) during pregnancy is the third most common cause of maternal death from non-obstetric cause with an incidence of 0.01%–0.05%.⁴ There is no difference of management in pregnant patients over aSAH patients.⁵ The possibility of repetitive bleeding during the rest of pregnancy in patients with an untreated aneurysm is as high as 33%–50% and contributes 50%–68% maternal death.

AVMs are responsible for about 50% of SAH in pregnant women. An elevated cardiac output and hormonal effects have been involved in the possibility of rupture of AVMs in the last trimester.⁶ If untreated, an AVM in the pregnant woman may pose a threat to the mother and the fetus.

Neoplasm

Primary central nervous system neoplasm pathology occurs in approximately six in 100,000 females with the same frequency in both pregnant and non-pregnant women.⁷ Meningiomas are the most common tumor during pregnancy which contains estrogen and progesterone receptors and grows faster during pregnancy.⁸ However, the growth of tumors and subsequent clinical manifestations are generally accelerated during pregnancy because of a multitude of factors such as increased vascularity, hormonal influence, peritumor edema and immune-related changes. Choriocarcinoma is an aggressive gestational tumor that metastasizes to the brain. Glioma is less common but usually carries a worse prognosis. Patients may present with focal or generalized seizures or the sign of increased intracranial pressure.

Shunt surgeries

Pregnancy is incorporated with the surpassing extent of shunt-related complications that may require shunt emendation. Patients' gestation age, clinical scenario, and imaging features guide the management in these patients. In the first two trimesters, shunt surgery can be performed as in non-pregnant patients (i.e. ventriculoperitoneal shunt); however, in the last trimester, a ventriculoatrial shunt or third ventriculostomy may be scrutinized as alternatives to avoid possible injury to the uterus or other abdominal viscera and an undue risk of induction of labor.

Traumatic brain injury

Approximately, trauma complicates one in every 12 pregnancies and is the principal cause of non-obstetric maternal death and may involve spinal or cranial injury.⁹ Incidence of trauma during pregnancy is 8%, 40%, and 52% in the first, second, and third trimester, respectively. Transportation accidents, falls, physical attack, and burn injuries are the familiar etiologies. Gravid uterus tends to protect from gastrointestinal injuries, but increased tissue vascularity aggravates splenic and retroperitoneal hemorrhage.

The early and aggressive protocol-based resuscitation is the cornerstone of management after traumatic brain injury (TBI). The indications of performing neurosurgery or opting for conservative management after TBI are the same as in non-pregnant patients. A caesarean section may be performed to improve maternal hemodynamics. A single episode of hypotension is associated with a worse outcome in this subset of patients in comparison with patients who never had hypotension.¹⁰ Systolic blood pressure <90 mm Hg should be aggressively managed, and cerebral perfusion pressure to be targeted between 50 and 70 mmHg. Intracranial pressure to be kept <20 mmHg and managed with osmotic diuretics such as hypertonic saline, mannitol (0.25–1 g/kg), and raising the head end of the bed by 15°–20°. Consider the Cerebral spinal fluid (CSF) drainage method to decrease Intracranial pressure (ICP) in severe TBI with Glasgow Coma Scale (GCS) 6 during the first 12 h after injury.¹⁰ Prolonged prophylactic hyperventilation is not recommended.¹⁰ Early hyperventilation is not desired as it causes cerebral ischemia, so normocarbida should be maintained in the first 24 h and thereafter. A computed tomography (CT) scan can be delayed in patients with hypotension owing to abdomen bleeding, and they should undergo emergent laparotomy first after an urgent craniotomy. Routine monitoring in mild to moderate head injury is not recommended; however, case-by-case assessment may be warranted. Other neurological monitoring techniques such as jugular venous oxygenation, cerebral oximetry, and cerebral microdialysis are being used in TBI patients, but their use in pregnant polytrauma patients is yet to be established. Dexmedetomidine and lidocaine are effective in blunting systemic and cerebrovascular response to tracheal suctioning in mechanically ventilated patients with severe TBI.¹¹

Spinal surgeries

Only a handful of reports exist in the literature about spinal surgeries during pregnancy. Fifty-six percent of women are reported to have low back ache during gestation.¹² Lumbar Disk Herniation (LDH) with features of nerve root compression is exceedingly rare, occurring in only one in approximately 10,000 pregnancies.¹² Most of these conditions resolve on their own after a few weeks or after delivery of the fetus, thus averting the challenge of performing spinal surgery in the prone position. Spinal conditions such as the cauda equina syndrome or any progressive neurologic disease require urgent spinal surgery. Akin to intracranial tumors, preexisting spinal tumors may show accelerated growth and become symptomatic during pregnancy. Spontaneous spinal epidural hematoma may occur owing to congenital or acquired bleeding disorders, peritumor bleeding, spinal AVMs, or vasculitis. LDHs are most common in individuals between the ages of 35–55 years, and more than 30% of women will be older than 30 years when they become pregnant, which may be the cause of more patients reporting with this condition.^{12,13}

Imaging during pregnancy

Radiation exposure is a concern, and exposure should be minimized whenever possible. Radiation exposure between 2

and 7 wk is a risk for teratogenic effect on the fetus. After the period of organogenesis, it may cause childhood cancer, microcephaly, and growth restriction. Radiation exposure upto 50–100 mGy (5–10 rads) is considered safe.¹⁴ CT scanning (<2 mrad) and cerebral angiography (>2 mrad) expose the fetus to radiation during the catheter placement if abdominal shielding is not applied. An unshielded fetus will be exposed to 30% of the maternal absorbed dose. A single plain chest radiograph (0.02–0.07 mrad) is safe even in the first trimester.¹⁵ Use of advanced imaging equipment and limited fluoroscopy and use of abdominal shielding are very helpful to decrease the dose of the total radiation. Dose reduction upto 80–97% can be achieved by the use 0.5-mm lead apron and by shielding the abdomen anteriorly and posteriorly.¹⁶

Anesthesia management during pregnancy

The decision to carry out neurosurgery or neurointervention in a pregnant patient requires a multidisciplinary and patient-individualized approach. The risk of proceeding with the surgery needs to be balanced against the risk to the growing fetus. Several considerations, such as the nature of the lesion, site of the lesion, neurological status of the patient, age of gestation, and the possibility/risks of adopting a conservative approach, exist. As always, maternal neurosurgical concerns take prime importance and the decision to proceed with or defer the surgery should be taken with collaboration with the neurosurgeon, neuroanesthesiologist, and the obstetrician. When the decision to perform a neurosurgical surgery/procedure is made, three distinct clinical scenarios can be present: neurosurgery performed with a view to maintain the fetus in utero (early pregnancy), cesarean delivery before the neurosurgical procedure, and neurosurgical procedure followed by cesarean delivery at a later date. Although there are no clear guidelines, 32 weeks are generally used as the cutoff for safe fetal delivery along with the neurosurgical procedure.

Aneurysm clipping

In case of a ruptured aneurysm during pregnancy, common practice is to proceed with craniotomy and clipping to secure the aneurysm and prevent further rebleeding. In aneurysm pregnant patient there is a gradual shift from craniotomy and clipping to coil-embolization in most centres. Patient outcomes are better if clipping or coiling is performed during pregnancy in cases of ruptured aneurysms.⁴ Patients with unruptured aneurysms may be kept under close monitoring, and surgical intervention may be deferred until after the delivery of the fetus. During pregnancy, maternal outcomes are probably better with coil embolization compared with craniotomy and clipping.¹⁷ Fetal risk of radiation exposure, especially in the first trimester, remains a valid concern.

AVM resection

Like with unruptured intracranial aneurysms, patients with AVM without bleeding should be kept under close neurological

monitoring, and surgical resection may be deferred after pregnancy. Furthermore, evidence of the improved maternal outcome after surgery even in cases of AVM with bleed lacks. The judgment is best made in a case-to-case basis after careful consideration of the size, location, and overall clinical status of the patient.

Neoplasm resection

Benign intracranial neoplasm can be resected after delivery of the fetus at term if neurological condition of the pregnant woman remains stable. Malignant neoplasm and benign lesion with clinical deterioration require craniotomy and excision, irrespective of the age of gestation. An awake craniotomy is gaining popularity as the standard of care in resecting tumors that are adjacent to eloquent brain areas. A good scalp block is the key to a successful awake craniotomy. Supplemental local anesthetics may be infiltrated at pin insertion sites with careful consideration of the reduced local anesthesia requirement during pregnancy and maximal allowable dose. A background infusion of dexmedetomidine, fentanyl, or propofol for additional analgesia and sedation is useful during the opening and closing stages of the awake craniotomy. An elevated circulatory blood volume with raised cardiac output in advancing gestation age can cause unexpected and significant blood loss.

Spinal surgeries

The level of spinal surgery, gestational age, maternal neurologic status, and consent of the patient should be taken into consideration for the favorable time of spinal surgery. For patients at or after 34–36 weeks of gestation, delivery should be conducted before spine surgery if there is ongoing neurologic deficit. In an urgent state, such as rapidly ongoing motor deficits, spine surgery followed by cesarean section can be performed. For patients at or before 34–36 weeks, surgical treatment should be considered.

A steroid injection into the epidural space in the second or third trimester of pregnancy can be considered for symptomatic relief. The position of the patient is critical during surgery. Using Relton–Hall laminectomy frame with side supports in the knee/elbow prone position, patients had undergone safe surgery.

Patient preparation for surgery

Akin to any other surgery involving general anesthesia, anesthetic management begins with requisite history taking, clinical examination, and laboratory investigations. Additional tests involve those related to the fetus such as gestational age, fetal maturity, and overall assessment of fetal well-being. Small doses of anxiolytic may be considered in extremely anxious patients but only when close monitoring facilities are present. Routinely administered premedication drugs include non-particulate antacids such as sodium citrate, prokinetic drugs such as metoclopramide, and gastric acid-lowering agents such as ranitidine (anti-histaminic) or omeprazole (proton pump inhibitor).

Intraoperative management

Intraoperative monitoring consists of the routine American Society of Anesthesia (ASA) monitors along with the fetal heart rate monitoring. If surgery requires craniotomy, invasive arterial pressure monitoring is recommended. Two wide-bore intravenous catheters are mandatory. A central venous catheter may be inserted depending on the nature of surgery, presence of comorbid illnesses, and if intraoperative vasopressor use is anticipated. Every case is a potential difficult airway, and necessary preparations should be completed before induction of anesthesia.

Vigilance must be exercised while positioning the patient to avoid any compression on the gravid uterus. This can also lead to epidural venous engorgement and increased surgical bleeding. During the first and early part of the second trimester, surgery can be performed in the prone position as there is minimal aortocaval compression by the gravid uterus.¹⁸ In fact when pregnant patients were positioned prone by letting the abdomen hang freely, there was actually better relief of compression on the large maternal vessels by the gravid uterus compared with sitting or lateral positions.¹⁹ One of the pitfalls of prone positioning is helplessness to obviously monitor the fetal status or conduct the emergent cesarean section for fetal distress. Lateral positioning has also been used well during the late second and third trimester of pregnancy.²⁰ Four-post Wilson frame has also been used for prone surgery; two posts are placed just below the clavicles on the chest and other posts centered on Anterior Superior Iliac Spine (ASIS) to support the pelvis. Posterior fossa tumor surgery in a pregnant lady in the sitting position has also been described.²¹

Tracheal intubation is commonly facilitated with 6.0- to 7.0-mm ID cuffed endotracheal tube in most patients. Induction and tracheal intubation are the most censorious moments for intraoperative aneurysmal rupture, with an incidence of 1–2%, which is higher in patients with inconvenient airways.²² Some approaches that can be used to decrease this hypertensive response to laryngoscopy and the risk of rupture include the following: administration of drugs, such as esmolol and lidocaine, that block or eliminate the hypertensive response and deep anesthetic plane (high doses of anesthetics with Bispectral Index (BIS) monitoring) at the time of intubation.²² This target can be attained by using remifentanyl, both as a bolus administration, immediately before potent stimuli, and continuous infusion, adjusting the dose for the respective degrees of stimulation. However, the attempt to reduce the hypertensive response to laryngoscopy and tracheal intubation can increase the risk of acute fetal distress by reduction in maternal Mean Arterial Pressure (MAP) and the fetal heart rate. To guarantee the superior control during those moments, intraoperative invasive blood pressure monitoring is desirable. There are theoretical concerns of fetal acidosis with prolonged propofol infusion, even though there are several reports of its safe use during pregnancy as a part of total intravenous anesthesia both inside the operating rooms and in the neuroradiology laboratories. No large trial has demonstrated any deleterious effect of using nitrous oxide intraoperatively. There is some evidence from animal-based studies that nitrous oxide may contribute to

teratogenesis by inhibition of methionine synthase and reduction of the uterine blood flow; thus, it may be prudent to avoid nitrous oxide during periods of organogenesis.

Ephedrine crosses the placenta and stimulates fetal metabolism by a direct adrenergic effect and stimulating endogenous release of fetal catecholamines, so phenylephrine (50–100 µgm) is considered the drug of choice to treat maternal hypotension. Hypotension should be aggressively treated because adequate uteroplacental perfusion is dependent on normal maternal blood pressure.

With an ongoing pregnancy, a lower dose of 0.25–0.5 gm/kg of mannitol is administered because larger doses may result in fetal dehydration and dyselectrolytemia. Similarly, the use of hyperventilation to lower ICP during pregnancy is controversial and no evidence-based guidelines exist. PaCO₂ normally decreases to about 28–32 mm Hg during pregnancy because of physiological hyperventilation. Reducing CO₂ levels further may cause reduction of the placental blood flow and an undesirable left shift of the maternal oxyhemoglobin dissociation curve. When neurosurgery is carried out in pregnant patients, it may be best to maintain PaCO₂ levels close to the baseline values, and any further hyperventilation can be avoided.

In patients with unruptured aneurysms, cases of aneurysmal rupture after lumbar puncture have been outline in the literature.²³ Puncture of the dura mater can diminish intracranial pressure and activate the rupture of an aneurysm.

Neurointerventional procedures during pregnancy

Coiling for intracranial aneurysms and embolization for AVMs are becoming more common compared with the conventional craniotomy-based surgical techniques in the last decade. The duration of the procedure should be kept short minimizing the amount of radiation (less than 5 rad).

Case reports of fetal hypothyroidism due to maternal exposure to iodine contrast is present but do not have any clinical relevance.²⁴ Iodinated contrast media has not been found to be teratogenic in animal studies but has not been studied in humans, although the risk should be assumed to be small. Hence, this agent may be used perioperatively.

Several procedures, such as diagnostic digital subtraction angiography, coiling for an aneurysm, and embolization for AVM may be performed under local anesthesia or intravenous sedation. To slow the blood flow in an AVM feeding artery before the injection of glue for embolization of an AVM, induced hypotension can be achieved with vasodilators drugs. The accuracy of glue injection is facilitated by lowering the systemic arterial pressure with vasoactive agents, general anesthetics, or even by brief adenosine-induced cardiac pause to allow the glue, the short time needed to set.²⁵

Normal perfusion pressure breakthrough in postoperative period accounts for <5% of patients and is managed by preventing postoperative hypertension. Protamine should be present inside the suite for rapid heparin reversal in the event of an acute intracranial hemorrhage. Reversal of antiplatelet activity is achieved with platelet transfusion in the event of acute bleed in these patients.

To conclude, neuroanesthesia management during pregnancy is challenging, and the basic principles of neuroanesthesia and obstetric anesthesia need to be adhered to. Every patient is different and may pose unique challenges both in terms of medical decision-making and anesthesia delivery. A holistic approach by a multidisciplinary team consisting of the neuroanesthesiologist, neurosurgeon/neuroradiologist, obstetrician, and neonatologist is essential for good maternal and fetal outcomes.

Conflicts of interest

All authors have none to declare.

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