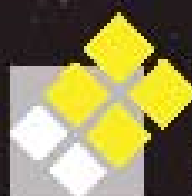


NSAIDs

Strategies for Minimising Harm



bpac nz
better medicine

Felix Hoffmann

Toward safer use of NSAIDs

Cover story...

During one particularly productive fortnight in August 1897 Felix Hoffmann, a German chemist with the Bayer Company, earned the curious distinction of 'discovering' one of the most useful substances known to medicine, and then one of the most deadly.

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All information is intended for use by competent health care professionals and should be utilised in conjunction with pertinent clinical data.

Do You Agree With Our Recommendations

Check to see if you agree with our recommendations and then review our reasoning on the following pages.

1. I consider NSAIDs as second-line therapy after non-pharmacological interventions and alternatives with less risk of harm.	AGREE / DISAGREE
2. When considering NSAIDs, I always try to identify high-risk patients and respond appropriately.	AGREE / DISAGREE
3. I advise low-dose NSAIDs when they are used for analgesia.	AGREE / DISAGREE
4. I advise diclofenac or naproxen when NSAIDs are used as anti-inflammatories.	AGREE / DISAGREE
5. I use the lowest effective dose of NSAIDs for the shortest duration needed.	AGREE / DISAGREE
6. I am not advising patients to use COX-2 inhibitors until their role is more clearly understood.	AGREE / DISAGREE

bpac^{nz} : working toward safe effective clinical outcomes by promoting primary care interventions that are evidence-based, patient-centred, cost-efficient and context-sensitive.

Main recommendations for safe, effective practice.

bpac^{nz} offer the following recommendations to enhance the safe effective use of NSAIDs:

1. Consider NSAIDs as second-line therapy after non-pharmacological interventions and alternatives with less risk of harm

Non-pharmacological interventions are important in every pain management strategy (Page 3). Paracetamol is recommended as the analgesic of first choice in most situations because it has a good safety profile, however NSAIDs are useful for patients who do not get good results from these first-line interventions. Some guideline extracts illustrating this principle are included in Appendix C.

2. When considering NSAIDs, identify high-risk patients and respond appropriately

There is a significant incidence of GI, renal and cardiovascular adverse effects from NSAID use. It is possible to identify those people who are at higher risk of these effects and respond with more appropriate prescribing and monitoring. An NSAID risk factor tool is provided on your desktop resource.

3. Advise low-dose ibuprofen when NSAIDs are used for analgesia

Low-dose ibuprofen (less than 1200mg per day) has a good safety profile and has a similar analgesic effect to other NSAIDs. This makes ibuprofen our choice of NSAID for pain relief in conditions such as osteoarthritis. Low-dose diclofenac or naproxen are suitable alternatives.

4. Advise diclofenac or naproxen when NSAIDs are used as anti-inflammatories

When NSAIDs are required for inflammatory arthritis such as rheumatoid arthritis, or crystal arthritis such as gout, we prefer diclofenac or naproxen.

5. Use the lowest effective dose of NSAID for the shortest duration needed

The risk of serious GI adverse effects increases with dose. Adverse GI effects occur at a fairly consistent rate throughout the duration of NSAID use. Therefore limiting the dose and duration of exposure to NSAIDs to the lowest dose for the shortest duration needed reduces the risk. The use of paracetamol along with NSAIDs can allow lower NSAID dose, and is associated with similar efficacy but lower risk of GI adverse effects.

6. Do not advise COX-2 inhibitors until their role is more clearly understood

At the time of writing (December 2004) there is intense debate about the safety and efficacy of COX-2 inhibitors. We intend to cover the use of COX-2 inhibitors in a follow-up to this POEM. Our feeling, at the moment, is that it is prudent to avoid the use of COX-2 inhibitors until the situation becomes clearer.

Toward safer use of NSAIDs

The aim of this POEM is to support the safer use of non-steroidal anti-inflammatory drugs (NSAIDs) including COX-2 inhibitors. It provides information for prescribers and pharmacists to consider and discuss with their patients. It offers recommendations to improve the safety of NSAID use and provides some useful tools to assist decision making.

NSAIDs weighing potential benefits against risks of harm

The analgesic and anti-inflammatory properties of non-steroidal anti-inflammatory drugs have made them popular with prescribers and with consumers. They are available over the counter from supermarkets and pharmacies. However, as with all medications, the potential benefits of NSAIDs must be weighed against the risks of harm.

There is considerable international evidence that people are suffering from adverse drug reactions (ADRs) from NSAIDs and much of this is due to inappropriate prescribing. For example, 6.8% of all patients over the age of 16 years admitted to two large hospitals in Liverpool, UK, were suffering from ADRs. Thirty per cent of these were caused by NSAIDs (including aspirin) (Pirmohamed, 2004). On average one in 1200 patients taking NSAIDs for at least two months will die from gastroduodenal complications. They would not have died had they not taken NSAIDs (Tramer, 2001).

Consider NSAIDs as second-line therapy after non-pharmacological interventions and lower risk alternatives

Associated with the sensation of pain are a wide range of personal issues, such as fear, impaired function and a misunderstanding of the effect of pain on the rate of recovery. Non-pharmacological interventions such as exploration of a patient's beliefs and expectations, exercise and in some cases physical therapies can make an essential contribution to pain relief and reduce the need for medications.

Paracetamol is presented as the first-line pharmacological intervention for pain relief in most guidelines. This is appropriate given its good benefit / harm profile. NSAIDs are useful when analgesia with paracetamol is inadequate or in conditions where inflammation is a feature. When used primarily for analgesia it is often advantageous to keep the dose of NSAIDs low by continuing with the paracetamol (Appendix C). Topical NSAIDs have been shown to do less harm than oral NSAIDs and evidence is emerging that they may be just as efficacious at least in the short term (Bandolier, (11) 2004).

Question: Are the anti-inflammatory effects of NSAIDs beneficial for the management of soft tissue injuries?

Answer: Probably not, although there are conflicting findings and opinions. "Because inflammation is a necessary component in the healing process, decreasing inflammation may prove counterproductive. Also, many tendon injuries called 'tendonitis' are, in fact, degenerative and not inflammatory conditions. An analysis of the pathophysiology and healing of musculoskeletal injuries questions the use of NSAIDs in many treatment protocols. Because NSAIDs have profound side effects, they should not automatically be the first choice for treating musculoskeletal injuries" (Stovitz, 2003).

Minimising Gastrointestinal Adverse Effects

NSAID use exposes people to increased risk of adverse GI events ranging from dyspepsia to GI perforation or haemorrhage.

Scope of the problem

Dyspepsia is common in NSAID users, occurring in 5-50% of people (depending on the definition). Dyspeptic symptoms however correlate poorly with the risk and presence of more serious complications. Serious upper GI adverse events such as GI haemorrhage or perforation have an incidence of around 2% per year in chronic NSAID users at average risk. This rises to 10% per year in "high risk" patients (CCOHTA, 2004). These rates are thought to be 3 to 4 times the rates in non-NSAID users (Hernandez-Diaz, 2000).

Factors influencing the risk of serious adverse GI events

Both patient characteristics and prescribing factors influence the risk of adverse GI events.

Patient factors which increase the risk of serious GI events:

- Increasing age, in particular age >65 years
- Past history of GI ulceration
- Presence of co-morbidities, in particular CVD

These factors, particularly the first two, are associated with a higher risk of serious GI problems irrespective of NSAID use. NSAID use increases the risk still further.

Prescribing factors which increase the risk of adverse events:

- Concomitant prescribing of: steroids, anticoagulants, bisphosphonates, low-dose aspirin
- Higher dose NSAID use
- Particular NSAID used (see page 5)

Strategies to reduce the risk of serious GI events

For all NSAID users:

- Choose an NSAID with a lower risk of adverse GI events.
- Use the lowest effective dose of NSAID, for the shortest duration needed.
- Do not prescribe more than one oral NSAID concurrently. Do not co-prescribe low-dose aspirin with another NSAID unless absolutely necessary.
- Do not prescribe NSAIDs for those with a current or past history of GI ulceration.
- Use paracetamol along with NSAIDs to reduce NSAID dose and risk of GI adverse effects.

For higher risk users who cannot avoid NSAID use:

- Co-prescribe a gastro-protective agent (a PPI or misoprostol).

Statements are based on recommendations made by the U.K. Committee on Safe use of Medicines (CSM) and the New Zealand Guidelines Group (NZGG).

Some evidence pertaining to these recommendations is presented on the following pages.

Do not prescribe NSAIDs in those with a current or past history of peptic ulceration

People with a history of peptic ulceration who also take NSAIDs have 17 times the risk of further GI bleeds or perforation compared to the general population.

People with a past history of peptic ulceration are already at a higher risk for a further GI bleed or perforation than the general population, with a risk approximately nine times higher. Use of an NSAID adds further to this risk. One study quantified the relative risks compared to those who had no history of ulceration or NSAID use (Rodriguez 1994).

NSAID use	History of ulcer	Relative risk
Yes	No	5.4 (4.4-6.8)
No	Yes	8.7 (7.4-10.3)
Yes	Yes	17.2 (10.0-29.6)

Such an increased risk prompted the CSM to recommend that non-selective NSAIDs should not be prescribed at all in those with a past history of peptic ulceration, as well as those with current ulceration.

Choose an NSAID with a lower risk of adverse GI effects

Ibuprofen in doses <1200mg/day seems to have a lower risk of adverse GI effects than other NSAIDs. Consider low-dose ibuprofen first when choosing an NSAID primarily for analgesic effect. Low-dose diclofenac or naproxen are suitable alternatives. Ibuprofen is thought to be a less potent anti-inflammatory agent than other NSAIDs, for conditions with a prominent inflammatory component (e.g. acute gout) consider diclofenac or naproxen.

There is evidence of different gastro-toxicities of different NSAIDs. Ibuprofen is consistently found to have the lowest risk in epidemiological studies although this may be due to the tendency to prescribe it at lower equivalent doses to other NSAIDs.

Relative risk of gastrointestinal complications with NSAIDs, relative to ibuprofen or non-use from three different epidemiological studies:

Drug	Henry et al.	MacDonald et al.	Rodriguez et al.
Non-use			1.0
Ibuprofen	1.0	1.0	2.1 (0.6-7.1)
Aspirin	1.6 (1.3-2.0)		
Diclofenac	1.8(1.4-2.3)	1.4(0.7-2.6)	2.7(1.5-4.8)
Sulindac	2.1(1.6-2.7)		
Naproxen	2.2(1.7-2.9)	1.4(0.9-2.5)	4.3(1.6-11.2)
Indomethacin	2.4(1.9-3.1)	1.3(0.7-2.3)	5.4(1.6-18.9)
Piroxicam	3.8(2.7-5.2)	2.8(1.8-4.4)	9.5(6.5-13.8)
Ketoprofen	4.2(2.7-6.4)	1.3(0.7-2.6)	3.2(0.9-11.9)

Table adapted from Bandolier, The Oxford Pain Internet Site.
www.jr2.ox.ac.uk/bandolier/booth/painpag/nsae/nsae.html#Heading4

Use the lowest effective dose, for the shortest duration needed

The risk of serious upper GI problems is dose related, as shown in the table (adapted from Hawkey, 2003):

NSAID	Daily Dose (mg)	OR (95% CI)
Ibuprofen	<1200	1.1 (0.6, 2.0)
	1200-1800	1.8 (0.8, 3.7)
	>1800	4.6 (0.9, 22.3)
Diclofenac	<75	2.2 (0.8, 5.8)
	75-150	3.2 (1.9, 5.5)
	>150	12.2 (5.6, 26.7)
Piroxicam	<10	9.0 (2.1, 39.2)
	11-20	12.0 (6.5, 22.1)
	>20	79.0 (9.9, 931.8)

“At doses of < 1200mg/day, gastrointestinal risks (of ibuprofen) may not be significantly elevated above background” (Hawkey, 2003).

Most of the analgesic effect of NSAIDs is obtained at lower doses (Hawkey, 2000), so there is rarely any benefit from increasing doses of NSAIDs in attempts to improve pain relief. Higher doses may improve anti-inflammatory effects however. Clinically this is most apparent for ibuprofen; analgesic effects are apparent at doses < 1200mg/day but for more marked anti-inflammatory effects doses of 1600-2400mg/day may be needed (BNF). The regimen for taking higher doses of ibuprofen may effect compliance.

The risk of adverse GI effects is relatively constant throughout duration of NSAID use. Therefore limiting the duration of use will limit the exposure to risk (MacDonald, 1997). In the clinical setting this means we should be carefully reviewing the duration and dose of NSAIDs on each prescription. The patient may still get good control of pain and/or inflammation on a lower dose of NSAID with the addition of paracetamol if needed.

Do not prescribe more than one NSAID concurrently

Risks of using more than one NSAID appear to be additive and this includes low-dose aspirin. The risk of serious events more than doubles when aspirin is co-prescribed with another NSAID (CSM 2002).

Low dose aspirin and other NSAIDs

Regarding concurrent use of aspirin the CSM advises: “The combination of a non-aspirin NSAID and low-dose aspirin may be associated with an increased risk and should only be used if absolutely necessary.” If it is considered absolutely necessary the Lothian guidelines advise a combination of low-dose diclofenac plus low-dose aspirin plus omeprazole (Lothian, 2004).

Ibuprofen may negate the protective effects of low-dose aspirin if used concurrently, this may occur because of competitive binding at the site of action of aspirin on the COX-1 enzyme (Castella-Lawson, 2001). Studies on whether this possible effect is of clinical relevance have been conflicting, with further clarification of the issue needed (Kimmel, 2003).

Gastroprotection for higher risk users of NSAIDs

Patients who are at higher risk of GI adverse events and cannot avoid NSAIDs should receive co-treatment with either a proton pump inhibitor (PPI) or misoprostol. Omeprazole is usually preferred because it is more readily available in NZ and better tolerated than misoprostol.

Patients who are at higher risk of GI adverse events

NICE defines high-risk patients as:

- Aged over 65 years,
- Using concomitant medications known to increase the likelihood of upper gastrointestinal adverse events (e.g. anticoagulants, steroids, low-dose aspirin and possibly biphosphonates),
- Serious co-morbidity (e.g. CVD), or
- Requiring the prolonged use of maximum recommended doses of standard NSAIDs

Gastroprotection

Three agents have shown some efficacy in gastroprotection: PPIs, Histamine H₂ receptor antagonists (H₂RAs), and misoprostol, a prostaglandin E₁ analogue. Of these misoprostol has the most evidence of efficacy, reducing the risk of serious GI complications by 40% as compared to placebo over six months (Silverstein, 1995).

PPIs have shown efficacy in preventing endoscopically diagnosed ulcers, with pooled results showing risk reductions in the region of 59%. It is generally viewed that these endoscopic results will translate into clinical benefits; however there are currently no trials assessing actual clinical outcomes (Micklewright, 2003).

Standard dose H₂RAs have not been shown to reduce the risk of endoscopically defined gastric ulcers. High dose H₂RAs (e.g. ranitidine 300mg BD) have shown some efficacy but this has not been verified with clinical outcome studies.

Current New Zealand guidelines recommend either misoprostol (200mcg QID) or a standard dose PPI (e.g. omeprazole 20mg daily) for cytoprotection. It is noted PPIs are better tolerated than misoprostol (NZGG, 2004).

Question: Does enteric coating of NSAIDs reduce the risk of serious GI complications?

Answer: No. There is no convincing evidence these formulations are safer, and there is concern such formulations could increase the risk of lower GI adverse effects (Davies, 1999).

Minimising Renal And Cardiovascular Adverse Effects

Cardiovascular effects

NSAIDs cause salt and water retention, which may raise blood pressure and increase the risk of heart failure, especially in those with pre-existing heart disease. Low-dose aspirin does not appear to have this effect.

Salt and water retention is a common side effect of NSAIDs. This is thought to be mediated by enhancement of renal sodium absorption, as a result of COX (largely COX-2) inhibition (Hawkey, 2003). This occurs to some degree in all NSAID users, but results in clinically apparent oedema in less than 5% of people (Whelton, 1991). However it can elevate blood pressure by an average of 3-5 mmHg, which at a population level may contribute to excess cardiovascular mortality (Hawkey 2003). Blood pressure elevation is more likely in those with pre-existing hypertension and NSAIDs may reduce the effectiveness of diuretics, beta blockers and ACE inhibitors.

Due to these renal effects, and possibly other effects on vasculature, NSAIDs may induce heart failure in susceptible persons. The risk of heart failure approximately doubles in NSAID users, and up to 19% of heart failure admissions may be due to NSAID use (Page, 2000). Such findings raise the possibility that NSAIDs may cause as much cardiovascular disease as they do ulcer complications (Hawkey, 2003).

The risk of heart failure appears to be dose related, and the risk is much higher in people with pre-existing heart disease; therefore risk reduction strategies include:

- Use the lowest effective dose of NSAID
- Prescribe NSAIDs with caution in those with heart disease; with careful monitoring
- Monitor blood pressure in those with pre-existing hypertension, particularly if they are taking beta blockers or diuretics

Question: Are NSAIDs other than aspirin cardioprotective?

Answer: "In general, these drugs, when used at a conventional analgesic dosage, inhibit reversibly platelet COX activity by 70 to 90%. This level of inhibition may be insufficient to block adequately platelet aggregation in vivo, because of the very substantial biosynthetic capacity of human platelets to produce TXA₂" (Patrono et al. 2004).

Question: If a person gets dyspepsia with one particular NSAID are they likely to get this with all NSAIDs?

Answer: Not necessarily. For some people dyspepsia may be specific to a particular NSAID and switching to another NSAID may be beneficial.

Renal failure

People who have reduced renal blood flow due to dehydration, renal disease or CHF are at risk of acute renal failure with NSAIDs. If NSAIDs cannot be avoided they should be used at low doses for short durations with careful monitoring.

Acute renal failure can be caused by NSAID use, usually in people with pre-existing reduced renal blood perfusion or impaired renal function. This is due to inhibition of production of vasodilatory renal prostaglandins, which are necessary for maintenance of renal perfusion in such at risk people (Whelton 1991).

Griffen et al. 2003, estimate the attributable rate of acute renal failure at 0.25% per year. The risk appears to be dose related. Situations in which risk is increased include:

- Congestive Heart Failure
- Severe liver disease
- Chronic renal disease
- Nephrotic syndrome
- Dehydration (protracted)
- The elderly (age-related renal impairment)

Strategies to decrease risk include:

- Use NSAIDs cautiously in such patients, avoid if possible
- Use NSAIDs at low doses
- Check renal function at baseline and periodically*

*Remember calculated creatinine clearance is a more accurate measure of renal function than a serum creatinine - use the bpac calculator.

Drugs that affect renal blood flow, e.g. ACE inhibitors, or which may cause dehydration, e.g. diuretics, increase the risk of renal failure when used with NSAIDs. The combination of **NSAID + ACE inhibitor + diuretic** is particularly **dangerous** and has been termed “the triple whammy”. This drug combination should be avoided for those who have other risk factors (Australian Drug Bulletin).

The adverse effects, if anyone should ask you, are GI and Renal and Cardiovascular.

The POET

Appendices

Appendix A:

Common NSAIDs and their doses

Drug	Dose Range	Indications	Notes
Ibuprofen	200-400mg 3-4 times per day (usually 1200-1600mg per day) 1600-2400mg may be needed for RA, maximum 2400mg per day	Rheumatoid Arthritis (RA) Osteoarthritis (OA) Inflammatory pain Dysmenorrhea Fever Headache	- Available OTC max. 1200mg per day - Available OTC for pain/fever in children - Weaker anti-inflammatory effects than other NSAIDs, Not suitable for prominent inflammatory conditions e.g. acute gout
Diclofenac	75-150mg per day in 2-3 divided doses 150-200mg per day may be used for RA short term max. 200mg per day	Rheumatoid Arthritis (RA) Osteoarthritis (OA) Ankylosing spondylitis Acute gout Analgesia: e.g. Inflammatory pain, Dysmenorrhea	Available OTC in 25mg doses
Naproxen	250-500mg bd maintenance dose usually 250mg bd. max. 1250mg per day acute gout or migraine: 750 mg initially then 250mg 8hrly	Rheumatoid Arthritis (RA) Osteoarthritis (OA) Ankylosing spondylitis Acute gout Dysmenorrhea Migrain Musculoskeletal pain Inflammatory pain	- Available OTC - Naproxen sodium more rapidly absorbed, may be better for acute pain relief

Information from BNF 2004, Medsafe data sheets and Australian Medicines Handbook 2002.

Appendix B:

Clinically relevant NSAID drug interactions

Drug Used With NSAID	Interaction	Recommended Actions
ACE inhibitors	↓ antihypertensive effect ↑ risk of renal impairment and hyperkalaemia	Avoid combination if renal hypoperfusion or impairment exists Monitor BP, weight, Cr, K+
ACE + Diuretics	↑ risk renal failure	Dangerous combination - avoid
Other antihypertensives	↓ antihypertensive effect	Monitor BP
Alendronate	↑ risk GI ulceration	Use with extreme caution
Aspirin	↑ risk GI ulceration	Consider need for co-therapy carefully Use lowest effective dose for shortest possible duration
Corticosteroids	↑ risk GI ulceration	Consider need for co-therapy carefully Use lowest effective dose for shortest possible duration
Cyclosporin, tacrolimus	↑ risk of cyclosporin nephrotoxicity	Monitor renal function
Diuretics	Possibly reduced diuretic effect ↑ risk of renal impairment	Monitor BP, weight and renal function
Lithium	↓ clearance of lithium, so ↑ risk of toxicity	Monitor lithium levels and renal function
Methotrexate	↑ risk of methotrexate toxicity (unlikely with low-dose methotrexate)	Avoid combination if methotrexate is used in antineoplastic doses
K+ sparing diuretics, K+ supplements	↑ risk of hyperkalaemia	Monitor K+, esp. in elderly/impaired renal function
Warfarin	Non-selective agents: ↑ risk GI bleeding Parecoxib, celecoxib, meloxicam : Possible ↑ INR	Avoid combination if possible Monitor INR

Based on information in Australian Medicines Handbook, 2003

Appendix C:

Alternatives to NSAIDs

A simple scheme for pain relief in adults (adapted from Bandolier)

Doses may need to be varied to suit patient needs.

For patients who can take NSAIDs

Pain	Analgesic
Mild	Paracetamol (1G)
Moderate	Paracetamol (1G) plus Codeine (60mg) or Ibuprofen (400mg)
Severe	Paracetamol (1G) plus Codeine (60mg) plus Ibuprofen (400mg)



Wait for two hours



Pain	Analgesic
Mild	None
Moderate	Ibuprofen (400mg)
Severe	Ibuprofen (400mg)

Wait two hours and repeat cycle ←

For patients who cannot take NSAIDs

Pain	Analgesic
Mild	Paracetamol (1G)
Moderate	Paracetamol (1G) plus Codeine (30mg)
Severe	Paracetamol (1G) plus Codeine (60mg)



Wait for four hours



Pain	Analgesic
Mild	Paracetamol (1G)
Moderate	Paracetamol (1G) plus Codeine (30mg)
Severe	Paracetamol (1G) plus Codeine (60mg)

Wait four hours and repeat cycle ←

Osteoarthritis

Non-pharmacological therapies should be considered as the foundation of treatment:

Exercise and physical therapy have been found to be beneficial. Joint bracing/taping and the use of insoles may also be beneficial for knee arthritis, although evidence is limited.

Regular paracetamol: Paracetamol is recommended as a first line agent when drug treatment is required.

Regular paracetamol plus other drugs: If regular paracetamol is not producing adequate pain-relief consider adding low-dose ibuprofen, codeine or tramadol if appropriate.

Other treatments that may be beneficial:

Topical NSAIDs: have been found to be beneficial for the short-term treatment of osteoarthritis (up to two weeks) but not for the longer term. They are best used for short periods during flare-ups in the disease (Lin 2004).

Glucosamine: There is some evidence for a beneficial effect of glucosamine on symptoms, although the size of the effect needs further study (Clin. Evid.).

Steroid injection (knee): Steroid injections have been found to be beneficial in pain reduction for up to 24 weeks (Arrol 2004).

Hyaluron injection (knee): Benefits of hyaluron have been demonstrated for up to six months (Clin. Evid.).

Rheumatoid Arthritis

Guidelines on the management of RA can be found at www.prodigy.nhs.uk/guidance

Key features of this guidance are:

- Paracetamol should always be considered for first-line use for pain relief
- Disease-modifying antirheumatic agents (DMARDs) should be introduced early to suppress disease activity
- Intra-articular corticosteroids may avoid the need for NSAIDs, particularly if the disease is localised, while waiting for DMARDs to take effect

Question: Do NSAIDs modify the course of rheumatoid arthritis?

Answer: No. NSAIDs can relieve symptoms of pain, stiffness and swelling but they are not DMARDs.

Chronic Low Back Pain

This is difficult to treat with only limited success for various strategies. Clinical Evidence (2003) summarises the effectiveness of various treatments:

Beneficial

Exercise

The optimal type of exercise (e.g. extension/strengthening/postural/stabilisation) is not yet defined; - evidence is conflicting

Intensive multidisciplinary treatment programmes

Likely to be beneficial

Analgesics (paracetamol, opioids).

There are surprisingly few studies comparing different analgesics with placebo.

One study found tramadol superior to placebo; other studies compared pain relief with an NSAID vs. paracetamol, and NSAID vs. opiate and found no significant difference

Antidepressants

Back schools in occupational settings

Behavioural therapy

Massage

NSAIDs

Trigger point and ligamentous injections

Unknown effectiveness (either conflicting or insufficient evidence available)

Acupuncture

Electromyographic feedback

Epidural steroid injections

Lumbar supports

Muscle relaxants

Physical conditioning programmes

Spinal manipulation

TENS

Likely to be ineffective or harmful

Facet joint injections

Traction

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