Managing pain in pregnancy

Some uncomfortable decisions

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Pain during pregnancy is complicated by diagnostic dilemmas, including different presentations due to physiological and anatomical changes, concerns about imaging, and therapeutic challenges because of contraindications and uncertainties about maternal and fetal drug safety.

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Why are GPs so important?

The teleological role of intrapartum pain aside, pregnant women present to their primary practitioner with pain of varying source, severity and implication. Pain is an ubiquitous symptom and the most commonly used drugs in pregnancy are analgesics.

In pregnant women presenting with pain, the GP may play a role as:

- a diagnostician
- a therapist or manager of acute pain, chronic pain or acute-on-chronic pain
- an adviser and counsellor about disease-related and drug-related matters.

Sound knowledge about causes of moderate to severe pain and its implications for immediate and long-term maternal and fetal wellbeing is required. The presenting complaints and features in pregnant women may differ or be misleading compared with those in nonpregnant women, creating diagnostic dilemmas. A modified approach to imaging and physical, psychological and pharmaceutical therapies is often required.

What painful conditions present in pregnancy and what is the significance of moderate to severe pain?

Although animal and human studies support the concept of 'pregnancy-induced analgesia', with upregulation of postpartum central oxytocin signalling a possible mechanism for the low rate of persisting pain in the perineum or caesarean wound, this is of little relevance to clinical practice. Aside from labour, delivery, postpartum and incidental pain (e.g. trauma, surgery or headache), pregnancy may:

- adversely influence or leave unchanged a range of painful conditions (e.g. low

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Key points

- **Pain during pregnancy is extremely common.**
- **Spine and pelvic girdle musculoskeletal pain and nerve entrapment syndromes can present for the first time in pregnancy and other painful abdominal and pelvic visceral conditions occur more frequently during pregnancy.**
- **Nonpharmacological therapies should be considered as initial treatment, together with analgesic drugs of established safety, prescribed in the lowest therapeutic dose for the shortest possible time.**
- **All drug prescribing in pregnancy requires consideration of the risks to the fetus as well as the mother. These risks vary with gestational age, dose, duration of exposure and the specific drug.**
- **GPs play a crucial role in the management of pain in pregnancy as a primary diagnostician or therapist, resource provider and adviser, or co-ordinator of care.**

back pain,[1] rheumatoid arthritis, sickle cell crises)
- promote new painful conditions (e.g. pelvic girdle pain,[1] urinary tract infection, nerve entrapment syndromes [Figure])
- be associated with obstetric events causing moderate to severe pain (e.g. miscarriage, severe pre-eclampsia, placental abruption)
- change the therapeutic management of both old and new pain.

There are associations between acute pain and the development of chronic pain and postnatal depression that justify heightened surveillance.

Musculoskeletal pain affects up to two-thirds of pregnant women, and this pain is of new onset in 25% of women.[2] The more common areas of musculoskeletal pain in pregnant women are:

- upper limb (carpal tunnel syndrome in the hand due to median nerve entrapment)
- chest or upper abdomen (costochondral pain or intercostal neuralgia along the anterior rib cage); the incidence of pain at these sites has not been reported but misdiagnosis of other intrathoracic or intra-abdominal pathologies (e.g. cholecystitis) is likely unless history and examination are thorough
- lower or upper back (muscle, joint and disc pain are common, occurring in up to 50% of pregnant women; sacroiliac pain is also common, occurring in up to 20% of pregnant women, but coccydynia or symphyseal diastasis are much less frequent, with an incidence of approximately one in 600)
- groin (stretching of pelvic ligaments or ilioinguinal nerve entrapment)
- lower limb (thigh pain from 'meralgia paraesthetica' due to lateral cutaneous nerve of the thigh entrapment)
- lower abdomen and pelvis.

Intra-abdominal pain is frequently a diagnostic dilemma, as there is an increase in risk of some pathologies (e.g. acute cholecystitis, renal tract infection) and common conditions arise (e.g. constipation, gastro-oesophageal reflux). In early pregnancy, severe pelvic pain may be gynaecological (e.g. miscarriage, ruptured ectopic pregnancy, degenerating fibroid, ovarian cyst accidents), gastrointestinal or arise from another organ system.

In late pregnancy, organ displacement by the gravid uterus can lead to altered pain localisation (e.g. right upper quadrant pain in acute appendicitis, low back pain from renal or retroperitoneal pathologies and abruption of a posterior placenta). Other pregnancy-related conditions may also present at this stage – for example, the acutely tender uterus of placental abruption, the rhythmic nature of pain due to premature

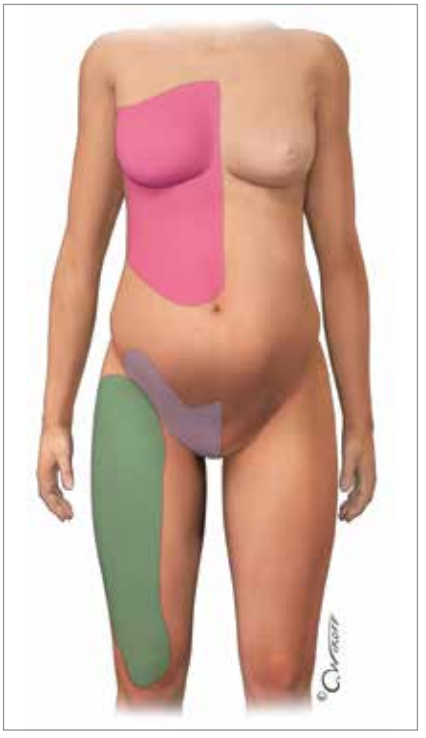

Figure. Surface anatomy of nerve entrapment syndromes in the trunk, groin and thigh.

labour or right anterior/posterior chest pain from liver capsule distension in severe pre-eclampsia.

New-onset headache, depending on severity, warrants exclusion of serious causes by neurological examination and even toxicology or cranial imaging. Severe pre-eclampsia must be screened for if the woman is beyond the first trimester.

How far should outpatient investigation and management be pursued?

Good communication with the patient and health carers underpins pain management. Women with known chronic pain and cancer pain are likely to need considerable support, including the integrated care of physiotherapists, psychologists, pain specialists and other medical practitioners. Modification of management plans and drug therapies may be appropriate. Balancing the best interests of mother and baby is complex. Severe pain warrants referral and hospital admission.

In addition to history, examination and laboratory tests, the safety of imaging is a consideration, although imaging should rarely be omitted if clinically important. Ultrasound is the preferred initial modality in most circumstances.[3] MRI appears safe in pregnant women, despite the absence of long-term follow-up studies, with caution applied to those in the first trimester. Radiation risk varies with the dose and fetal gestational age, the critical periods being those of organogenesis (four to 10 weeks) and early brain development (10 to 17 weeks), with biological injury much less likely after 26 weeks. Fetal exposure can be reduced with pelvic apron shielding, minimisation of x-ray beam time and modifications to computed tomography (CT).[4] CT involves higher radiation exposure than standard x-ray but restricted or selective use (e.g. head and chest only) has not been associated with abortion, teratogenicity or childhood cancer. Even abdominal or pelvic noncontrast CT in the first trimester does not necessarily exceed levels of radiation exposure at which the risk significantly increases, so this may occasionally be indicated in women with trauma or renal colic. However, a small radiation dose-dependent increase in the absolute risk of childhood cancer mandates discussion with a radiologist before this is performed. Radioiodine isotopes may be contraindicated in pregnancy, depending on the timing and dose exposure, and iodinated contrast media (unlike gadolinium) appear to be safe but are often still avoided. Seeking expert advice before referral for imaging is recommended.[3,4]

Some pregnant women with debilitating and prolonged pain (e.g. nerve entrapment pain, pelvic girdle pain, mechanical low back pain) can be reassured that full resolution is very likely postpartum. Women presenting with acute pain that is severe enough to require opioid analgesia must be referred for immediate investigation in a suitable hospital environment.

Which physical, behavioural and other therapies are useful?

Pain in pregnancy may be reduced and quality of life improved with use of nonpharmacological therapies, either as primary or adjunctive modalities. A psychosocial and functional evaluation is a mandatory part of pain assessment, helping to identify strategies that avoid or minimise pharmacological therapy and guiding management when drug therapies fail or decline in efficacy. Chronic back pain or pre-existing acute discitis warrant preventive strategies such as regular physiotherapy and improvement of tone in paravertebral and abdominal muscles.

Myofascial pain responds well to heat, passive stretching and massage. Cold packs can relieve headache. Exercise (especially aquatic), physiotherapy and mobilisation aids or supports (e.g. sacroiliac belts for pelvic symphysis diastasis) are valuable in controlling low back and pelvic girdle pain.[1,2] Transcutaneous electrical nerve stimulation and acupuncture may be effective for myofascial or nerve entrapment pain.

Local anaesthetic injection, with or without corticosteroid, is considered very safe in appropriate doses, so is suitable for myofascial trigger points, wound neuroma, symphyseal diastasis and peripheral nerve blocks. Epidural analgesia may be appropriate for severe intercostal or back pains and use of corticosteroid injections are controversial, but best supported by data in pregnant women experiencing new-onset lumbar root compression.

Which analgesics are safe in pregnancy?

All drug prescribing in pregnancy requires consideration of the risks to the fetus as well as the mother. These risks vary with gestational age, dose, duration of exposure and the specific drug. Discussing with the patient the risks and benefits is good practice. It may be the case that omitting a drug may prove more harmful than introducing it. The obstetric implications of the use of other drugs, such as legal drugs (e.g. alcohol, nicotine), illicit drugs (e.g. cannabis) and prescribed drugs (e.g. antidepressants), should also be discussed.

Selecting 'time-proven' analgesics is sensible, as is avoiding, if possible, those without time-proven support of safety in

the first trimester (see Table). Paracetamol is the safest analgesic and nonsteroidal anti-inflammatory drugs (NSAIDs) are generally of no or low risk. Knowledge of where to locate resources that detail current, valid information about less commonly used analgesics is essential. Unfortunately neither the Australian Drug Evaluation Committee classification of drugs in pregnancy nor the drug's product information is of much clinical value. There are several potential sources of information, in particular the state obstetric drug information service, a local tertiary maternity hospital pharmacy advisory service, online resources such as MotherSafe, a respected compendium, the *Australian Medicines Handbook* and the Therapeutic Goods Administration website.[5-9]

Paracetamol

Paracetamol in nontoxic doses should be first-line therapy for pregnant women. Despite a lack of controlled data, it has no known teratogenicity or later fetal effects and is compatible with breastfeeding. Patients should be made aware of the multiple trade names and combinations so that safe regimens avoiding liver toxicity are used.

NSAIDs

NSAIDs vary in risk. Low-dose aspirin is used for specific medical conditions and is considered safe, but high doses are avoided because of platelet-inhibition and an apparent increase in the risk of neonatal intracranial haemorrhage before 35 weeks' gestation. There is weak evidence that traditional NSAIDs may impact on fertility and the first trimester (miscarriage) but they are of particular concern after 28 to 32 weeks' gestation. At this stage there is an increased risk of oligohydramnios, fetal renal impairment, intracranial haemorrhage and premature closure of the ductus arteriosus, leading to persistent pulmonary hypertension (15-fold increase).[10,11] There are insufficient controlled data for the use of cyclo-oxygenase-2 specific inhibitors in pregnancy.

Table. Analgesic drug recommendations in pregnancy and breastfeeding*

Drug	Recommendation in pregnancy	Recommendation in breastfeeding
Paracetamol	Compatible throughout	Compatible
Aspirin	Avoid at conception and chronic high-dose use during pregnancy	Potential toxicity – caution short-term use only
Diclofenac	Avoid after 28 to 32 weeks' gestation	Compatible
Indomethacin	As diclofenac	Probably compatible
Ibuprofen	As diclofenac	Compatible
Naproxen	As diclofenac	Compatible
Ketoprofen	As diclofenac	Compatible
Ketorolac	As diclofenac	Compatible
Celecoxib	Insufficient data – caution as per diclofenac	Compatible
Tramadol	Probably avoid in the first trimester, thereafter low risk (neonatal abstinence syndrome possible)	Probably compatible
Tapentadol	No data – caution	No data – caution
Morphine	Compatible but possible neonatal depression at birth and neonatal abstinence syndrome with third trimester use	Probably compatible
Codeine	As morphine but less effective	Probably compatible
Pethidine	As morphine but always use alternative opioids if possible	Compatible, prefer alternatives
Methadone	As morphine	Probably compatible
Oxycodone	As morphine	Probably compatible
Fentanyl	As morphine	Probably compatible
Amitriptyline	Low risk throughout	Compatible
Carbamazepine	Compatible if used for epilepsy but try to avoid (risk of malformations)	Compatible
Gabapentin	Limited evidence suggests low risk	Limited data – probably compatible
Pregabalin	Insufficient data – caution	Limited data – probably compatible
Ketamine	Low risk throughout	Probably compatible
Clonidine	Probably avoid in the first trimester	Probably compatible
Bupivacaine	Compatible	Compatible
Ropivacaine	Compatible	Compatible
Lignocaine	Compatible	Compatible

* The information in this Table is the author's own practical recommendations based on the information available from the major compendium on this topic combined with the latest clinical reviews, studies and pharmacokinetic studies.

Opioids

Opioids, both oral and parenteral, have apparent short-term safety in pregnancy, although several issues may arise. The number of women who are prescribed opioids (one in seven in the USA), are opioid-dependent or are opioid-abusers (one in 250 hospitalised pregnant women in the USA) is increasing in many countries.[12,13] These women have higher rates of premature labour, fetal growth retardation, stillbirth and inhospital maternal death. Maternal withdrawal symptoms, neonatal respiratory depression and neonatal abstinence syndrome are possible if opioids are used near the time of birth.[11] The use of methadone and buprenorphine maintenance of opioid dependence requires multidisciplinary planning and care, with the application of typical pharmacological 'analgesic ladders' when escalating treatment of acute pain.

Some epidemiological database studies suggest early pregnancy exposure to opioids may be associated with an increased risk of birth defects.[14] Nevertheless, weak opioids such as codeine are generally considered reasonably safe, despite pharmacogenetic variance in demethylation to morphine and hence response (lack of effect or excessive effect in poor metabolisers and ultra-rapid metabolisers of CYP2D6, respectively). Although unresolved, basic research raises the possibility that in-utero exposure to opioids has implications for drug-seeking behaviour in later life.[15]

Other nonopioid analgesics

Other analgesics are often of value for pain in pregnancy, although there are no long-term neurodevelopmental data available for many of these drugs. Animal studies show that tramadol is very unlikely to cause fetal abnormalities, especially after organogenesis, although high dosing near delivery should be avoided.[16] Generally it has a favourable benefit to risk assessment, but relative contraindications include increased seizure risk (e.g. pre-eclampsia) and risk of serotonin syndrome. There is no information as yet about tapentadol.

Ketamine and lignocaine are safe, potent and useful inhospital analgesics. Clonidine, amitriptyline and nortriptyline, various serotonin and noradrenaline reuptake inhibitors and the gabapentinoids can be useful in specific situations, but require consultative discussion with other specialists and the patient. Gabapentin has not been shown to cause major malformations in animal studies and appears acceptable based on limited human experience,[17] whereas information about pregabalin is insufficient.

Conclusion

GPs have a crucial role to play in the management of pain, whether as a primary diagnostician or therapist, resource provider and adviser, or co-ordinator of care. Pain during pregnancy is extremely common. Spine and pelvic girdle musculoskeletal pain and nerve entrapment syndromes can present for the first time in pregnancy and some painful abdominal and pelvic visceral conditions occur more frequently in pregnant women.

Pain is a warning of many important obstetric conditions and events. As initial treatment, nonpharmacological therapies should be considered along with analgesic drugs of established safety, prescribed in the lowest therapeutic dose for the shortest possible time. Use of less well-evaluated drugs need discussion with experts and the patient to determine mutually agreed plans. Severe acute pain during pregnancy is always a flag for a serious and even life-threatening condition, so after initial treatment it usually mandates immediate referral of the patient for secondary or tertiary care by appropriate specialists. PMT

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