Maternity Guideline

Antenatal and Postnatal Analgesia
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**Antenatal**

For relief of mild to moderate pain
- **Paracetamol** 1g PO QDS

For relief of moderate to severe pain
- **Dihydrocodeine** 30mg PO QDS

**Intrapartum**

See ‘Analgesia in Labour’ guideline

Simple analgesics include
- **Paracetamol** 1g PO QDS
- **Dihydrocodeine** 30mg PO QDS

Additional analgesia includes
- Entonox
- Pethidine
- Epidural analgesia (link to guideline)
- Remifentanil patient controlled analgesia (link to guideline)

**In hospital**

Unless contraindicated, all patients should be prescribed PRN
- **Paracetamol** 1g PO/IV QDS
- **Ibuprofen** 400mg PO QDS

*After caesarean section, these should be prescribed regularly (QDS) rather than as required*

Additional analgesia
- **Oramorph** 10-20mg PO 2hrly PRN after caesarean section
- **Oramorph** 5-10mg PO 2hrly after vaginal delivery

If known sensitivity / intolerance to Morphine or NSAIDs consider
- **Dihydrocodeine** 30mg PO QDS PRN or
- **Tramadol** 50-100mg PO/IM QDS PRN

**Postnatal**

In hospital

Unless contraindicated, all patients should be prescribed PRN
- **Paracetamol** 1g PO QDS
- **Ibuprofen** 400mg PO QDS

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Additional analgesia
- **Oramorph** 10-20mg PO 2hrly PRN after caesarean section
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If known sensitivity / intolerance to Morphine or NSAIDs consider
- **Dihydrocodeine** 30mg PO QDS PRN or
- **Tramadol** 50-100mg PO/IM QDS PRN

**On discharge**

- **Paracetamol** 1g PO QDS
- **Ibuprofen** 400mg PO **TDS** (NOT QDS)

If intolerant to NSAIDs or additional analgesia required
- **Dihydrocodeine** 30mg PO QDS PRN
  *(Supplied in 14 tablet pack as TTA)*
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Background

Traditionally codeine has been used extensively for provision of antenatal and postnatal analgesia. However, there has been a recent death of a breast-fed infant, due to morphine toxicity, following maternal use of codeine [1], and 3 fatalities in children under 18 where codeine has been prescribed after tonsillectomy. This has led the Medicines and Healthcare Products Regulatory Authority (MHRA) and European Medicines Agency (EMA) to issue advice contraindicating its use in women who are breastfeeding [2,3].

CYP2D6 Polymorphism

Codeine has no analgesic effect in its parent form and relies on its metabolism to active metabolites, partly through the cytochrome (CYP2DP) pathway. The CYP2DP pathway is subject to genetic variation. 7-10% of Caucasians are classified as poor metabolisers, in that they convert very little codeine into morphine and have little or no pain relief [3]. Some individuals are ultra-rapid metabolisers and consequently are extremely sensitive to the analgesic properties and side effects of codeine. The prevalence of ultra-rapid metabolisers varies by ethnicity: Africans / Ethiopians 29%, Greek 6% and Caucasian 5%. [3] The case report of a breastfeeding mother taking codeine resulting in neonatal death, is thought to be due to ultra-rapid production of morphine. [4] Genetic testing is currently impractical and therefore the advice is to avoid codeine use in all women who are breast feeding.

What are the alternative options?

NON-OPIOIDS

Both paracetamol with the addition of non-steroidals (NSAIDs) in the postnatal period (unless there are contraindications) should provide the mainstay of analgesia in this group of women. Paracetamol is considered safe in pregnancy. Non-steroidals, including ibuprofen and diclofenac, are considered safe in the postnatal period in breast feeding women.

OPIOIDS

Morphine

Morphine is active in its parent form. It has been used extensively in pregnancy and in the postnatal period, and is licensed for use. It is subject to first pass metabolism and therefore an oral dose is approximately half as potent as an intramuscular dose.

Dihydrocodeine (DHC)

DHC has similar analgesic activity to codeine; however, unlike codeine which is a pro-drug displaying no analgesic properties itself, the analgesic effect of dihydrocodeine appears to be mainly due to the parent compound [5] and is largely unaffected by an individuals metabolising capacity [6]. Dihydrocodeine (DHC) is metabolised to dihydromorphine (DHM) by CYP2DP, but only a small proportion of DHC becomes DHM. A study examining urinary metabolites showed that even in “extensive metabolisers” <10% of metabolites were derived from DHM [7].

Another study examining 26 patients who died of self harm considered the role of DHC metabolites in DHC related deaths. [8] From the levels measured, they concluded that DHM and DHM-6-glucuronide have less influence on causing death than DHC itself, suggesting that the degree of side effects such as respiratory depression may not be influenced by genetic variations in metabolism. However, until more data is available regarding the metabolism of dihydrocodeine, the advice from UK Medicines Information (UKMi) is that DHC, in the breastfeeding mother should be at the lowest effective dose for the shortest duration [9]. All breastfed infants should be monitored for opioid adverse effects regardless of the maternal dose. If significant opioid adverse
effects develop in the mother, this could suggest the possibility that she is an ultra-rapid metaboliser and that the risk of adverse effects in the infant may be increased.

**Tramadol**

Tramadol produces analgesia by 2 mechanisms – an opioid effect and an enhancement of serotonergic and adrenergic pathways. It has fewer typical opioid side effects (e.g. less respiratory depression and constipation) but the drug can cause psychiatric disturbances, which may be dependent of its metabolites. Tramadol is also metabolised by CYT2DP to an active O-desmethyl metabolite. A case report describes an adult patient who took a single 100mg dose of tramadol and developed ataxia, dilation of the pupils, numbness and dysphoria lasting approximately 4 hours. The patient was phenotyped for CYP2D6 activity, and was determined to be an extensive metaboliser with very high CYP2D6 activity. The authors suggested the reaction may be due to high concentrations of the active O-desmethyl metabolite of tramadol [10]

The BNF suggests ‘amount in breast milk probably too small, but manufacturer suggest avoid’. Studies have demonstrated that tramadol and its metabolites are found in breast milk, even after single dose [11]. However, a study examining milk samples from 75 mothers who were 2 to 4 days postpartum, demonstrated that an exclusively breastfed infant would receive maternal weight-adjusted dosages of 2.24% of tramadol and 0.64% of its metabolite. No behavioural adverse effects were observed in the breastfed infants [12]. Likewise comparing poor and extensive metabolisers the study showed that the relative and combined infant dose remained below the suggested 10% threshold for drugs in breast milk, irrelevant of metabolising capacity of the mother [13]. Detectable levels (>12 micrograms/L) of tramadol were found in samples of breast milk collected 10 hours after a 50 mg maternal dose of intravenous or oral tramadol. No other clinical details or milk levels were reported.

The UKMi concludes that tramadol **is considered acceptable** in breast feeding based on low levels in breast milk when prescribed at the lowest effective dose for the shortest duration. However, it is important to note that 50% of the general population do not tolerate tramadol due to the side effects experienced.

**The overall recommendation** from the UKMi regarding dihydrocodeine and tramadol is:

- As it is not practical to genotype all breastfeeding mothers and infants, weak opioids, specifically dihydrocodeine or tramadol, can be considered for a breastfeeding mother.

- This should be at the lowest effective dose and for the shortest duration and regular use of any opioid beyond 3 days should be under close medical supervision.

- If significant opioid adverse effects develop in the mother, this could suggest the possibility that she is an ultra-rapid metaboliser and that the risk of adverse effects in the infant may be increased.

- All breastfeeding mothers, regardless of ethnicity, should be informed of the potential problems and advised to stop breastfeeding if symptoms develop and seek medical advice.
**Antenatal analgesia**

Correct management of pain during pregnancy is essential to minimise the risk of adverse outcome to the mother and baby. Inadequate treatment of pain can lead to the development of anxiety and depression; which can impact on a woman’s physical and psychological wellbeing. Reluctance to treat a woman’s pain can also result in increased use of inappropriate over-the-counter medication or herbal remedies.

If possible, all drugs should be avoided during the first trimester. The embryo is most vulnerable to teratogenic effects during organogenesis (4-10 weeks’ gestation). All medicines in pregnancy should follow a risk versus benefit assessment and be used sparingly, to try and reduce any adverse effects on the developing fetus. Non-pharmacological interventions should be considered first line; for example adequate rest, hot and cold compresses, massage, aromatherapy, acupuncture, physiotherapy, relaxation and exercise.

**Paracetamol**

- 1g PO 4-6hrly (max 4 doses per 24 hours)

Paracetamol is the first choice analgesic for treatment of mild to moderate pain. It can be prescribed, but is also available as an over-the-counter medicine. Some studies have demonstrated associations between the use of paracetamol antenatally and adverse outcomes for the fetus [17,18] but current advice is that it remains safe for use during pregnancy. [14] 1g of paracetamol can be given orally, or intravenously if this is more appropriate, up to four times per day.

**Non-steroidal anti-inflammatories (NSAIDS)**

- 400mg **ibuprofen** PO 8hrly (max 3 doses per 24 hours)

The use of NSAIDs should be avoided during pregnancy where at all possible. If an NSAID is clinically indicated, then ibuprofen is preferred but should not be taken after 30 weeks’ gestation as it can lead to neonatal pulmonary hypertension.[16] NSAIDs can also reduce fetal urine production leading to a reduced amniotic fluid volume. NSAIDs should be used at the lowest effective dose for the shortest possible duration.

**Low dose aspirin (75mg PO once daily), used as prophylaxis against pre-eclampsia in high risk women, has not been shown to be associated with adverse effects on the fetus.**

**Dihydrocodeine (DHC)**

- 30mg PO 4-6hrly (max 4 doses per 24 hours)

Opioid analgesics can be used during pregnancy for the short-term treatment of moderate to severe pain, when paracetamol has not been effective. Dihydrocodeine has similar analgesic activity to codeine and is the first choice when opioid analgesia is required antenatally.

There is inadequate data on human pregnancy exposure to dihydrocodeine to rule out teratogenic risks completely, although the limited data available do not indicate an increased risk of fetal toxicity. Indiscriminate use should be avoided. [15]

Opioid use, especially around the time of delivery, may lead to neonatal respiratory depression. Long-term use of opioid analgesia can lead to neonatal withdrawal symptoms; therefore the lowest effective dose dihydrocodeine should be used for the shortest possible time.
Opioids can exacerbate constipation, nausea and vomiting, which may already be a problem in the pregnant woman. The risk and severity of side effects should be weighed up against the amount of pain the woman is experiencing.

**Alternative analgesia for inpatients**

When women are admitted acutely to the antenatal ward with severe pain and require additional analgesia, then consider:

- Oramorph 5-10mg PO 2hrly PRN
- Morphine 5-10mg IM 4hrly PRN

If a woman is admitted in early labour then consider:

- Pethidine 50-100mg IM 4hrly PRN

**Discharge medication for antenatal patients**

Patients can be advised to purchase paracetamol over-the-counter on discharge. If necessary then they can be prescribed dihydrocodeine as a TTA.

- **Dihydrocodeine** 30mg PO QDS PRN (*Supplied in 14 tablet pack as TTA*)
For Epidural analgesia and Remifentanil PCA in labour please refer to the appropriate guideline.

**Postnatal analgesia**

Analgesia can be subdivided into 2 groups of women:

1. Following Caesarean section or abdominal surgery
2. Following vaginal delivery

**IN HOSPITAL**

**1. Following Caesarean Section**

**Regular analgesia** is important. Unless intolerant of paracetamol, all women should be prescribed regular paracetamol – 1g orally or intravenously, four times a day (QDS)

Unless there are contraindications all women should also be receive diclofenac 100mg rectally (PR) at the end of surgery, followed by ibuprofen 400mg oral QDS (taken with food). There should be an interval of ideally 10-12hrs (minimum 8hrs) between the dose of diclofenac 100mg and the first oral does of Ibuprofen.

Non-steroidals affect renal function, platelet function, and can exacerbate asthma (in approximately 10%). In addition they may cause gastric irritation / ulcers.

Non-steroidals (diclofenac and ibuprofen) are contraindicated in women with a known hypersensitivity and should be avoided in the following circumstances:

1. If there has been significant haemorrhage, the women is hypovolaemic, and / or there is a risk of ongoing haemorrhage
2. In impaired renal function or moderate / severe pre-eclampsia
3. In women with severe asthma
4. In women with asthma known to be exacerbated by non-steroidals or aspirin
5. In women with a history of gastric ulceration

Paracetamol, diclofenac and ibuprofen on the day of surgery should be prescribed on the front of the drug chart, and the prescription for continuing regular doses started the following day.

**TTAs should be written up before the woman leaves CDS where possible.**

**Opioid analgesia**

In hospital, **Oramorph** should be the opioid of choice, and the only opioid prescribed, for all women unless they have a history of previous sensitivity / intolerance.

Oramorph should be prescribed in a dose of 10-20 mg orally 2hrly as required.

Morphine 10mg intramuscularly 1hourly PRN may be prescribed alongside to be given if necessary e.g. if a woman is vomiting, but with clear documentation that Morphine should not be given together by 2 different routes.

For women who are intolerant of morphine consider:

- Dihydrocodeine 30mg orally 4-6hrly as required (maximum 4 doses per day)
• Tramadol 50-100mg orally or intramuscularly 4-6 hourly as required (to a maximum of 400mg in 24hrs).

2. Following vaginal delivery:

Paracetamol and ibuprofen (if no contraindications) may be prescribed either regularly or as required.

Opioid requirements are likely to be less than after an operative delivery and therefore Oramorph at a dose of 5-10mg orally 2hourly PRN should be prescribed.

If women have a history of intolerance to morphine then dihydrocodeine or tramadol (as above) may be considered.

ON DISCHARGE FROM HOSPITAL

The majority of women requiring analgesia on discharge should be receive a TTA pack of paracetamol and ibuprofen (unless there are contraindications to non-steroidal).

If additional analgesia is required e.g. if women still require Oramorph in hospital or cannot take non-steroidal, they should be discharged with a TTA pack containing 14 tablets of dihydrocodeine 30mg 4-6 hourly PRN (maximum 4 doses per day).

Tramadol may be considered if the woman is known to be intolerant to dihydrocodeine.

*Do not prescribe Oramorph as a TTA to postnatal women.*

**SUMMARY: POSTNATAL ANALGESIA**

- Unless contraindications all women should be prescribed:
  -  **Paracetamol** 1g PO / IV QDS
  -  **Ibuprofen** 400mg PO 6hrly

- After Caesarean section these drugs should be prescribed regularly QDS rather than ‘as required’.

- Additional analgesia in hospital:
  - **Oramorph** 10-20mg 2hrly PRN after operative delivery, or 5-10mg PO 2hrly after vaginal delivery
  - If known sensitivity / intolerance to Morphine consider:
    - **Dihydrocodeine** 30mg PO QDS PRN or
    - **Tramadol** 50-100mg PO/ IM QDS PRN.

**On discharge TTA pack of:**

- **Paracetamol** 1g PO QDS PRN
- **Ibuprofen** 400mg TDS PRN (if no contraindications)

- If additional analgesia required:
  - **Dihydrocodeine** 30mg PO QDS (supplied in 14 tablet pack as TTA)
References


4. Pattinson KTS. Opioids and the control of respiration. BJA 2008; 100(6):747-758


15. UKMi: Medicines Q&A: **Can opioids be used for pain relief during pregnancy?**
   [http://www.medicinesresources.nhs.uk](http://www.medicinesresources.nhs.uk)