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.
- If the oral route is unavailable NSAIDs may be given rectally (diclofenac), by intramuscular injection (ketorolac) or by intravenous injection (parecoxib)

Indications:
- Day stay surgery- may be combined with paracetamol and used in a PRN capacity Obstetric surgery- may be used following Caesarean section.
- Gynaecology surgery- may be used peri-operatively.
- Gynaecology/Oncology – Not for routine use in the first 24 hours post major oncology surgery while renal function and haemostasis are established. May be added to the post operative pain management regimen when haemostasis and renal function are not compromised.

Caution: Not to be used pre-operatively

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
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Precautions:
- Avoid double dosing of more than one NSAID

Interactions:
- Important pharmacokinetic interactions occur between NSAIDs and warfarin, lithium, oral hypoglycaemics, phenytoin, methotrexate, digoxin, aminoglycosides, cyclosporin, and probenecid. 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.

Dosage and Administration:
- **Diclofenac**: 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.
- **Parecoxib**: 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.

Contraindications
- Patients with poor urine output particularly pre-eclamptic women with impaired renal function ie serum creatinine >70umol/l. It is reasonable for RN’s to withhold NSAIDs if a patient has poor urine output.
- Patients with poorly controlled hypertension particularly post-natal women with pre-eclampsia. Tramadol may be initiated as an alternative analgesic.
- Patients may be trialed 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.

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.

Risk rating: Low. Review every 5 years.

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**REVISION & APPROVAL HISTORY**
Reviewed and Endorsed Therapeutic & Drug Utilisation Committee 9/12/14
Approved Quality & Patient Safety Committee 15/7/10
Reviewed and Endorsed Therapeutic & Drug Utilisation Committee 20/4/10
Approved Quality Council 20/2/06

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