Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

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Analgesic use for non-labour pain during pregnancy

Non-labour pain such as headache and musculoskeletal pain are common complaints during pregnancy. Like most drugs, analgesics (including paracetamol, nonsteroidal antiinflammatories (NSAIDs) and opioids) readily cross the placenta. Potential risks of analgesic use may put practitioners off prescribing or recommending use during pregnancy. Whichever analgesics are chosen, the lowest effective dose for the shortest amount of time should be used to minimise any potential risks to the developing foetus. This bulletin aims to address the use analgesia during pregnancy and associated risks.

Paracetamol is the analgesic of choice for the treatment of mild to moderate pain during any stage of pregnancy. The mechanism of action is unclear but it is thought to act by inhibiting prostaglandin synthesis in the central nervous system. Paracetamol is metabolised in the liver to a toxic metabolite. The low concentrations of this that result from normal dosing are removed by conjugation with glutathione.

To date, there is no clear evidence to indicate that paracetamol use in pregnancy is likely to harm the developing foetus at any stage of pregnancy.

NSAIDs, such as ibuprofen and diclofenac, inhibit prostaglandin synthesis and are anti-inflammatory analgesics. Use of NSAIDs in the first and second trimesters (prior to week 28) is considered relatively safe and does not appear to be associated with an increased risk of adverse foetal outcomes. However, there may be an increased risk of spontaneous abortion (observational studies - controls were not matched for maternal age, which itself is associated with spontaneous abortion).

The use of NSAIDs after week 28 of pregnancy is contraindicated as they are known to cause adverse foetal cardiovascular effects including premature closure of the ductus arteriosus and neonatal pulmonary hypertension. They are also associated with oligohydramnios with reduced foetal renal function. NSAIDs can inhibit uterine contraction, prolong the length of gestation and delay the onset of labour when given late in pregnancy. At the time of parturition, they can also be associated with excess bleeding in both the mother and the infant.

Codeine is a 'weak' opioid that is used to treat mild to moderate pain. It is inactive and is metabolised by cytochrome P450 2D6 in the liver to morphine, from which it derives its main analgesic effects. On average, approximately one tenth of a dose of codeine is converted to morphine in the body. It may be used at any stage during pregnancy where use of paracetamol alone provides insufficient pain relief.

The use of codeine near term or during labour may cause problems for the foetus and neonate. Like other opioid analgesics, codeine via morphine (from in utero exposure) can cause respiratory depression in the newborn. Neonatal withdrawal symptoms such as tremor, jitteriness, diarrhoea and poor feeding have also been reported in infants following maternal use of large doses of codeine taken throughout pregnancy.

Tramadol is a synthetic opioid analogue (approximately equivalent in strength to codeine) that is used to treat mild to moderate pain. In addition to acting on the opioid receptors, it also has a significant effect on serotonin and noradrenaline receptors in the descending inhibitory pain pathways of the spinal cord. There are very limited data on the use of tramadol during the first trimester of pregnancy.

Tramadol, like other opioids, has the potential to cause neonatal withdrawal symptoms. Due to the limited data, it should be avoided during pregnancy unless there are compelling clinical reasons for use.

Morphine is a 'strong' opioid that is used to treat moderate to severe pain where use of regular paracetamol plus codeine is ineffective. Morphine may be used during pregnancy when clinically indicated.

To date, there are no reports of major congenital defects being associated with the therapeutic use of morphine during human pregnancy. However, regular use and use near term or during labour has been associated with neonatal withdrawal symptoms and respiratory depression.

Table: Recommendations and cautions of analgesic use during pregnancy

	Recommendations	Cautions
Paracetamol	Use first-line at any stage of pregnancy	None expected with standard dosing
NSAIDs	Use up to week 28 of pregnancy if an antiinflammatory is clinically indicated	Avoid from week 28 onwards - risk of premature closure of the ductus arteriosus and other adverse foetal outcomes
Codeine	Use at any stage of pregnancy when stronger pain relief than paracetamol is required	Use near term may be associated with withdrawal symptoms in the neonate and respiratory depression
Tramadol	Limited data, avoid use unless there are compelling clinical reasons	Use near term may be associated with neonatal withdrawal symptoms and respiratory depression
Morphine	Use at any stage of pregnancy when maximum doses of paracetamol plus codeine are insufficient	Use near term may be associated with withdrawal symptoms and respiratory depression in the neonate