Chapter 10
Musculoskeletal system

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1 Arthritis

NSAIDs, paracetamol and codeine are indicated for both rheumatoid and osteo-arthritis. The use of DMARDs (disease modifying antirheumatic drugs) is beneficial in rheumatoid arthritis. DMARDs include methotrexate, azathipurine, ciclosporin, antimalarials, leflunomide, and cytokine modulators.

1.1 Hydroxychloroquine

Rare risk of ocular toxicity; the following recommendations exist.

Before treatment:

- Assess renal and liver function
- Ask patient about visual impairment
- Record near visual acuity of each eye
- Initiate hydroxychloroquine treatment if no abnormality detected

During treatment:

- Monitor visual acuity annually
- Seek medical advice if vision becomes impaired
- Routine slit-lamp examination for children

1.2 Cytokine modulators

e.g. adalimumab, etanercept, and liximab

The use of cytokine modulators is associated with sometimes severe infection risk such as tuberculosis, septicaemia, and hepatitis b reactivation.

Tuberculosis
Patients should be evaluated for tuberculosis before treatment. Active tuberculosis should be treated for at least 2 months before starting therapy. Patients should be advised to seek prompt medical attention if symptoms suggestive of tuberculosis (e.g. persistent cough, weight loss, and fever) develop.

Blood disorders
Patients should be advised to seek medical attention if symptoms suggestive of blood disorders (such as fever, sore throat, bruising, or bleeding) develop

2 Hyperuricaemia and gout

Acute attacks of gout are usually treated with high doses of NSAIDs. Colchicine is an alternative in patients in whom NSAIDs are contra-indicated. Aspirin is not indicated in gout. Long-term control is achieved with allopurinol, or febuxostat (if allopurinol is not tolerated or is contra-indicated).

2.1 Febuxostat

Serious hypersensitivity reactions
Rare but serious risk of hypersensitivity reactions, including Stevens-Johnson syndrome and acute anaphylactic shock with febuxostat. Patients should be advised of the signs and symptoms of severe hypersensitivity; if these occur febuxostat therapy must be stopped indefinitely. Most cases occur during the first month of treatment.

3 Neuromuscular disorders

Anticholinesterases, immunosuppressant therapy, and corticosteroids have a place in the treatment of myasthenia gravis.

Skeletal muscle relaxants such as baclofen, diazepam, and tizanidine, are licensed for the relief of chronic muscle spasm or spasticity associated with multiple sclerosis, or other neurological damage.

3.1 Baclofen

Intrathecal treatment
Cautions: coagulation disorders; previous spinal fusion procedure; malnutrition (increased risk of post-surgical complications)

Pump implantation should be initiated within 3 months of a satisfactory response to intrathecal baclofen testing. Important to monitor patients closely during screening and immediately after implantation. Resuscitation equipment must be available for immediate use.

Treatment cessation
Avoid abrupt withdrawal – discontinue by gradual dose reduction of at least 1-2 weeks; risk of hyperactive state, exacerbation of spasticity, and psychiatric reactions.

Driving and skilled tasks
Drowsiness may affect performance of skilled tasks e.g. driving; effects enhance by alcohol.

4 NSAIDs (HIGH RISK)

NSAIDs reduce the production of prostaglandins by inhibiting the enzyme cyclo-oxygenase. Selective inhibition of cyclo-oxygenase-2 is associated with less gastro-intestinal intolerance, but greater cardiovascular risk.

4.1 WARNING SIGNS

(patient to report immediately to a doctor)

- Black stools or 'coffee ground' vomit, suggesting chronic gastrointestinal bleeding
- Iron deficiency anaemia due to GI bleeding (fatigue, dizziness, pale skin, shortness of breath)
- Progressive unintentional weight loss or difficulty swallowing
- Pregnancy and breastfeeding (contraindicated)
- Oedema
  (swollen ankles or feet)
- Unexplained, recent dyspepsia
- Worsening of asthma

4.2 MONITORING

- Blood pressure (especially after dose changes)
- Renal function
- Liver function
- Haemoglobin in those with risk factors for GI bleeding

4.3 DRUG INTERACTIONS

- Possible increased risk of convulsions when given with quinolones
- Possible enhanced anticoagulant effect of coumarins and phenindione
- Possible enhanced effects of sulfonylureas
- Increased risk of bleeding with dabigatran, heparins, SSRIs, venlafaxine, antiplatelets
- Increased risk of nephrotoxicity when given with ciclosporin, tacrolimus, diuretics (also antagonism of diuretic effect)
- May reduce excretion of lithium or methotrexate (increasing risk of toxicity)
- Increased side effects with concomitant use of other NSAIDs, aspirin
- NSAIDs antagonise hypotensive effect of beta-blockers, calcium-channel blockers, ACEI-inhibitors, angiotensin-II receptor antagonists, alpha-blockers, nitrates

4.4 OTHER POINTS

- All patients of any age prescribed NSAIDs for osteoarthritis or rheumatoid arthritis or patients over 45 years who are prescribed NSAIDs for lower back pain should be co-prescribed gastro-protection (e.g. a proton pump inhibitor)
- NSAID should be taken with or just after food

NSAIDs and cardiovascular events

All NSAID use (including COX-2 inhibitors) can be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke), the greatest risk may be in those receiving high doses long term. COX-2 inhibitors, diclofenac and ibuprofen are associated with an increased risk of thrombotic events. The lowest effective dose of NSAID should be prescribed for the shortest period of time to control symptoms.

NSAIDs and gastro-intestinal events

All non-selective NSAIDs are associated with serious gastro-intestinal toxicity; the risk is higher in the elderly. Piroxicam, ketoprofen, and ketorolac are associated with the highest risk; indometacin, diclofenac, and naproxen are associated with intermediate risk, and ibuprofen with the lowest.

More than one oral NSAID should not be used at a time, and NSAIDs associated with a low risk should be started at the lowest recommended dose.

The combination of a NSAID and low-dose aspirin can increase the risk of gastro-intestinal side-effects; this combination should be used only if necessary and the patient should be monitored closely.

Asthma

Any degree of worsening of asthma may be related to the ingestion of NSAIDs, either prescribed or (in the case of ibuprofen and others) purchased over the counter. Medical advice must be sought.

4.5 PIROXICAM

Increased risk of gastro-intestinal side effects and serious skin reactions

The CHMP has advised that piroxicam should:

- be initiated only by experienced physicians
- not be used as first-line treatment
- be limited to the symptomatic relief of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis
- not exceed 20 mg daily dose
- no longer be used for the treatment of acute painful and inflammatory conditions
- reviewed 2 weeks after initiating treatment
- be prescribed with a concomitant gastro-protective agent

Note: Topical preparations containing piroxicam are not affected by these restrictions