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Review Article

Anesthesia Methods in Pregnant Women: A Review Study

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ABSTRACT

Background: Manage and deal with the pregnant patient undergoing anesthesia for surgical non-obstructed surgery, assess the effects of non-obstetric surgeries on both fetus and mother during pregnancy, and measures to prevent it.
Methods: A review search study was currently managed in PubMed, MEDLINE, Embase, Science gate, Elsevier, Scientific report, Google Scholar, and Cochrane Evidence-Based Medicine Reviews, after obtaining approval from the ethics committee of Tehran University of Medical Sciences. All the reviews identified were restricted to human studies and available in English.
Results: Elective surgery ideally should be avoided during pregnancy while emergency surgery should proceed with consideration for the anesthetic implications of the altered physiology of pregnancy. Caution must be taken during anesthetic application and Airway management.
Conclusion: Pre-oxygenation is essential and consider the rapid-sequence induction accompanied with cricoid pressure to lower the incidence of aspiration. Lower MAC values of the volatile anesthetic should be used and medications titrated to preferably produce beneficial effects only.

During pregnancy, "about 2% of pregnant women may require non-obstetric surgery". Appendicitis, cholecystitis, herniated disks, trauma, and cancer surgery are the most common diagnoses [1]. Such surgeries can be performed either as an emergency or as an elective procedure. The complications of anesthesia affect both the mother and the fetus, while the disorder itself might have a detrimental effect on the mother's wellbeing. Another factor to consider is the surgery's timing in relation to the gestational age of the mother [2]. Any condition that can occur in pregnant women needs urgent surgical care, an interdisciplinary management should be optimized to achieve optimum protection for both mother and fetus in order to prevent teratogenous medications, fetal acidosis, and hypoxemia, as well as adverse pregnancy consequences such as miscarriage, stillbirth, or premature birth.

The anesthetic and surgical procedures will be altered as a consequence of various physiological and hormonal modifications that occur during pregnancy period [3]. Evidence shows that surgery during pregnancy is safer than previously believed. It is recommended that non-obstetrical elective surgery be deferred after delivery whenever possible.

If this isn't feasible, the operation can be performed in the middle of the third trimester, depending on the urgency of the symptom (due to a lower incidence of teratogenicity, which occurs more frequently during the first trimester of pregnancy, or preterm labor, which occurs more frequently in the third trimester) [4].

The large portion of these alterations are caused by the mechanical effects of the enlarging uterus, hormonal changes associated with gestation, elevated metabolic demands, and low resistance placental circulation, which may be problematic in the non-pregnant state [3].

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The most significant changes for the anesthetists are summarized below:

During pregnancy, the cardiovascular system undergoes changes such as "an increase in intravascular volume and changes in hematology" [5]. Cardiac output (CO) starts increasing early during pregnancy, (CO) raises to 75%, this increase in cardiac output is coming as a result to the increased oxygen requirement due to the increased metabolic demands of the fetus [6]. While myocardial contractility remains constant, systemic vascular resistance tends to decrease, primarily as a consequence of progesterone's effects and the presence of the lower-resistance placenta [6]. Physiologic hypotension might be present between weeks 14 and 24 due to the decrease in systemic vascular resistance, systemic blood pressure diminished secondary to the reduction in systemic vascular resistance influenced by positioning, systole, diastole, and mean blood pressure [7]. "The uterus is enlarged in size and emerges out of the pelvis to encroach upon the abdominal viscera" that might result in aortocaval compression especially during the supine position [8]. "The vena cava is compressed by the gravid uterus" resulting in decreased cardiac preload and output. Supine hypotension can negatively affect venous stasis in the legs, eventually leading to ankle edema, varicose veins, and a higher risk of venous thrombosis [7].

Blood volume expands within the first trimester and reaches to 35 to 50 % at term [8]. "Erythrocyte mass also increases by approximately 30% [6]. The heart undergoes unusual hypertrophy because of increased blood volume [3]. Also, "changes in the renin-angiotensin-aldosterone system facilitate the sodium absorption and water retention causing the maternal intravascular fluid volume to increase in the first trimester" [8]. The additional increased intravascular fluid volume helps for the future compensation of estimated blood loss in vaginal delivery [7].

Total protein reduction reaches to 10% compared with non-pregnant levels while the red cell volume has increased only 25% [7], resulting in a condition called physiologic anemia of pregnancy, so uteroplacental blood flow is improved due to this reduction in blood viscosity [3].

Coagulation changes occur from the first weeks of pregnancy [3]. Platelet turnover is enhanced and similarly are the clotting factors [3], including an increase in pro-coagulant factors V, VII, VIII, IX, X, XII, fibrinogen [9]. Von Willebrand factor also increases leading to a state of hyper-coagulablity.

The Fibrinolytic system is inhibited due to the higher levels of plasminogen activator inhibitor and the lower levels of plasminogen activator levels during pregnancy [6]. levels of endogenous anticoagulant protein S decline throughout pregnancy [9]. This hyper-coagulable state increases the risk of thromboembolism in the pregnant woman [10]. Low molecular weight heparin is the drug of choice in the prevention and treatment of VTE during pregnancy because it has fewer side effects and a lower placental cross, discontinuation of treatment or change to heparin at 6 weeks of pregnancy is recommended to prevent embryonic exposer [3,10].

Respiratory changes: The mucosa of the nasopharynx becomes edematous and hyperemic as estrogen levels rise, resulting in hypersecretion and an increased risk of epistaxis [11]. Also "The anatomical changes related to both weight gain and edema of the upper airway and vocal cords, which occur secondary to the generalized increase in capillary permeability, complicate airway control in pregnancy" [8], with the enlarged hazard of bleeding present during manipulation of the upper airway leading to difficult ventilation and intubation of the trachea [12].

As local vascularity and permeability increase, "topical drugs delivered into the nasopharynx and upper airway may be more readily accessible to the bloodstream". However, there is no confirmation that inhaled agents cause elevated toxicity during pregnancy [6].

If the mechanical pressure from the gravid uterus increases, the cartilaginous attachments between the ribs and the sternum relax, the thoracic cavity compromises structurally "increase in the subcostal angle, chest diameter, and rise in the diaphragm". Total lung capacity, functional residual capacity, and residual volume all decrease as a result of these changes [11].

The enlarging uterus pushes the abdominal content and diaphragm upward limiting the free space for normal lung expansion, result of this the functional residual capacity (FRC) is reduced by 20% [13]. This reduction comprises almost equivalent reductions in both the expiratory reserve volume (ERV) and residual lung volume (RV), by the same time the oxygen consumption is raised to 20% - 40%, this reduced reserve of oxygen with expanded metabolic demand predispose pregnant women to the risk of hypoxia, hypercarbia, and other respiratory complications [13].

At full term minute ventilation is increased by half, outcomes in a state of respiratory alkalosis, which facilitate oxygen delivery and carbon-di-oxide removal from the fetal circulation [6,13].

"With dilatation of the renal pelvis, calyces, and ureters", the kidney and renal collection systems grow in size during pregnancy. Subsequently, the glomerular filtration rate increases to half within the first trimester [11], as a result creatinine clearance is raised to 50% [3]. A physiologic drop in serum creatinine, blood urea nitrogen, and uric acid concentration occurs as a result of hyper-filtration [3]. "Changes in renal physiology have a profound effect on drug pharmacokinetics". Also, the bladder capacitance decreases over time as a result of pressure exerted by the expanding uterus, resulting in urinary frequency, urgency, and incontinence [11].

Progesterone-mediated smooth muscle inhibition has an important effect on the gastrointestinal tract [6], in which they adopt dysrythm leading to nausea and vomiting [8]. After mid-gestation, intestinal emptying is prolonged, leading to a state of increase in intra-gastric pressure due to the gravid uterus's external compression with delayed emptying [6], a decline in lower esophageal sphincter resting muscle tone resulting in substantial upsurge in gastro-esophageal reflux [11].

"While gastric emptying is normal during pregnancy, the risk of gastric content aspiration rises (especially after the 15th week)", particularly in patients who suffer from heartburn [3]. Pregnant women are at an elevated risk of regurgitation when general anesthesia is induced (all pregnant women should be considered as a full stomach), aspiration of gastric contents, and developing acid pneumonitis, therefore consideration must be given to prevent aspiration and lowering the pH of gastric fluid [12].

The drug's teratogenicity is determined by the dosage, course, and period of exposure [3]. Large studies show that no significant difference in the rates of congenital abnormalities in babies of those who have undergoes surgery during pregnancy compared with controls [14]. The timing of exposure is critical; an all-or-nothing phenomenon occurs within the first 15 days of human gestation, and structural defects can occur during organogenesis [3]. "Pregnancy is associated with higher sensitivity to inhalational anesthetics, with alveolar concentration reductions reaches 40%". Similarly, the sensitivity to intravenous agents is also increased [3].

Nitrous oxide affects the B12 metabolism [15], it has a known effect on DNA synthesis since it inhibits methionine syntheses (3). It's better to remain away from nitrous oxide during pregnancy since it's not required for safe and successful anesthesia.

According to some reports, Benzodiazepine use by mothers for a long time has been linked to cleft palate defects [15], while midazolam has not been linked to congenital defects, it is best to avoid it during the first trimester [16], single doses are tolerable.

Thiopentone rapidly crosses the placenta, but it does not sedate the neonate [17]. However, propofol is much more common as an option because it is more effective and does not seem to affect the umbilical cord gestation in early pregnancy [18].

Ketamine and other agents that augment uterine tone are better to avoid, since it rapidly crosses the placenta [17].

Short-term exposure to opioids is secure, but long-term exposure to opioids can cause withdrawal symptoms to the fetus [18].

For these patients, remifentanil is an excellent option since, unlike other opioids, it is quickly metabolized by nonspecific blood and tissue esterases [4]. But special attention must be taken to the accompanying transient hypotension.

"Neuromuscular blocking agents are ionized and cross the placenta in most cases". Also, their action may be prolonged during pregnancy, (plasma cholinesterases are diminished to 25%) [3-4], while recovery from succinylcholine is not prolonged [18], which make it the best choice for anesthesia induction.

"All induction agents opioids, neuromuscular blocking agents, and volatile anesthetics are not teratogenic when used in clinical doses and maternal physiology is controlled" [18].

Anesthetic consideration:

Tracheal intubation: The common cause of maternal mortality in relation to the anesthesia were problems in the management of the airway [19]. Difficult tracheal intubation due to the edema of the airway and friability of oropharyngeal tissues [3]. Upper respiratory tract mucosa becomes more vascular which increases airway bleeding probability and swelling. So, tracheal intubation may be challenging when these anatomical changes occur. The insertion of the laryngoscope becomes more difficult with enlarged breasts, this can alter the view of the vocal cords [20-21]. Since pregnant women desaturated rapidly than non-pregnant women because of the high oxygen consumption and metabolic requirement of the growing fetus, so pre-oxygenation with 100% oxygen and rapid sequence induction must be an essential step during induction to prevent the rapid hypoxia [22-23].

During pregnancy, Regional anesthesia via peripheral nerve and neuraxial blocks is usually recommended. Blocks like these are effectual and significantly used during surgeries. If neuraxial blocks are used, the provider must be aware of the risk of sympathetic block causing induced maternal hypotension [24]. Regional anesthesia is preferred to general anesthesia where feasible. Although, there is no evidence showing that this type of anesthesia influences the outcome of pregnancy. But, obesity and edema may obscure the anatomical landmarks, the softened hormonally Inter-spinal ligaments cause difficulty with epidural loss resistance techniques [4], "Since the volume of the epidural and subarachnoid spaces is decreased due to aorta-cavel compression (which induces engorgement of the epidural venous plexus)", which results in an extra distribution of local anesthetic that infused in neuraxial block [18]. Although neural tissue is more sensitive to local anesthetics, lower doses are needed, which increases the risk of toxicity [8]. In the presence of hypervolemia, severe maternal hypotension can occur; it should be treated with "intravenous fluids, left lateral tilt, and a vasoconstrictor such as ephedrine or phenylephrine" [18].

Due to the extreme developing fetus, pain management during pregnancy is challenging [25]. The main goal of

acute pain control during pregnancy is to protect maternal-fetal homeostasis while avoiding the harmful effects of analgesics on the developing fetus. Any pharmacological treatment for acute pain in a pregnant woman must be adjusted to their individual circumstances (consideration must be taken for pregnancy stage, risk-benefit of drug, teratogenicity, and potential for premature labor) [25]. Several treatment options are considered relatively safe during pregnancy, except during the time of organogenesis [26].

Opioids are a common treatment option for mild to extreme acute pain in pregnancy, they cross the placenta and blood-brain barriers with a possibility of fetus exposure [25]. Given opioid is associated with risk of maternal respiratory depression [27]. To prevent fetal dependence, it is preferred that patients be weaned from opioids as soon as possible. "Babies born with opioid dependency will have low birth weight, respiratory depression, and serious drowsiness, which can lead to feeding issues" [12].

Tramadol is a synthetic centrally acting typical opioid. Its biologically active metabolites and excreted by the kidney [28-29]. Tramadol crosses the placenta, it's batter to avoid during early pregnancy [25,30].

Using codeine during pregnancy was related to a higher risk of elective and emergency cesarean sections, as well as postpartum hemorrhage [31].

"The non-steroidal anti-inflammatory drugs use in early pregnancy is thought to be related to increased fetal loss", single doses are tolerable and gives no harm [18]. Ibuprofen, naproxen, and diclofenac are examples of non-steroidal anti-inflammatory drugs (NSAIDs) that are widely used during pregnancy [32-33]. NSAIDs have a direct effect on implantation and pregnancy maintenance, according to animal studies [33-34]. The use of non-steroidal anti-inflammatory drugs (NSAIDs) thought to be connected to increased risk of congenital malformations and miscarriage. NSAIDs will quickly cross the placenta and have a long half-life in the fetus [33]. Avoiding use during the first trimester and the last trimester of pregnancy [25].

Acetaminophen is considered safe in pregnancy [12]. While it's one of the most commonly prescribed analgesics and antipyretics during pregnancy, several clinical studies have recently shown some negative effects on the fetus [45]. Acetaminophen exposure during the first 8–14 weeks of pregnancy has been shown to influence fetal reproductive growth and trigger neurodevelopmental disorders [35-36].

Fetal consideration: Intrauterine asphyxia is the most significant risk factor for the embryo during maternal surgery. It's such a challenge for the anesthesiologist to maintain normal maternal hemodynamics and oxygenation during surgery. The critical points that must be handled are maternal oxygenation, hyper or hypocarbia, hypotension, and uterine hypertonus [4]. Short-term hypoxia is tolerable, but long-term hypoxia may cause uteroplacental vasoconstriction and reduced perfusion, resulting in fetal hypoxia, acidosis, and death [3]. "Fetal respiratory acidosis, uterine vasoconstriction, and decreased uterine blood flow can all be caused by maternal hypercapnia, which can occur during spontaneous ventilation or deep stages of anesthesia" [3,7,18]. "Extreme positive pressure ventilation may induce hypocapnia in the mother, as well as increased intra-thoracic pressure, decreased venous return, and decreased uterine blood flow" [18]. The maternal oxyhemoglobin dissociation curve is shifted to the left, subsequently decrease oxygen discharge to the embryo.

Because of the passive dependency of the placental circulation on maternal systemic arterial pressure, any reduction in maternal arterial pressure will result in decreased uteroplacental blood flow and fetal ischemia [7]. Intravenous fluid given must be sufficient and necessary for the surgical blood loss [7]. Uterine hypertonus is related to a rise in uterine vascular resistance, which decreases uterine blood flow.

Anesthetic management: The maternal response to stress may be impaired by physiologic changes during pregnancy. Pregnant women consume more oxygen and have less oxygen reserves. As a result, they are at risk of hypoxia during brief apnea episodes.

The main risk during anesthesia induction is the aspiration of gastric contents, that means rapid sequence induction of general anesthesia must be considered with cricoid pressure which to some degree decrease the probability gastric aspiration. The anesthesiologist should perform good arrangements including airway assessment, adequate pre-oxygenation, good positioning, antacid prophylaxis to lower the acidity of gastric content, and never forget the fully equipped theater with all anesthetic instruments with a well-trained staff [37].

Aortocaval compression can be avoided by taking a lateral posture where possible, or by tilting in the supine position [18], "in relation to extra weight, breast engorgement, and increased vascularization, which may predispose to bleeding during intubation, airway control, mask ventilation, and laryngoscopic intubation can all be difficult", It's possible that a smaller tracheal tube would be needed (usually size 6-6.5 is used) [18].

Pre-oxygenation is vital in pregnant patients, and it should be maintained for at least 3 minutes with a close-fitting mask since hypoxia progresses three times faster during pregnancy. Hypoxia can easily compromise placental blood flow [11,18].

Preoperatively, sufficient hydration and blood supply for transfusion should be ensured [38]. Tocolytics and deep venous thrombosis prophylaxis can only be used if there are known or perceived contractions [38-39].

Induction of anesthesia should be accomplished after pre-oxygenation with 100% for at least three min. usually, propofol is the best anesthetic induction choice.

"In order to sustain placental blood flow, the hemodynamic effects of induction must be expected and minimized" [40]. For muscle relaxation, Succinylcholine is the drug of choice that is most used, since it facilitates the rapid sequence intubation, "non-depolarizing neuromuscular blocking agents do not cross the placenta" [11,40]. The introduction of sugammadex make rocuronium another suitable choice for induction [17].

Ventilation should be directed at keeping the PCO2 in the usual range for pregnancy after airway securing.

Manipulation of the uterus should be less as much as possible [38]. If needed, fetal monitoring should be done for the first 24 weeks of pregnancy [7-8]. When it comes to fetal heart rate monitoring, close contact between the anesthesiologist and the obstetricians is critical. The baseline fetal heart rate ought to be the key measure for fetal well-being during general anesthesia since the majority of the drugs used induce general anesthesia will abolish fetal heart rate variability [8].

Loss of fetal heart rate variability during general anesthesia is not always indicative of fetal distress, it may be to the predicted anesthetic impact on the fetal autonomic nervous system [7]. During maintenance, volatile anesthetic agent should be reduced "pregnancy is associated with raised sensitivity to the volatile anesthetic agent".

"To avoid maternal catecholamine release and reduced uteroplacental perfusion", light anesthesia and pain should be avoided. Extubation must be performed in the lateral position with the patient fully awake [18]. Regional anesthesia should be used if it's possible, it's better to continue pain management, if an epidural catheter is used [3].

Laparoscopic surgery commonly increases in pregnancy. The indications for surgery are similar to non-pregnant patients [41], and can be done in any trimester of pregnancy, but they are safer during the second and early third trimester [3,41]. Laparoscopic surgery is related to a shorter hospital stay with a faster return to daily activities and appears to be safe and effective as open surgery without increasing adverse perinatal outcomes [42]. Laparoscopic surgery during pregnancy has a high success rate and a low risk profile. There are some issues about fetal health. Direct fetal/uterine damage and fetal acidosis from insufflated carbon dioxide absorption are two possible injury mechanisms. Maternal cardiac production and uteroplacental perfusion may also suffer from increased intra-abdominal pressure [7]. Laparoscopic surgery is contraindicated in placental abruption, imminent delivery, ruptured membranes, and uncontrolled eclampsia [16]. The potential for respiratory compromise as a result of diaphragm displacement, as well as the risk of peritoneal absorption of carbon dioxide, is the source of concern about carbon dioxide insufflation. Usually, 15 mm Hg pressure is applied without triggering contrary maternal/fetal outcomes [43]. The fetal and uterine status, as well as end-tidal PCO2 and maternal arterial blood gases, should all be controlled.

Methods

A review search study was currently managed in PubMed, MEDLINE, Embase, Science gate, Elsevier, Scientific report, Google Scholar and Cochrane Evidence Based Medicine Reviews, after obtaining approval from the ethics committee of Tehran University of Medical Sciences (IR.TUMS.SPH.REC.1399.236). References reviews and manual searching of recently published books, articles in relation to the subject (surgical non-obstetrical anesthesia) was started at (Dec.2021).

All the reviews identified were restricted to human studies and available in English.

The study involved all pregnant women that experience non-obstetrical surgeries during pregnancy urgent and cold cases.

Results and Conclusion

Elective surgery ideally should be avoided during pregnancy, especially during the first trimester, while emergency surgery should proceed with consideration for the anesthetic implications of the altered physiology of pregnancy. The symptoms, nature, and location of the surgical procedure should all determine the anesthetic technique used. The risk of miscarriage and preterm labor should be handled with the obstetrician prior to surgery. Caution must be taken during anesthetic application, airway management and intubation can be difficult due to the extra weight and increased vascularization, potentially resulting in edema and bleeding. Pre-oxygenation is essential and considering the rapid-sequence induction with cricoid pressure to decrease the incidence of aspiration (preoperative antacid prophylaxis to lower gastric acidity). lower MAC values of the volatile anesthetic should be used and medications titrated to preferably produce beneficial effects only should be given. Light anesthesia and pain should be prevented and avoidance of the aortocaval compression by lateral position.

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