

# PJ PRACTICE CHECKLIST

## TOPICAL ANALGESICS

Several new OTC topical analgesics have been launched recently. This card reviews the use of this group of compounds, explaining how the different types of drugs work, when one of the newer NSAIDs might be most appropriate and when oral therapy is the best treatment

### HOW POPULAR ARE TOPICAL ANALGESICS?

Recent data from the Prescription Pricing Authority suggest that some 10 per cent of the total costs of all analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) relates to topical NSAIDs. Over-the-counter sales of topical NSAIDs are also substantial, and with the recent downregulation of a number of such products from prescription only to pharmacy status, this market is likely to expand.

### HOW DIFFERENT ARE THE CURRENTLY AVAILABLE TOPICAL ANALGESICS?

Topical analgesic formulations in current use fall into three broad categories: (i) traditional formulations, generally referred to as rubefacients, based on long-established salicylate and nicotinate esters, capsaicin or other capsicum extracts and derivatives; (ii) formulations based on the newer NSAIDs, including diclofenac, felbinac, ibuprofen, ketoprofen and piroxicam; and (iii) a miscellaneous group of agents such as benzydamine, mucopolysaccharide polysulphate (which the manufacturer claims should be classified as an NSAID but is not generally recognised as such) and salicylamide. Cooling sprays may conveniently be included in this miscellaneous category.

While all of the topical products probably share the same non-specific mode of action as analgesics, there are substantial differences in their specific biochemical activities.

### WHAT ARE THE LICENSED INDICATIONS FOR THE TOPICAL ANALGESICS?

Licensed indications vary somewhat from product to product but broadly include muscular pain and stiffness, sprains and strains, and pain associated with rheumatic and non-serious arthritic conditions.

### HOW DO TOPICAL ANALGESICS WORK?

The traditional explanation for the analgesic action of topical products containing agents such as the nicotinate and salicylate esters and capsaicin is that of counter-irritancy. This is usually linked to the most widely accepted theory of pain sensation and control, namely, the gate-control theory. This theory suggests that there is input control to incoming nerve impulses so that only modulated information reaches the brain and that the central nervous system integrates all the incoming information. This input control is thought to take place in the substantia gelatinosa and the processed information is then conveyed to the transmission T cells deeper in the spinal cord.

Counter-irritants initiate signals which compete with pre-existing impulses in obtaining access to the central nervous system. The gate theory predicts that massaging a painful area will stimulate the thick myelinated nerve fibres and close the gate to incoming information. T cell activity is depressed and pain relief ensues. However, this fails to account for the pain relief which continues well after the

massaging is stopped. Massage is also thought to bring pain relief by stimulating local circulation and diluting accumulated mediators of pain.

### IF COUNTER-IRRITANCY IS IMPORTANT, HOW DO NSAIDS WORK?

By inhibiting cyclo-oxygenase enzyme, NSAIDs interfere with the synthesis of prostaglandins which sensitise pain receptors. Much of the specific analgesic and anti-inflammatory action of the NSAIDs is attributed to this mechanism of action although this explanation does not succeed in ranking the available NSAIDs in terms of analgesic efficacy. Selectivity of action against cyclo-oxygenase enzyme isoforms (COX-1 and COX-2) does not provide a full answer either. For example, two NSAIDs might have similar cyclo-oxygenase blocking activity but very different analgesic and anti-inflammatory potencies. Other mechanisms postulated for how NSAIDs work include membrane stabilisation with inhibition of lysosomal enzyme release, and inhibition of generation of superoxide anion in activated neutrophils.

### TO WHAT EXTENT ARE TOPICALLY APPLIED NSAIDS ABSORBED?

Only a few per cent of a dose of topically applied NSAID is absorbed into the systemic circulation. However, some studies suggest that levels in tissues in close proximity to the area of application may be higher following topical application than

after oral administration of conventional doses. Contradictory results have also been reported.

### HOW EFFECTIVE ARE TOPICAL NSAIDS?

The British National Formulary suggests that topical NSAIDs may provide some slight relief of pain in musculoskeletal conditions. Several placebo-controlled studies have indeed shown that topical NSAIDs are effective in providing modest pain relief in a variety of painful conditions, including acute sprains and osteoarthritis. Better data are available to support clinical efficacy of the newer NSAIDs (ibuprofen, piroxicam, ketoprofen, diclofenac and felbinac) than the older agents. However, there is little evidence from comparative studies to show that any of the newer NSAIDs are better than the traditional rubefacients. On theoretical grounds, NSAIDs are preferable to paracetamol or the nicotinate and salicylate esters in the presence of inflammation (eg, soft tissue injury).

### WHY ARE TOPICAL NSAIDS SO POPULAR?

A major concern with oral NSAIDs is that a significant proportion of patients develop gastrointestinal problems, including ulceration and gastrointestinal bleeding, when given these drugs. Elderly patients are at particularly high risk. Topical application is thought to be safer for such patients.



## TREATMENT GUIDELINES

- In the presence of soft tissue injury, and hence inflammation, an oral NSAID should be recommended (in addition to rest and immobilisation), provided that there are no major contraindications, ie, a history of hypersensitivity to NSAIDs (including aspirin), a history of gastrointestinal ulceration or bleeding, or serious renal problems. Ideally, treatment should start with oral ibuprofen but aspirin is an acceptable alternative. Once inflammation is under control, a switch to a topical formulation is reasonable. Any of the newer NSAIDs would be satisfactory.

In patients with a history of GI ulceration but not of hypersensitivity to NSAIDs or serious renal problems, treatment may be initiated with a topical NSAID because systemic levels are unlikely to be high enough to cause serious GI complications. It is, however, important to ensure that excessive applications are avoided since case reports of renal problems have followed such use. Oral paracetamol may be a useful supplement to such therapy.

- Some 10 per cent of asthmatics are claimed to be hypersensitive to aspirin and hence possibly to other NSAIDs. Those affected should avoid topical NSAIDs. Asthmatics without a history of aspirin hypersensitivity are unlikely to react adversely to topical NSAIDs.
- In other painful conditions (osteoarthritis, painful muscles), there is little justification for preferring the topical NSAIDs over the traditional rubefacients (salicylate and nicotinate esters). Oral ibuprofen and paracetamol are reasonable alternatives under such circumstances provided the necessary precautions are observed.

## WHEN TO REFER

1. Patients with suspected bone fractures
2. Patients with visible joint inflammation, although this does not preclude counter-prescribing an oral NSAID
3. Patients who have not responded to oral NSAIDs
4. Patients with a history of hypersensitivity to oral NSAIDs and not responding to paracetamol or non-salicylate rubefacients
5. Children under 12

## POINTS TO REMEMBER

1. In the presence of inflammation, an NSAID is preferable to paracetamol
2. In the presence of inflammation of acute onset, an oral NSAID is preferable to a topical NSAID
3. In patients with a history of hypersensitivity to aspirin, both oral and topical NSAIDs should be avoided
4. In otherwise healthy subjects with myalgia, any topical rubefacient or a topical NSAID would be appropriate although the former would be more cost-effective

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