IN THE NAME OF GOD

Pharmacotherapy in Low Back Pain

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Low back pain is a symptom, not a disease, and has many causes

It is extremely common.

Approximately 40% of people say they have had low back pain within the past 6 months,

Most episodes resolve with or without treatment and the great majority of people who have back pain do not seek medical care.

Studies have shown approximately 90% of people who develop acute LBP experience a resolution of the symptoms within 6 weeks.

Nonspecific Low Back Pain

Nearly 85% of those who seek medical care for low back pain do not receive a specific diagnosis.

The majority of these patients are likely to have a multifactorial cause for back pain, which includes deconditioning; poor muscle recruitment; emotional stress; and changes associated with aging and injury such as disk degeneration, arthritis, and ligamentous hypertrophy.

This type of back pain can be given many names; nonspecific low back pain, simple backache, mechanical low back pain, lumbar strain, and spinal degeneration are a few of the common names for this condition.

By definition, the history and physical examination do not suggest a more specific diagnosis, and diagnostic tests used to exclude other likely causes of the symptoms are negative.

Treatment of Low Back Pain

Most studies of the various treatments for low back pain, particularly chronic low back pain, unfortunately have shown **limited efficacy**.

Even the most commonly prescribed treatments, such as medications, exercise, and manipulation, in large trials tend to show improvements of only **10 to 20 points** on a 100-Point Pain Visual Analog Scale.

For this reason, most clinicians use **multiple treatments** on a particular patient in the hope that their cumulative effect will provide sufficient pain relief and an improvement in symptoms

Reassurance and Patient Education

Reassurance that there is no serious underlying pathology, that the **prognosis is good**, and that the patient can stay active and get on with life despite the pain can help counter negative thoughts and misinformation that the patient might have about back pain. Providing empathy and a strong therapeutic alliance will improve **adherence to treatment and better outcomes**

Behavioral treatment/ cognitive behavioral approach

Pharmacotherapy
Management strategies

Includes management of the **underlying disease** process causing the pain and symptomatic treatment. Both the management strategies should run in parallel.

Pharmacotherapy is the first way to pain control in LBP , can play a substantial role in both strategies.

It is essential to **individualize the pharmacotherapy** because the effect, side-effect and toxicity profile for each drug shows marked variation from person to person.

Each medication is given in **adequate doses** for the appropriate length of time. A medication should not be abandoned and regarded as being ineffective until the maximum possible dose that does not produce significant side effects is reached.

Once **adequate pain relief** is obtained, the **dose should be maintained for 2 to 3 weeks,** while encouraging **appropriate exercise** and normal activity

If pain control is not achieved with adequate doses of a drug, it is advisable to discontinue that drug.

Summary of the groups of medications to treat low back pain based on the types of pain.

Type of pain	Drug class	Drug group-options
Nociceptive / Somatic • back pain with or without referred pain	Simple analgesics	Paracetamol
	Compound analgesics	Paracetamol + codeine
	NSAIDs	Diclofenac
	COXIBs	Celecoxib, Etoricoxib
	Opioids	Tramadol
Neuropathic / radicular pain • Burning back pain • Radicular leg pain	Anticonvulsants	Gabapentin, Pregabalin
	Antidepressants - TCAs (Tricyclic antidepressants.)	Amitriptyline, Prothiaden
	- SNRIs (Serotonin and norepinephrine reuptake inhibitors)	Venlafaxine, Duloxetine
	Opioids	Tramadol, Oxycodone

Pain types

- **Pain types**

  While doing the pain assessment, the medical practitioner has to decide whether the pain is nociceptive,neuropathic or a combination of both. The choice of medication for nociceptive or neuropathic pain is different. Nociceptive pain is the pain that occurs in response to potential or actual tissue damage. Patients tend to describe it using simple terms. In the context of back pain, nociceptive pain concentrates in the back and can refer diffusely into the legs.

  Neuropathic pain is defined as pain derived from a nervous system lesion. It has typical pain qualities that include burning and shooting. In the context of back pain, neuropathic pain presents as radicular pain (pain radiating down the leg), due to injury to the spinal nerve by disc prolapse and / lateral canal stenosis.

Analgesics

- Simple analgesia Paracetamol is the first line of treatment especially if back pain is mild as it is has few side effects and is widely available. **Do not exceed> 4g / day**
- If simple analgesics are not effective, compound analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs)/COX-2 selective inhibitors can be used.
- In view of the long-term side-effects of NSAIDs, these drugs should only be used for **short-term duration (up to three months) or during flare-ups**.
- There is insufficient data on the use of NSAIDS in **chronic low back pain ?**

NSAIDS

- NSAIDS are not more effective than paracetamol or other drugs for ALBP.!
- No single NSAIDS overcome the others in terms of effectiveness also COX 2 inhibitors.
- strong evidence that various NSAIDS are equally effective .
- Silghtly more effective than placebo in CLBP.
- Cox2 inhibitirs associated with increased cardiovascular risk.
- *American pain society : good short term efficacy with moderate effect for ALBP.*

Drug class	Drug	Recommended dosage	Side effects	Cautions and contraindications	Comments
Simple analgesic	Paracetamol	0.5-1 g every 4-6 hours to a max of 4g daily	Rare	Hepatic impairment, alcohol dependence	- Preferred drug particularly in elderly patients - Liver damage following overdosage
NSAIDs	Mefenamic acid	500 mg 8 hourly	Peptic ulcer, GI bleed, Platelet dysfunction, Renal failure, Hypertension, Allergic reaction in susceptible individuals, Increase in CVS events.	Gastroduodenal ulcer, Asthma, Bleeding disorder, Renal dysfunction, Ischaemic heart disease, Cerebrovascular disease, Inflammatory bowel disease,	**Current data suggest that increased CV risk may be an effect of the NSAID/coxib class. Physicians and patients should weigh the benefits and risks of NSAID/coxib therapy.**
	Diclofenac	75-150 mg daily in 2-3 devided doses			
	Naproxen	500 mg initially then 250 mg 8 hourly			
	Meloxicam (Mobic®)	7.5 – 15mg daily			
COX-2 inhibitor	Celecoxib (Celebrex®)	200 mg daily 400mg daily in acute pain	Renal impairment, Allergy reaction in susceptible individuals, Increase in CVS events.	Ischaemic heart disease, Cerebrovascular disease, Contraindicated in hypersensitivity to sulphonamides	Associated with a lower risk of serious upper Gastrointestinal side-effects

Opioids

- Weak opioids such as Tramadol (an atypical opioid) where the use of NSAIDs are contraindicated or not effective
- . In a metaanalysis it was found to be helpful for short-term treatment of chronic low back pain , probably equivalent to antidepressants, and may be slightly better than NSAIDS in decreasing pain, there is **no evidence to show it improves function**.

- short-acting opioids to treat **acute low back pain ??**. The use of opioids for chronic nonmalignant pain is much more controversial

- In elderly patients, chronic opioid therapy may have fewer lifethreatening risks than long-term daily use of NSAIDs/ COX-2 inhibitors. Tramadol,, may be useful as a single agent in combination nociceptive and neuropathic pain.

- The use of intermittent injections of potent opioids such as pethidine for chronic back pain is strongly discouraged as it can lead to the development of dependency.
- Opiate side effects occur in more than half the participants. include nausea, constipation, somnolence, dizziness, and pruritus.
- There are numerous guidelines that suggest using safe prescribing habits (e.g., a maximum 7-day supply on prescriptions for opioids .

Muscle relaxants

- The use of muscle relaxants remains **controversial**. One reason is that it is unclear what role muscle “spasms” play in low back pain.
- *Other experts do not believe that pain in the low back is generally caused by muscles.*
- *Despite this controversy, 35% of patients who visit a primary care physician for low back pain are prescribed muscle relaxants. They seem to be effective.*
- *American pain society : good short term efficacy with moderate effect for ALBP.*
- *These medications fall into three classes of drug: the **benzodiazepines, the nonbenzodiazepines that are antispasmodics, and antispasticity medication***

Benzodiazepines

- The mechanism of action for **benzodiazepines** is the enhancement of gamma-aminobutyric acid (GABA) inhibitory activity.
- to be effective for both acute and chronic low back pain for short-term pain relief (trials generally lasted from 5 to 14 days).
- Adverse effects sedation, dizziness, and mood disturbances. Rapid withdrawal can cause seizures.
- These medications have serious abuse and addiction potential, and they are not recommended for low back pain except in unusual cases for a **short time**.
- **No evidence** exists to support that they are **more effective than other** muscle relaxants such as cyclobenzaprine.

Nonbenzodiazepines/ Antispasmodics

Medications with **multiple mechanisms** of action.
Cyclobenzaprine has a structure similar to that of tricyclic antidepressants and is believed to act in the brainstem.

The mechanism of action of Methocarbamol is not known but could be as a result of central nervous system depression.
Effective for patients with **acute low back pain for short-term** pain relief (usually 2 to 4 days' duration).
The most common **side effects** are drowsiness and dizziness.
Currently, no evidence shows that one is more efficacious than another.

Little literature exists on the use of muscle relaxants **for chronic pain**. The drug manufacturers in this class state that they are **not for long-term** use.

Non benzodiazepines/Antispasticity drugs

Baclofen is a GABA derivative that inhibits transmission at the spinal level and brain. One study has shown this medication to be effective for **short-term pain relief** in those with **acute low back pain**.

Dantrolene works on the muscle, blockading the sarcoplasmic reticulum calcium channels. A small study of 20 patients found it to be effective for **acute low back pain**. It does not have the drowsiness side effect of the other muscle relaxants, but there is a risk of severe **hepatotoxicity.**

Tizanidine, a centrally acting alpha^2-agonist developed to treat spasticity, has been shown to be effective for acute low back pain in multiple trials. No studies support its use for chronic low back pain.

Antidepressants

Tricyclic antidepressants (amitriptyline) are an effective treatment for many painful conditions, such as diabetic neuropathy, postherpetic neuralgia, fibromyalgia, and headaches.

No adequate studies show whether they are effective for the treatment of acute low back pain. Multiple studies and reviews have shown their effectiveness, however, for **chronic low back pain**.

The most common side effects seen with the use of tricyclic antidepressants are dry mouth, blurry vision, constipation, dizziness, tremors, and urinary disturbances.

The selective serotonin reuptake inhibitors, SSRI (fluxetine) **are not effective** in treating chronic low back pain, which is consistent with the findings in studies for other painful conditions, such as diabetic neuropathy.

The selective serotonin and norepinephrine reuptake inhibitors, SNRI (duloxetine)are effective for **chronic LBP.**

Antidepressants

TCA (Tricyclic antidepressant)	Amitriptyline	Start with 10-25 mg nocte. Increase weekly by 25 mg/d to a max of 150 mg/d	Anticholinergic effects eg. Dry mouth, drowsiness, urinary retention, arrhythmias	Not recommended in elderly patients and patients with cardiac disease, glaucoma, renal disease
SNRI (Serotonin and norepinephrine reuptake inhibitor)	Duloxetine	Start with 60mg once daily, increase to a maximum of 120 mg/ day in evenly divided doses.	GI disorders, excessive sweating, CNS disorders eg. dizziness, fatigue, insomnia, somnolence, blurred vision, dysuria	Concomitant use with MAOIs, potent CYP1A2 inhibitors. Hepatic or severe renal impairment. Uncontrolled narrow-angle glaucoma

Anti-convulsants

The anticonvulsants, particularly gabapentin and pregabalin, are widely used for neuropathic pain. Large randomized controlled trials have not yet been conducted with these medications for the treatment of low back pain.
One study of topiramate showed small improvement in chronic low back pain. Side effects include sedation and diarrhea.

Anti-convulsants	Gabapentin (Neurontin®)	300-3600 mg/d. Day 1 : start at 300mg nocte. Day 2 : 300 mg bd. Day 3 : 300 mg tds. Thereafter, increase by 300 mg/d every 1-7 days	Drowsiness, Dizziness, GI symptoms and mild peripheral oedema	Dose adjustment needed in renal impairment
	Pregabalin (Lyrica®)	Start with 150mg/d (in 2 divided doses). If needed increase to 300mg/d after 3-7 days intervals, if needed increase to 600mg/d after 7-day interval.	Drowsiness, Dizziness, GI symptoms and mild perpheral oedema	Dose adjustment needed in renal impairment

Systemic Steroids

- IV, IM or Oral
- Multiple studies have found them **not to be effective for axial (nonradicular) low back pain.**
- In radicular LBP single IM dose or tapered oral dose of CS have **not been found to be superior to placebo.**
- In a RCT 8 mg IV dexamethasone had greater reduction in VAS pain score, which was **not clinically significant**.
- IV bolus of 500 mg methylprednisolone provided a small and transient improvement in leg pain during first 3 days.
- Side effects: arythmia, circulatory collapse with IV methylprednisolone > 500 , flushing , hypertension , hyperglysemia.

Herbal Medicines

Several herbal medicines **are used** in the treatment of low back pain. Literature studies in this area tend to be of **low quality**, but several herbal preparations seem to **reduce pain more than placebo**, including *Capsicum frutescens (cayenne) in a topical preparation, Salix alba (white willow bark), and Harpagophytum procumbens (devil's claw).*

Topical medication

- Topical NSAIDs are effective for acute musculoskeletal disorders. However, there is no evidence supporting its long term use.

LEG pain greater than back pain / sciatica, disc herniation /Lumbosacral Radiculopathy

Radicular symptoms can be the result of overt mechanical compression of a nerve root or a chemically mediated inflammatory process. Nucleus pulposus is highly antigenic as a result of being in an immunoprotected setting in nonpathologic states. When the fluid of the nucleus pulposus is exposed to neural tissue of the spinal canal and neuroforamen through a defect in the annular fibers, an autoimmune-mediated **inflammatory cascade** begins. The inflammatory mediators generated can cause swelling of the nerves.

The mechanism of mechanical compression of the nerve roots has also been studied.Compression of nerve roots can induce structural and vascular changes as well as inflammation. Neural compression can result in impairment of intraneural blood flow, with subsequent local ischemia and formation of intraneural edema. This can set off an inflammatory cascade similar to that described previously.

conservative management of lumbosacral radiculopathies

- **Use nonsteroidal anti-inflammatory drugs (NSAIDs) to help reduce inflammation and to provide pain relief. In a review NSAIDs have not been found to be effective in patients with radiculopathy. (small effect size)**
- **No definite support exists for oral steroids in the treatment of acute radiculopathy. Moderate quality research support for use of CS to pain relief in the short term.**
- **The neuropathic pain agents (anticonvulsants and tricyclic antidepressants) are often used for radicular pain. Small studies have found gabapentin and topiramate to be associated with small improvements in pain scores.**
- **In a recent meta-analysis of the use of NSAIDs, corticosteroids, tricyclic antidepressants, and anticonvulsants, data showed no efficacy with any of these medications over placebo in chronic radiculopathy,**
- **Opioids may be used for pain relief, although their effectiveness is suboptimal in neuropathic pain, with some suggestion that they should be used only in severe cases. Opioids for acute radiculopathy have limited effectiveness.**
- **Tumor necrosis factor alpha inhibitors, no significant pain relief, limited clinical; value.**
- **Epidoral steroid injection**

Pharmacotherapy Guidelines summary

Recommendations for the prescription of medication vary depending on the class of medication and symptom duration.

Most guidelines (93%) recommend the use of nonsteroidal anti-inflammatory drugs (NSAIDs) for patients with acute and chronic LBP considering the risk of adverse events (e.g., renal, cardiovascular, and gastrointestinal).

For paracetamol/ acetaminophen, while most guidelines recommend in favor of this medication 57%), five guidelines (36%) advise against the use of paracetamol.

Most guidelines (87%) recommend weak opioids **for short periods**, if there is no improvement with NSAIDs or other treatments. The guidelines recommend opioids for acute LBP (61%), chronic LBP (38%),

For antidepressants, most guidelines (75%) recommend its use for patients with **chronic LBP** where necessary.

For muscle relaxants, most guidelines (54%) recommend this medication for **acute LBP** (50%), chronic LBP(33%), In contrast, five guidelines(45%) recommend against muscle relaxants.

Two guidelines mentioned the use of herbal medicine for LBP (13%); one recommends its use for patients with chronic LBP , but the other recommends against it for any type of LBP .

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Clinical practice guidelines for the management of non-specific low back pain in primary care: an updated overview

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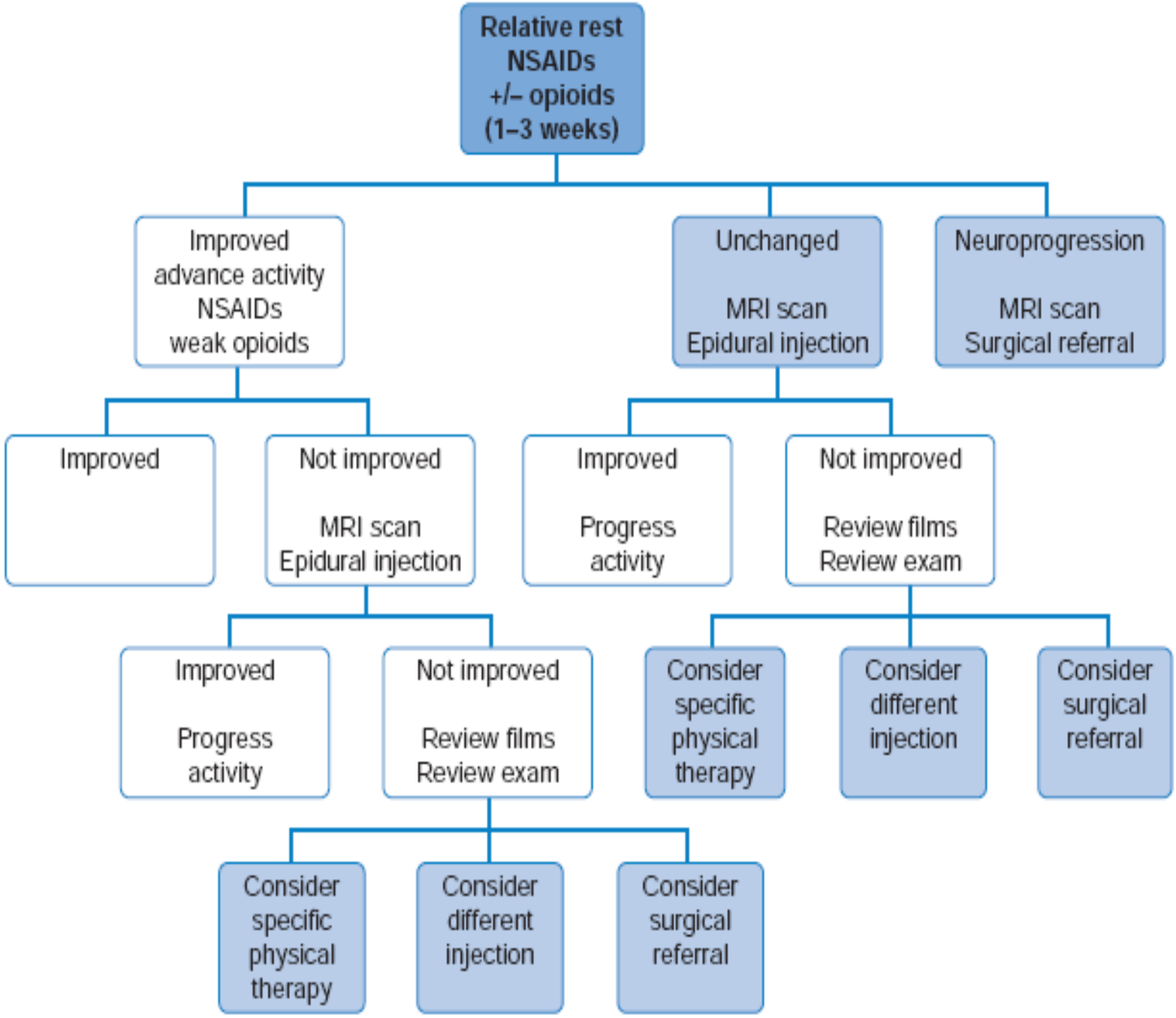
Relative rest
NSAIDs
+/– opioids
(1–3 weeks)
Improved
advance activity
NSAIDs
weak opioids
Unchanged
MRI scan
Epidural injection
Neuroprogression
MRI scan
Surgical referral
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