NON STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) AND COX-2 INHIBITORS IN THE ACUTE POST OPERATIVE PAIN SETTING

Role:

- Managing moderate pain
- Opioid sparing effect

Action:

- Decreasing levels of inflammatory mediators generated at the site of tissue injury. Inhibition of prostaglandin synthesis
- May have other mechanisms of action independent of any effect on prostaglandins including effects on basic cellular and neuronal processes.
- Anti-pyretic

Pharmacology:

- Cyclo-oxygenase (COX) is present in 2 forms, COX-1 and COX-2. Inhibition of COX-1 is associated with impaired gastric cytoprotection and antiplatelet effects. Inhibition of COX-2 is associated with anti-inflammatory and analgesic action. Reduction in glomerular filtration rate and renal blood flow is associated with both COX-1 and COX-2 inhibition. Nonselective NSAIDs bind both COX-1 and COX-2 isoforms. COX-2 inhibitors selectively bind the COX-2 isoform. COX-2 may be associated with less risk of thrombosis.
- If the oral route is unavailable NSAIDs may be given rectally (diclofenac), by intramuscular injection (ketorolac) or by intravenous injection (parecoxib)

Indications:

- **Day surgery-** simple post-operative pain relief in combination with paracetamol
- **Obstetrics (e.g. perineal pain or after pains)** - simple post-delivery pain relief in combination with paracetamol
- **Obstetric surgery** - may be used following caesarean section up to a maximum of one week
- **Gynaecology surgery** - may be used peri-operatively or post-operatively with caution.
- **Gynaecology/Oncology** surgery- may be used peri-operatively or post operatively with caution.
- **May be used pre-operatively** with caution and approval of surgical team.

Contraindications:

- Known sensitivity especially asthma sufferers (NSAIDs are not contraindicated in all asthma sufferers)
- Renal impairment
- Active bleeding or increased risk of bleeding, thrombocytopenia
- Gastric ulceration or history of gastric ulceration
- Patients with an epidural catheter insitu who are also on heparin are at increased risk of epidural or spinal haematoma formation, hence should not be prescribed NSAIDs.
- Cardiac failure
- NSAIDS (e.g. Ibuprofen) – Cat C in pregnancy - There is insufficient experience about the safety of use of NSAIDs in humans during pregnancy. NSAID should, therefore, not be used during the first 6 months of pregnancy unless the potential benefits to the patient outweigh the possible risk to the foetus.

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NON STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) AND COX-2 INHIBITORS IN THE ACUTE POST OPERATIVE PAIN SETTING cont'd

- Cox 2 inhibitors (Celebrex) - There is no information on the use of celecoxib in pregnant women. Celebrex use is not recommended in pregnancy unless it is considered clinically essential (see information on animal studies). No studies have been done to evaluate the effect of celecoxib on the closure of the ductus arteriosus in humans. In animal studies, both COX-1 and COX-2 (e.g. Celebrex) - have been shown to be present in the ductus arteriosus of fetal lambs and to contribute to maintenance of patency. Therefore, use of Celebrex during the third trimester of pregnancy should be avoided, and Celebrex should not be used during the first and second trimesters of pregnancy unless the potential benefit to the mother justifies the potential risk to the fetus.

Precautions: (Please seek advice from medical/surgical/O&G team)

- Patients with poor urine output particularly pre-eclamptic women with impaired renal function i.e. serum creatinine >70umol/l. It is reasonable for RN/RM to withhold NSAIDs if a patient has poor urine output.
- Patients with poorly controlled hypertension particularly post-natal women with pre-eclampsia.
- Patients may be trialled on NSAIDs if they are asthmatic but have received aspirin or other NSAID previously without exacerbation to their asthma.
- Concomitant use of anti-platelet agents e.g. aspirin >600mg/day, clopidogrel, dipyridamole
- Age >65 years: the risk and severity of NSAID associated side effects is increased in elderly people.
- NSAIDs should only be given in pregnancy if the maternal benefits outweigh the potential fetal risks, at the lowest effective dose and for the shortest duration possible. Please seek advice from O&G medical team prior to prescribing NSAIDs for a pregnant woman.

Drug Interactions:

- Important pharmacokinetic interactions occur between NSAIDs and warfarin, lithium, oral hypoglycaemic, phenytoin, methotrexate, digoxin, aminoglycosides, cyclosporine, and probenicid.

Dosage and Administration:

- **Diclofenac: (COX-1)** PR maximum daily dose 200mg (i.e. 100mg twice daily) for no more than 2 days followed by 150mg orally for maximum of 3 days (i.e. 50mg three times daily). The patient should be reviewed if ongoing diclofenac is thought necessary.
- **Naproxen: (COX-1) 250mg qid for 5 days max then review.**
- **Ibuprofen: (COX-1) 400mg tds for 5 days max then review.**
- **Parecoxib: (COX-2)** IV for a single dose intra-operatively for day stay and moderate surgery cases. Parecoxib should be utilised as per the guidelines of **one** dose only. Any subsequent dose of NSAID or COX-2 may be given 12 hours after this one-off dose of parecoxib.
- Oral NSAIDs and COX-2 inhibitors should be prescribed for administration after meals.
- Low body weight: **<** 55kg may require a reduction in the daily dose.

Avoid double dosing of more than one NSAID

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Adverse Effects

- Renal impairment: increased in the presence of factors such as pre-existing renal impairment, hypovolemia, hypotension, use of other nephrotoxic agents
- Bleeding: GIT or surgical. Studies have demonstrated that short term use of COX-2 inhibitors produce less clinically significant peptic ulceration than NSAIDS
- Bronchospasm
- Cardiac failure, fluid retention
- COX-2 inhibitors have been found to have a high adverse drug event profile when used chronically for arthritis and chronic pain sufferers.
- There is no similar evidence when COX-2 inhibitors are used for short periods in the acute post-operative setting

RISK RATING
Low

NATIONAL STANDARD
Standard 4 - Medications

REVISION & APPROVAL HISTORY
Reviewed and endorsed Therapeutic & Drug Utilisation Committee 28/4/21
Approved Quality & Patient Safety Committee 18/12/14
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