REVIEW ARTICLE

Neurosurgery and pregnancy

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Abstract

Pregnant patients rarely present with neurosurgical emergencies, but can cause significant morbidity and mortality to the mother and the foetus. Physiological changes of pregnancy in relevance to neurosurgery, effects of anaesthetic agents on the foetus, common neurosurgical emergencies, and anaesthetic implications both from obstetric and neurosurgical point of view are discussed in this review.

Key words: Aneurysm, subarachnoid haemorrhage, teratogenicity

INTRODUCTION

Neuroanaesthesia and neurosurgery in a pregnant patient is not commonly encountered in our day-to-day anaesthesia practice. Rarity of the combination of such cases poses several challenges to the anaesthesiologist. Various neurological conditions requiring neurosurgery may occur during pregnancy, labor or puerparium. Proper understanding of the maternal and fetal physiology, fetal drug pharmacology and principles of neuroanaesthesiology is of utmost importance. In this review, we will discuss neuroanaesthetic management of pregnant patients for different neurological conditions.

MATERNAL PHYSIOLOGICAL CHANGES COMPLICATING NEUROSURGERY

Physiological changes during pregnancy can complicate any kind of surgery and Neurosurgery is no exception. Anaesthetic exposure and surgical complications exposes both the mother and foetus at risk. There is little margin of safety for a pregnant patient undergoing complicated neurosurgery. Risk of fetal hypoxia, respiratory depression, cardiovascular complications and teratogenicity-related to anaesthesia and surgery is more attributed to altered maternal physiology. Physiological changes relevant to neurosurgery are tabulated in Table 1.

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Routine neurosurgery is rare during pregnancy. If the conditions permit, it is wise to wait until the completion of pregnancy. On the other hand, life-threatening neurosurgical conditions are to be treated promptly. Broadly five types of neurosurgical conditions can be encountered during pregnancy.

Intracranial aneurysm

Unruptured intracranial aneurysms occur in 3.2% of the general population[1] and subarachnoid haemorrhage (SAH) due to ruptured intracranial aneurysm is estimated to be 6-16/1,00,000 population. Prevalence of SAH from all causes is estimated to be 5.8/1,00,000 deliveries[2] in the obstetric population. Rupture of an aneurysm is heralded by sudden onset severe headache, other symptoms of increased intracranial pressure (ICP) and neurological deficit. Morbidity and mortality due to aneurysmal SAH is predicted by a number of scoring systems.[3] Mortality in such cases are attributed to vasospasm, raised ICP leading on to ischaemia, rebleeding, and surgical complications. In a pregnancy, SAH is associated with 35% risk of poor feto-maternal outcomes.[4] There are a number of clinical scenarios where the anaesthesiologist is involved in the management of pregnant patients:

1. Incidentally diagnosed unruptured aneurysm planned for lower segment caesarean section (LSCS)[5]

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Table 1: Physiological changes of pregnancy

Systems	Changes in pregnancy	Implications
Nervous system	↓MAC of inhalational anaesthetic	Modify dose of anaesthetics
	↓Local anaesthetic requirement	Pharmacological sympathectomy is detrimental
	Dependence on the sympathetic system for maintaining haemodynamic stability	
Cardiovascular system	↑HR, SV, CO	Difficulty in estimating blood loss
	↓SVR	Left uterine displacement
	Aortocaval compression	
Haematological system	Disproportionate increase in plasma volume	Physiological anaemia
	Hypercoagulability	Transfusion trigger and blood volume replacement
		Thromboembolic events
Airway and respiratory system	Increased mucosal vascularity and oedema	Difficult intubation
	↑Alveolar ventilation and oxygen consumption	Raised ICT during intubation
	Respiratory alkalosis	Epistaxis
	↓FRC	↑Oxygen requirement
		Rapid desaturation
		Hyperventilation not tolerated
		Decreased reserve for gas exchange
Gastrointestinal and hepatobiliary	↑Intragastric pressure and↓tone of LOS	RSI
	↑Placental ALP	Aspiration prophylaxis
	↑Gall bladder volume and↓contractility	Mimics obstructive pathology
		↑Chances of gall stone disease

MAC = Minimum alveolar concentration, HR = Heart rate, SV = Stroke volume, CO = Cardiac output, SVR = Systemic vascular resistance, FRC = Functional residual capacity, LOS = Lower oesophageal sphincter, RSI = Rapid sequence induction, ALP = Alkaline phosphatase, ICT = Intra cranial tension

2. Ruptured aneurysm for caesarean section[6,7]
3. Ruptured aneurysm planned for craniotomy/ endovascular procedure with continuing pregnancy[8,9]
4. Ruptured aneurysm undergoing craniotomy, followed by LSCS[10]
5. Lower segment caesarean section followed by craniotomy for a ruptured aneurysm[11]
6. Unruptured or ruptured intracranial aneurysm in pregnancy or puerparium planned for coil closure in neuroradiological suite[8,12]
7. Pregnant patient with a ruptured aneurysm for neurointensive care management.

Pregnancy is associated with increased propensity for aneurysm formation and rupture. Increased cardiac output associated with pregnancy imposes haemodynamic stress over the aneurysmal sac; weakening of the aneurysmal sac by the hormonal changes of pregnancy[13] and coexisting conditions such as preeclampsia, eclampsia[14] increases the risk for aneurysmal rupture. Increase in mean arterial pressure (MAP) or decrease in ICP (as may result with subarachnoid block [SAB]) is associated with an increase in transmural pressure and subsequently rupture of the aneurysm:

Transmural pressure = MAP - ICP.

MAP is increased by hypertension, preeclampsia, and sympathetic responses during airway manipulation, coughing and bucking. Whereas ICP is reduced by hyperventilation, mannitol, ventriculostomy/ dural puncture. In addition, factors such as positive end-expiratory pressure and valsalva manoeuver also affect transmural pressure.

The risk for rupture of the aneurysm is highest during 30-40th week of pregnancy, when the haemodynamic stress is the maximum. Rupture during induction of anaesthesia in the general population is <1% in present anaesthesia practice.[15] Asymptomatic aneurysms do not pose any excessive risk for rupture either during pregnancy or puerparium.[16] In a cross-over study in 244 patients the authors concluded that the risk of aneurysmal SAH is not increased during pregnancy, labor, and puerparium.[17]

Unruptured aneurysm

There are no objective data to say vaginal delivery is associated with an increased incidence of aneurysmal rupture, so LSCS is reserved only for obstetric reasons. However, valsalva manoeuver associated with bearing

down and auto-transfusion with every uterine contraction might increase the chances of aneurysmal rupture. Hence, labor analgesia with labor epidural should be provided to all patients planned for vaginal delivery.[18] Many authors in literature have safely used SAB for caesarean section, but there are cases of SAH with the use SAB.[19] Though unruptured aneurysm has a high incidence in the general population, and larger number of them receive neuraxial block performed in day-to-day practice, one shall expect a huge number of SAH after SAB. But the literature has very few reports of the same; hence, SAB can be considered safe of anaesthesia in patients with unruptured aneurysm.[5] Still epidural anaesthesia is considered the safest as there is no dural breach or fall in ICP. However, accidental dural puncture with a large bore epidural needle should be prevented. General anaesthesia is reserved for fetal distress; care should be taken on haemodynamics throughout the surgery.

Ruptured aneurysm

Ruptured aneurysm in pregnant women is usually treated like that in nonpregnant women, where the patient is taken up for immediate craniotomy or coil embolization depending on the clinical grades. Conservative management has high chances of rebleeding, feto-maternal mortality.[8] In a series of seven pregnant patients with a ruptured aneurysm, two patients underwent emergency LSCS, followed by the aneurysmal surgery, while the other five patients underwent craniotomy between 5th and 7th months of pregnancy, and subsequently delivered vaginally at term.[20] General anaesthesia is the technique of choice for LSCS whenever neurosurgical procedure is planned. However, there are case reports of successful use of neuraxial anaesthesia even in patients with SAH, who did not undergo neurosurgery simultaneously.

Anaesthesia in the radiological suite

Coil embolization initially reserved for patients with poorer grades and those unfit for extensive intracranial procedures, is no longer considered so. The safety and efficacy of coil embolization is established[21] and it is an effective option in pregnant patients with a ruptured or unruptured aneurysm. Procedure can be done under sedation and local anaesthesia at femoral cannulation site or can be done under general anaesthesia. Both of the techniques have their own advantages and disadvantages. Concerns are fetal radiation exposure, anaesthesia at remote location, contrast agent and anaphylaxis, contrast and renal dysfunction. Invasive blood pressure monitoring, vasoactive medications, access to the facility for emergency cesarean section and craniotomy should be available. Both thrombotic and bleeding complications are known to occur in patients undergoing coil closure, so provisions for initiation and reversal of anticoagulation should be available.

Arteriovenous malformation

Though congenital, arteriovenous malformations (AVMs) rarely present in childhood. Clinical manifestations appear commonly between age 25 and 45 years.[22] It can present as headache, rupture leading to SAH, cerebral ischaemia or stroke, seizure disorder and in few cases as congestive cardiac failure. Incidence of AVM in pregnant patients is the same as in the general population. Pregnancy as such does not have any influence on the progression of this disease. Ruptured AVM contributes to 50% of SAH,[23] which occurs in pregnancy and responsible for 5-12% maternal mortality. Intracranial AVM can be supratentorial, infratentorial or located deep inside brain structures.[24] Haemorrhage is common in small AVM's. From neurosurgical perspective: Patients with large AVM, large shunt flow and history of previous intracranial bleed are associated with poor postoperative outcomes.

In incidentally diagnosed unruptured or ruptured AVM with no new focal deficits and stable neurological course pregnancy can be continued, and definitive neurosurgical intervention is planned in the postpartum period. If a patient with ruptured AVM has progressive neurological dysfunction then, patient is planned for an emergency craniotomy or endovascular procedures depending on the medical condition of the patient and availability of resources. Maternal well-being becomes primary concern compared to fetal outcomes.

If a patient with unruptured AVM is planned for caesarean section then, central neuraxial analgesia would be safe. However, if the same patient is planned for combined craniotomy and LSCS, then general anaesthesia is the preferred technique.[25] Anaesthetic concerns for such cases are essentially the same as for intracranial aneurysms.

Intracranial tumours

Incidence of intracranial neoplasms in a pregnant patient is not different from general population.[26] Certain tumours manifest rapidly during pregnancy because of increased blood volume, which increases the volume of vascular tumours (e.g., meningioma's). Pregnancy is associated with increased salt and water retention, which increases chances of peritumoral oedema and hence increased ICP. Moreover, hormonal influences of pregnancy are associated with increased growth of certain neoplasms.[27]

Intracranial neoplasms generally present with headache, vomiting, seizures, and visual impairment. Headache and vomiting occur commonly in pregnant patients and hence nonspecific. Nevertheless, any pregnant patient with rapidly progressing headache, vomiting in second or third trimester, new onset seizures and visual disturbances are to be evaluated accordingly.

Gliomas are the most common malignant tumours, which occur in pregnancy. Low-grade gliomas like astrocytoma present with non-specific symptoms and grow slowly, so the main stay of treatment becomes steroid therapy, seizure prophylaxis with adequate follow up and definitive treatment after delivery. On the other hand, aggressive gliomas like glioblastoma multiforme grow rapidly and cause progressive neurological deficit. So in these patients, definitive treatment is never delayed. If the foetus is viable, neurosurgery can be performed after caesarean section or can be done at any time of gestation with adequate fetal monitoring. Salvage therapy like carmustine-impregnated wafers[28] can be used for localized chemotherapy. Carmustine is an alkylating chemotherapeutic agent, which exerts its effects by alkylating the RNA and DNA.[29] Systemic administration of carmustine is associated with systemic side effects and reduced efficacy; to overcome these problems a localized delivery of the chemotherapeutic agent is desirable.

Meningiomas appear to be the most common benign tumor, and they continue to grow during pregnancy. Unless they present with progressive neurological deficits treatment is mainly conservative in pregnant patients. Acoustic neuromas and pituitary adenomas are other common types of intracranial tumours.

Steroids decrease the vasogenic oedema associated with tumor growth, improve the patient symptomatically, increase the fetal surfactant formation,[30] but also have a risk of fetal adrenal hypoplasia. Antiepileptic drugs are used both for treatment and prophylaxis of seizures. Most of the antiepileptic drugs are teratogenic[31] with varying presentations in the newborn. Generalized chemotherapy is not an option in pregnancy; so localized chemotherapy can be used. Radiotherapy is associated with teratogenicity and childhood cancers but may be safely used.[32] Care should be taken to decrease the dose of radiation and to provide adequate fetal shielding. Gamma knife surgeries provide local radiation and awake craniotomy and can be performed safely.[33,34]

Management, like all other cases depends on the gestational age of the foetus. Anaesthetic technique for caesarean section depends on obstetric requirements. Various anesthetic techniques have been used in literature including, combined spinal epidural anaesthesia, general anaesthesia for meningioma excision at 25th gestational week in the sitting position[35] and general anaesthesia for LSCS followed by craniotomy for tumour excision.[36]

Trauma in pregnancy

Maternal mortality due to obstetric causes is gradually decreasing due to better obstetric management, coordinated team approach between obstetrician and anaesthesiologist and better awareness in the society. However, nonobstetric causes of maternal mortality are increasing worldwide. Trauma is the leading nonobstetric cause of maternal death during pregnancy[37] in United States. Out of this head injury is especially devastating and can increase the overall morbidity and mortality.[38] Motor vehicle accidents are the commonest cause of head injury in pregnant patients.[39] In most of the studies, it carries worst outcome in the foetus. Risk is due to the systemic effect of trauma on maternal altered physiology, mainly posttraumatic hypotension and hypoxia.[39] However, some studies showed contrasting result with no increase in mortality or morbidity due to traumatic brain injury in pregnancy.[40] Treatment can be conservative or surgical. Progressive deterioration of the symptoms is an indication for surgery. Maternal outcome has been reported better than fetal outcome in various case series.[29-31]

Spinal cord surgeries and cauda equina syndrome

Low backache is a common complaint in pregnancy, due to the physiological changes, which occur in pregnancy. Significant lumbar intervertebral disc herniation and neuralgia occurs in approximately 1 in 10,000 pregnancies. Impending cauda equina syndrome in such cases is even rarer (approximately 2% of prolapsed cases).[41] It usually presents with gradual onset of severe radicular pain, mostly unilateral, numbness in the sacral region, decreased sensations in specific dermatomes of lower extremities, paresthesias, decreased tone in lower limb, areflexia and bowel and bladder disturbances. Patients with severe back pain with no neurological deficit are managed conservatively with bed rest, physiotherapy, and simple analgesics.

Patients presenting with severe and progressing neurological deficits need to be taken up for surgery. Endoscopic micro-discectomy has advantage of not requiring anaesthesia, and pregnant patient can position herself comfortably in lateral or prone position.[41] Epidural anaesthesia for conventional open surgical decompression with the patient in prone patient is described in literature.[42] General anaesthesia and prone positioning may be required in certain cases of spontaneous epidural haematoma at thoracic or cervical level.[34] Han *et al*. suggest epidural anaesthesia as a safe option for spine surgeries; they also suggest prone position for patients in first and early second trimester of pregnancy and lateral position for late second and third trimester of pregnancy.[43] Positioning a pregnant patient in the prone position can be technically challenging, as excessive compression over the gravid uterus can precipitate preterm labor. Jackson table, Relton-Hall frame, and Wilson frame have been used in literature for positioning pregnant patients in the prone position.

FOETAL IMPLICATION IN NEUROSURGERY

Maintaining foetal well-being during neurosurgery is equally important. Special care should be taken to avoid drugs, which can cause fetal teratogenicity, to prevent fetal hypoxia, acidosis, and premature labor.

Teratogenicity

Organogenesis occurs during 3rd and 8th week of gestation, hence more vulnerable period for developmental anomaly. Drug exposure after 8th week is associated with only minor morphological abnormality.

Drugs and teratogenicity

Teratogenicity due to drugs depends on the kind, dose, and duration of exposure to that particular drug and also on the gestational age. For recapitulation Food and Drug Administration defined category of drugs in relation to fetal teratogenicity are shown in Table 2. Most of the anaesthetic agents fall in the category of B and C, that is, can be used safely with caution. Controversy exists regarding the use of nitrous oxide, benzodiazepines. Cocaine is the only anesthetic agent listed as known teratogenic agent. Different anaesthetic agent, their category and controversy are in Table 3.

Table 2: Food and drugs administration classification of drugs in pregnancy

Category	Drug characteristics
A	No risk for the foetus in any trimester
B	No risk for drugs given after 1st trimester
	Animal study-no risk
	Human study-no controlled study
C	Drugs given if benefit >risk
	Animal study-confirmed fetal risk
	Human study-no controlled study
D	Drugs given if benefit >risk
	Human study-confirmed fetal risk
X	Contraindicated in pregnancy

Radiation and teratogenicity

There are a number of radiological investigations for imaging in neurosurgical conditions. Concerns of radiation-induced teratogenicity, microcephaly and childhood cancers do exist. United Nations Nuclear Regulatory Commission states "0.5 rem" as the safe maximum dose of radiation to the foetus. Iodinated contrast material during pregnancy can cause transient hypothyroidism in foetus.[11] Common neuroradiological investigations and radiation exposure are shown in Table 4.

MAINTENANCE OF FETO PLACENTAL CIRCULATION

Fetal hypoxia and acidosis should be prevented. Factors that can precipitate fetal hypoxia can adversely affect fetal outcomes with poor Apgar and the neurobehavioral score. Uterine circulation is not auto-regulated and hence uterine perfusion is entirely dependent on MAP of the mother. Maternal hypotension, anxiety, pain, hypoxia, hyperventilation, hypercarbia all might compromise feto-placental perfusion and should be vigorously treated.

Tocolysis

There is no evidence that premature labor is associated with types of the anesthetic drugs and anaesthetic technique. Role of prophylactic use of tocolytics is controversial because of its own side effects. Nevertheless both intraoperative and postoperative tocolysis may be required in threatened preterm labor.

Table 3: Anaesthetic agents and teratogenicity

Drugs	Inference
Methohexitone, propofol, enflurane	Category B agent
Thiopentone, ketamine, etomidate, mannitol	Category C agent
Nitrous oxide	Probably teratogenic in animal studies
	Inhibition of methionine synthetase
	No teratogenic effect in a clinical concentration in human studies
	Neonatal depression on delivery with 70% N_2O
Benzodiazepines	Earlier studies showed increased risk for cleft lip and palate
	Subsequent studies failed to prove a causal relationship
	Long term administration to the mother can cause fetal dependence and withdrawal
Desflurane, sevoflurane, halothane, isoflurane, opioids, hypertonic saline	Category B and C
Local anesthetic	Category B and C except cocaine

Foetal monitoring

American Society of Anaesthesiologists guideline on foetal monitoring standards for nonobstetric surgeries state that surgery should be done at an institution with neonatal and pediatric services, an obstetric provider with cesarean delivery privileges should be readily available and qualified individual should be readily available to interpret the foetal heart rate. Type of monitor used is individualized on case-to-case basis.

Table 5 gives a comprehensive tabulation of various concerns from both neurosurgical and obstetric point of view.

CONCLUSION

To conclude, neurosurgical intervention in a pregnant patient is rare but poses too many challenges to the attending anaesthesiologist. Anaesthesiologist's should be aware of these concerns to provide optimal care to both the mother and foetus.

Table 4: Common neuroradiological investigation and radiation exposure to the foetus

Radiological procedure	Amount of radiation absorbed by foetus
CT scan head	<0.01 rem
Cerebral angiography	0.1 rem*[8]
Coil embolization	0.3 rem*[44]

Adequate shielding of the abdomen of the mother. CT = Computed tomography. * = The radiation absorbed by the foetus with adequate maternal abdominal shielding

Table 5: Summary of anaesthetic concerns

Neuroanaesthetic concerns	Obstetric anaesthetic concerns
Stable haemodynamics	Aspiration prophylaxis
Hyperventilation	Rapid sequence induction
Controlled hypotension	Potentially difficult airway
ICP reduction	Maintenance of feto placental circulation
	Feto placental drug transfer
	Avoid aorto caval compression
	Fetal monitoring
	Tocolysis if high risk of preterm labor
	Postpartum haemorrhage: Avoid inhalational agents and prefer total intravenous anaesthesia
	Dosage modifications (increased blood volume, Vd, decreased MAC requirements etc.,)
	Teratogenicity

ICP = Intracranial pressure, MAC = Minimum alveolar concentration, Vd = Volume of distribution

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