Pain Management in Pregnancy

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Introduction

- Nonobstetrical causes of pain during pregnancy are very common and can be incapacitating if not treated appropriately.
- 14% of women filled a prescription for an opioid at least once during the antepartum period and 6% of women received opioids throughout all trimesters.
- While there is increasing awareness and use of nonpharmacological approaches in the management of pain overall, the literature and discussion on their use in the pregnant patient with the unique consideration of mother and fetus are sparse.

Common Pain Presentations

- Throughout pregnancy, several anatomic and physiologic changes occur in the body.
- These changes can precipitate pain, which in some cases can lead to disability.
- Additionally, a pregnant state can exacerbate preexisting painful conditions.
- Pain conditions during pregnancy may be further grouped into a systems-based classification such as musculoskeletal, rheumatologic, neuropathic, and pelvicoabdominal pain syndromes.

Musculoskeletal and Rheumatologic Pain

- Low back pain is a common problem among pregnant women as it impacts approximately half of pregnancies.
- laborious work, a history of low back pain before pregnancy, and a previous history of pregnancy-related low back pain have been identified as risk factors for the development of pregnancy-related low back pain.

Management

- Postural Techniques and Physical Therapy
- Complementary and Alternative Medical Treatments (acupuncture, manual therapy, water therapy, transcutaneous nerve stimulation, stabilization belts, yoga)
- Medication Management
- Interventional Options and Evidence

Prognosis

- Within a few months after delivery, most women experience improvement of their pain symptoms.
- However, some women continue having residual pain.
- Specifically, in a prospective, 3-year follow-up study, about 20% of women reported that they continued to experience pain after pregnancy.

Joint Pain

- Healthy women can present with diverse musculoskeletal changes during pregnancy, such as joint pain.
- These symptoms usually raise suspicion of inflammatory diseases like systemic lupus erythematous (SLE) or rheumatoid arthritis.
- However, developing new-onset rheumatoid arthritis during pregnancy is rare, and some studies even suggest that pregnancy is protective against new onset rheumatoid disease.

Management

- The current literature on the management of joint pain in previously healthy pregnant women is limited.
- Presently, most of the available studies focus on managing joint pain in women with preexisting rheumatologic conditions.
- A multidisciplinary treatment plan directed by a rheumatologist is suggested for pregnant women with rheumatologic disease.

Neuropathic Pain—Carpal Tunnel Syndrome (CTS)

- The prevalence of CTS ranges from 2.3% to 35% in pregnant women.
- Hormonal changes associated with pregnancy and associated tissue edema have both been
- implicated.
- Electrophysiological changes in median nerve function have also been reported in asymptomatic pregnant women.

Management

- For the management of CTS, both activity modification and the use of splints in neutral position throughout the night have shown some success.
- Activity modification includes eschewing extreme flexion and/or extension and avoiding extended exposure to vibration.
- Thermoplastic night splints have been helpful, as several women have experienced symptom relief after two weeks of use.
- Physical therapy and NSAIDs have also been recommended for CTS. If CTS symptoms persist, therapy directed specifically towards edema reduction is suggested.
- Additionally, steroid injections have been suggested as they have been shown to offer relief in up to 80% of patients.
- In extreme cases, surgical decompression may be necessary.

Neuropathic Pain—Meralgia Paresthetica

- Meralgia paresthetica is a sensory mononeuropathy that specifically involves the lateral femoral cutaneous nerve of the thigh.
- It transpires when the lateral femoral cutaneous nerve is compressed, as it is then forced to pass under the tensor fascia lata at the inguinal ligament.
- Patients typically describe an insidious onset of a painful burning sensation on the lateral aspect of the thigh, aggravated during side-sleeping and prolonged sitting or standing.
- Examination will reveal an exaggerated lumbar lordosis and sensory deficit on the lateral aspect of thigh with preserved motor function and reflexes.

Management

- Typically, treatment is usually not needed for meralgia paresthetica and symptoms abate with delivery of fetus.
- Stretching exercises such as the “catcamel”position help alleviate pain temporarily.
- However, if symptoms persist, pain may be relieved by local infiltration of steroids and local anesthetics at the point of maximal tenderness or a lateral femoral cutaneous nerve block

Pelvic and Abdominal Pain

- The cause of pregnancy related pelvic pain is multifactorial.
- Pain seems to occur from increased motion in the pelvic girdle which is associated with increased ligamentous laxity,which occurs due to the influence of the hormones relaxin and estrogen.
- It has been proposed that there is a correlation between relaxin levels during pregnancy and pelvic pain. As a result of elevated relaxin concentrations, the symphysis pubis expands during the 10th to 12th weeks of pregnancy.
- This widening can be painful, as it allows for increased mobility of the joints.
- This pain is exacerbated by exercise and sometimes mechanical strain.
- Risk factors for pregnancy-related pelvic pain include strenuous work, previous low back pain, previous history of pregnancy-related pelvic pain, and previous trauma to the pelvis.

Management

- Patient education is an important part of managing pregnancy-related pelvic pain.
- Information regarding the condition not only helps to reduce fear, but also encourages patients to become an active part in their treatment and rehabilitation.
- These patients should be provided with material about ergonomics and physical activity for their pain.
- Women with pregnancy-related pelvic pain should avoidmaladaptive movements such as unequalweight bearing on legs, hip abduction, and activities that strain joints to their extreme.

Abdominal Nerve Entrapment—Anterior Cutaneous Nerve Entrapment Syndrome

- Abdominal pain in pregnancy has various origins, and while most complaints involve the abdominal viscera, the abdominal wall itself can be a source of chronic pain in pregnancy.
- Anterior Cutaneous Nerve Entrapment Syndrome (ACNES) usually is reported after surgery, as the small cutaneous nerve fibers become entrapped in skin incisions.
- Pain is described as very well localized and lateral to the umbilicus.
- Physical examination will demonstrate a positive Carnett's sign (pain worsened with Valsalva maneuvers such as a crunch or sit up) and alleviated with rest.
- In pregnancy, the increasing abdominal wall size can stretch the cutaneous nerves and cause chronic pain. It has been proposed that the changes in the thoracic and abdominal wall from uterine growth can lead to entrapment of the anterior cutaneous nerves.

Management

- Ultrasound-guided transversus abdominis plane (TAP) blocks or rectus sheath blocks can be used to alleviate pain from Anterior CutaneousNerve Entrapment Syndrome.
- The choice of which block to use is indicated by the location of the pain, and these blocks may be considered for both diagnostic and therapeutic approaches.

Intercostal Neuralgia

- Intercostal neuralgia may arise as a result of lesions at the level of the spinal cord, nerve trunks, roots, or terminals. It has been suggested that the enlarging gravid uterus, which leads tomechanical stretch on the lower intercostal nerves, can cause intercostal neuralgia.
- It has also been proposed that postural variations throughout pregnancy can assist in generating nerve root irritation when the nerves transverse the neural foramina.
- Intercostal neuralgia may manifest with radicular pain in the distribution of a thoracic root or intercostal nerve.
- Pain is described as a burning or radiating pain, associated with late gestation (increased uterine displacement), and occasionally followed by bouts of coughing, which can cause a secondary costochondritis.

Management

- In a review of the literature, topical lidocaine patches or creams, intercostal nerve blocks, and/or epidural steroid injections have evidentiary support for successful treatment for pregnant women with intercostal neuralgia.

FDA classification	Definition[a]	Examples
Category A	Controlled studies in women fail to demonstrate a risk to fetus. The possibility of harm to the fetus appears remote.	Multivitamins
Category B	Either animal studies have not demonstrated a fetal risk but there are no controlled human studies *or* animal studies have indicated an adverse effect that was not confirmed in controlled studies in women in the 1st trimester (and there is no evidence of risk in the later trimesters).	(i) PO acetaminophen (ii) Opioids: nalbuphine (iii) Local anesthetic: lidocaine
Category C	Teratogenic or embryocidal risk indicated in animal studies, but controlled studies in women have not been done *or* there are no controlled studies in animals or humans.	(i) NSAIDs: sulindac, naproxen (ii) Opioids: codeine, butorphanol, fentanyl, hydrocodone, levorphanol, methadone, morphine, oxycodone, and oxymorphone (iii) Antidepressants: fluoxetine (iv) Tricyclic antidepressants: amitriptyline, imipramine (v) Anticonvulsant: gabapentin (vi) Drugs used for migraine: metoprolol, propranolol, sumatriptan, nifedipine, and verapamil
Category D	Positive evidence of fetal risk, but use in pregnant woman is acceptable since the maternal benefit outweighs the risk to the fetus.	(i) NSAIDs: aspirin (ii) Steroids: cortisone (iii) Anticonvulsants: diazepam, phenobarbital, and phenytoin
Category X	Animal and human studies demonstrate fetal abnormalities *or* there is evidence of fetal risk based on human experience *or* both; the risk outweighs any possible benefit. The drug is *contraindicated* in women who are or may become pregnant.	(i) Antimigraine: ergotamine (ii) Antidepressants: paroxetine (iii) Anticonvulsants: valproic acid

Acetaminophen

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
Acetaminophen Risk factor: B when taken orally (C for intravenous use) *650 mg every 4–6 hours or 1 g every 6 hours.*	Use with caution Strong evidence against increased risk of miscarriage , serious birth defects , IQ, or physical growth . Associated with small increased risk of cryptorchidism in boys and childhood asthma	Use with caution Associated with small increased risk of cryptorchidism in boys and childhood asthma	Use with caution Associated with increased risk of childhood asthma	Safe to use No increased risk of hemorrhage if the drug is given to the mother at term in standard doses .	Safe to use The American Academy of Pediatrics (AAP) considers acetaminophen to usually be safe during lactation . Weak association with early infant exposure (first 6 months) with increased risk of childhood asthma ; more research is required.

NSAIDs

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
Nonsteroidal anti-inflammatory drugs (NSAIDs) See individual drugs in the class for more detailed information, as risks vary per drug.	Studies are mixed on prenatal and early pregnancy use of NSAIDs and risk of miscarriage. Nakhai-Pour et al. showed the association with NSAIDs as a class; however, Edwards and colleagues did not find this association. A more recent study, with more than 65,000 women also did not find an increased risk of spontaneous abortion following exposure to NSAIDs. One prospective study in pregnant patients with inflammatory rheumatic disease did not show a significant association with major birth defects nor harmful long-term effects caused by intrauterine exposure to these drugs when taken early to mid-pregnancy. On the other hand, Ericson and Källén observed an increase in cardiac malformations in women with rheumatic disease exposed to NSAIDs in the first trimester. There was no drug specificity for cardiac defects.	One prospective study in pregnant patients with inflammatory rheumatic disease did not show a significant association with major birth defects nor harmful long-term effects caused by intrauterine exposure to these drugs when taken early to mid-pregnancy.	Do not use. NSAIDs are generally linked to premature closure of the ductus arteriosus when taken in the third trimester of pregnancy, which in some cases may result in primary pulmonary hypertension of the newborn. Large doses taken by mothers in the week before delivery can increase risk of intracranial hemorrhage in premature neonates.	The use of NSAIDs as tocolytics has been associated with an increased risk of neonatal complications, such as patient ductus arteriosus necrotizing enterocolitis and intraventricular hemorrhage.	NSAIDs in general seem to be safe during breastfeeding.

Aspirin

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
(i) Aspirin Risk factor: D *60–100 mg daily is generally not associated with adverse outcomes.*	Use only if clearly indicated Three studies including 11,000 NSAID-exposed pregnancies did not find a significant increase in the frequency of congenital malformations, nor was there an effect upon infant survival compared with unexposed pregnancies. Low-dose aspirin therapy (81 mg/day) is generally free of maternal or neonatal complications. Weak evidence for increased associations with gastroschisis and IQ/attention decrements in children.	Use only if clearly indicated In one study, aspirin was dose-dependently associated with congenital cryptorchidism, particularly during the second trimester.	Do not use, especially if there is increased risk of premature delivery The use of high-dose aspirin close to delivery has been shown to increase the incidence of clotting abnormalities, in addition to neonatal and perinatal bleeding such as hemorrhage in the CNS in the newborn. Severe neonatal bleeding has been reported after premature delivery. Premature closure of the ductus arteriosus can result when using a full-dose aspirin in this period. Persistent pulmonary hypertension of the newborn (PPHN) is a potential complication of this closure.	Use only if clearly indicated	Use only if clearly indicated Data has suggested that low dose aspirin, 81 mg/day, is generally considered safe; however, aspirin should be used with caution. Doses above 150 mg are contraindicated.

Ibuprofen-Ketorolac

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
(ii) Ibuprofen Risk factor: C (prior to 28 weeks of gestation)/D (≥28 weeks of gestation) *400 mg every 4–6 hours as needed.*	Use with caution	Use with caution	Do not use Linked to premature closure of the ductus arteriosus, resulting in persistent pulmonary hypertension of the newborn (PPHN).	Use with caution	Safe for breastfeeding women to use. AAP classifies ibuprofen as usually compatible with breastfeeding.
(iii) Ketorolac Risk factor: C (prior to 28 weeks of gestation)/D (≥28 weeks of gestation) *Single IV dose: 30 mg. Weight <50 kg: 15 mg.*	Use with caution	Use with caution	Do not use Linked to premature closure of the ductus arteriosus, resulting in persistent pulmonary hypertension of the newborn (PPHN).	Use with caution	Use with caution AAP classifies ketorolac as usually compatible with breastfeeding.

Naproxen-Celecoxib

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
(iv) Naproxen Risk factor: C *500 mg every 12 hours.*	Use with caution One study found an association between naproxen use and orofacial clefts. However, the risk for these defects appears to be small.	Use with caution	Do not use Linked to premature closure of the ductus arteriosus, resulting in persistent pulmonary hypertension of the newborn (PPHN).	Use with caution	Safe for breastfeeding women to use. AAP classifies naproxen as usually compatible with breastfeeding.
(v) Celecoxib Risk factor: C (prior to 28 weeks of gestation)/D (≥28 weeks of gestation). *200 mg twice daily.*	Use with caution	Use with caution	Do not use Linked to premature closure of the ductus arteriosus, resulting in persistent pulmonary hypertension of the newborn (PPHN).	Use with caution	Use only if clearly indicated There is inadequate evidence to fully determine infant risk. Should only be used if the possible benefit outweighs the possible risk.

Opioids

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
Opioids See individual drugs in the class for more detailed information, as risks vary per drug.	Use with caution In general, short-term, episodic use of opiates appears to be safe in pregnancy. Few studies have evaluated opioid teratogenicity in the first trimester. Overall opinion is that there is minimal risk. However, one study showed an association with congenital heart defects, spina bifida, and gastroschisis. This study is limited by recall-bias. Opioid abuse and use of chronic opioids during pregnancy is associated with neonatal abstinence syndrome (NAS).	Use with caution In general, short-term, episodic use of opiates appears to be safe in pregnancy. Opioid abuse as well as use of chronic opioids during pregnancy is associated with neonatal abstinence syndrome (NAS).	Use with caution In general, short-term, episodic use of opiates appears to be safe in pregnancy. Opioid abuse as well as use of chronic opioids during pregnancy is associated with neonatal abstinence syndrome (NAS). Onset of withdrawal signs is sooner in infants exposed to opioids with shorter half-lives, such as morphine and oxycodone.	Use with caution Maternal opioids pass readily into fetal circulation and can cause fetal respiratory depression. Opioids should be avoided when delivery of a premature neonate is expected.	Use with caution The short-term use of opiates during breastfeeding appears to be safe. Infants should be closely monitored for signs of respiratory depression.

Morphine-Fentanyl

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
(i) Morphine Risk factor: C *15 mg, 30 mg tabs; 10 mg, 20 mg/5 mL elixir*	Use with caution No reports linking the therapeutic use of morphine with major congenital defects have been reported.	Use with caution Onset of withdrawal signs is sooner in infants exposed to opioids with shorter half-lives, such as morphine.	Use with caution Onset of withdrawal signs is sooner in infants exposed to opioids with shorter half-lives, such as morphine.	Use with caution	Use with caution AAP classifies morphine as usually compatible with breastfeeding.
(ii) Fentanyl Risk factor: C *Intramuscular, intravenous, intrabuccal, transdermal, or epidural*	Use with caution	Use with caution	Use with caution	Use with caution	Use with caution AAP classifies fentanyl as usually compatible with breastfeeding.

Hydrocodone-Codeine

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
(iii) Hydrocodone Risk factor: C	Use with caution	Use with caution	Use with caution	Use with caution	Use with caution Appears to be safe in breastfeeding as very little hydrocodone is transferred to the milk. However, there is inadequate evidence to fully determine infant risk. Should only be used if the possible benefit outweighs the possible risk.
(iv) Codeine Risk factor: C	Use with caution Birth defects (including some heart defects) have been reported with maternal use of codeine in the first trimester of pregnancies,. However, in another study, no effects were observed on infant survival or congenital malformation rate.	Use with caution	Use with caution	Use with caution The use of codeine during labor may produce neonatal respiratory depression.	Use with caution. AAP has classified codeine as usually compatible with breastfeeding. However, toxicity has been reported. The recommendation is to avoid long-term consumption of codeine-containing products during breastfeeding. Short-term therapy, such as 1-2 days, with close monitoring of the infant for symptoms of opioid toxicity is

Methadone

Drug	First trimester (weeks 1–12)	Second trimester (weeks 13–28)	Third trimester (weeks 28–40)	Labor	Postpartum and lactation
(v) Methadone Risk factor: C *Oral, subcutaneous, intramuscular, or intravenous*	Use with caution Methadone has been shown to have a favorable risk/benefit ratio if the user is a part of a comprehensive opioid dependence maintenance program during pregnancy. Methadone-maintenance has been associated with longer gestation and increased birth weights in comparison to nonmaintenance controls. If maintenance medication is necessary, treatment should begin with the lowest effective dose.	Use with caution Clearance of methadone increases during the second and third trimester, which may cause withdrawal symptoms and necessitate dose adjustment. Onset of withdrawal signs is longer in infants exposed to opioids like methadone.	Use with caution Clearance of methadone increases during the second and third trimester, which may cause withdrawal symptoms and necessitate dose adjustment. Onset of withdrawal signs is longer in infants exposed to opioids like methadone.	Use with caution	Use with caution Breastfeeding is likely safe, based on studies that show transfer to milk is extremely low. AAP classifies methadone as usually compatible with breastfeeding.

Conclusion

- With an ever-increasing rate in the rise of parturient utilizing opioid pain medications, it is reasonable to assume that many obstetricians may be uncertain about adequate treatment options to offer their population.
- Evaluation as well as effective management is limited by the relative contraindication of radiography in the workup and the risks to the fetus associated with pharmacologic therapy against providing effective analgesia to the patient.

Conclusion

- Evidence on nonpharmacologic strategies, while limited, is of value. If pharmacologic therapy is required, the decision to use itmust be based on the risks and benefits to the mother and the fetus.
- Management of these patients should be with a multidisciplinary team, providing all the therapeutic options to assure the wellbeing to the patient, minimize fetal teratogenicity, and avoid chronic symptoms and long-term disability.
- Nevertheless, an understanding of frequently occurring pain complaints along with quick diagnostic evaluation, risks of pain medications to the maternal-fetal unit, complementary alternative options, and expert consultation allows the obstetrician to easily help women achieve a more enjoyable and functional pregnancy.