Guidelines in focus

Chronic nonspecific low back pain: Rehabilitation

Lombalgia inespecífica crônica: reabilitação

Brazilian Association of Physical Medicine and Rehabilitation
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Description of the evidence collection method
The present study included a review of articles published in the Medline (PubMed) and other databases, without particular time limits. The search strategy was based on structured questions according to PICO (i.e., the acrostic formed by the initials of “patient”, “intervention”, “control”, and “outcome”). The following keywords were used:

- Question 1: Low back pain AND (analgesics OR paracetamol OR acetaminophen OR dipyrone);
- Question 2: (Chronic back pain OR chronic low back pain OR chronic lumbar pain OR back pain OR lumbar pain OR low back pain OR lumbago) AND (anti-inflammatory agents, non-steroidal OR NSAIDs OR aspirin OR indomethacin OR diclofenac OR piroxicam OR tenoxicam OR meloxicam OR phenylbutazone OR ibuprofen OR naproxen OR nimesulide OR cyclooxygenase 2 Inhibitors OR valdecoxib OR celecoxib OR etoricoxib);
- Question 3: (Opioids OR narcotics OR morphine OR oxymorphone OR hydrodormorphine OR tapentadol or morphine derivatives OR oxycodone OR hydrocodone OR fentanyl OR tramadol OR codeine OR buprenorphine OR methadone OR dextropropoxyphene) AND (low back pain OR back pain OR lumbar pain);
- Question 4: (Chronic back pain OR chronic low back pain OR chronic lumbar pain OR back pain OR lumbar pain OR low back pain) AND (antidepressant OR duloxetine OR venlafaxine OR amitriptyline OR nortriptyline OR clomipramine OR imipramine OR desvenlafaxine OR fluoxetine OR sertraline OR citalopram OR mirtazapine OR paroxetine OR tricyclic antidepressant OR dual antidepressant);
- Question 5: Low back pain AND (muscle relaxants OR cyclobenzaprine OR diazepam OR benzodiazepines OR carisoprodol OR tizanidine OR tetrazepam);
- Question 6: Low Back Pain AND (hyperthermia, induced OR diathermy OR ultrasonic therapy OR shortwave therapy OR ultrasound OR infrared rays OR microwaves);
- Question 7: (Transcutaneous electric nerve stimulation OR TENS) AND low back pain;
- Question 8: (Physical exercise program OR exercise therapy OR muscle stretching exercises OR exercise movement techniques) AND (low back pain OR chronic low back pain);
- Question 9: (Acupuncture or electroacupuncture) AND (low back pain OR lumbar myofascial pain);

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• Question 10: Human engineering AND low back pain;
• Question 11: Low back pain AND exercise;
• Question 12: (Low back pain OR lumbar and chronic pain) AND acupuncture and economics.

Those keywords were combined according to the subject addressed by the question topics (P.I.C.O.). Following an analysis of the located articles, those relevant to the study questions were selected and analysed to establish evidence with which to support the guidelines described herein.

Degree of recommendation and strength of evidence
A: Experimental or observational studies with greater consistency.
B: Experimental or observational studies with lesser consistency.
C: Case reports (non-controlled studies).
D: Consensus-based opinions without critical assessments; physiological or animal model-based studies.

Objective
To provide information with regard to the treatment of non-specific chronic low-back pain.

Introduction
The term lumbago is defined as low-back pain. This disorder affects both genders and varies from sudden pain to short episodes of intense pain. Low-back pain is classified according to the patient’s symptoms and the results of diagnostic tests, thus allowing for categories with some specificity relative to the prognosis1 (A).

Low-back pain is divided into two major types, specific and non-specific2 (A), and is considered specific when it can be attributed to a cause. The causes might be intrinsic, including congenital, degenerative, inflammatory, infectious, tumour-related, or mechanical-postural conditions, or extrinsic, including imbalances between functional loads and the effort required to perform tasks at work and in everyday life. Additionally, low-back pain can be caused by postural stress and acute injuries that induce structural deterioration2 (A). In contrast, when no cause can be identified, low-back pain is classified as non-specific or idiopathic2 (A).

The recommendations suggested in the present document apply to individuals with non-specific chronic low-back pain. Persistent pain of more than 12 weeks duration is classified as chronic2 (A).

These recommendations do not apply to individuals with histories of 1 or more prolapsed intervertebral discs and concomitant neurologic symptoms; spinal surgery; infectious spondylopathies; low-back pain due to inflammation, malignant or autoimmune disease; congenital spine deformities, except for lordosis and scoliosis; compression fractures due to osteoporosis; spinal stenosis; and spondylolysis or spondylolisthesis2 (A).

Currently, rehabilitation methods cannot be determined without relating the available interventions for low-back pain to economic considerations. For this reason, evidence-based guidelines help doctors and policy-makers to identify the most cost-effective treatments in order for patients to avoid both time and financial losses9 (A).

1. What is the benefit afforded by simple analgesics to the control of non-specific chronic low-back pain, and how long should these drugs be used?

Acetaminophen, at a dose of 1,000 mg four times daily per the oral route (PO) over four weeks, is inferior to sodium salicylate at a dose of 500 mg twice daily with regard to reducing pain and disability in individuals with chronic low-back pain of more than 6 months’ duration without associated neurologic symptoms4 (A).

A combination of acetaminophen (325 mg) and tramadol (37.5 mg), given PO 4 times per day over 91 consecutive days, improved chronic low-back pain and reduced the absolute risk by 88.4% (95% confidence interval (95% CI), 78-99%), thus benefitting 1 of every 9 individuals treated with this regimen (number needed to treat (NNT) = 9; 95% CI, 5-101). The adverse events reported in the treated group included nausea (13%), sleepiness (12.4%), and constipation (11.2%). One of every 8 patients exhibited adverse events5,6 (number needed to harm (NNH) = 8; 95% CI, 5-17) (A).

Evidence has been reported regarding the occurrence of severe drug-induced hepatitis as an adverse event at doses lower than 4 g5 (A).

Recommendation
Acetaminophen, given at a dose of 500 mg 4-6 times per day PO over 4 weeks, is recommended for individuals with non-specific chronic low-back pain4 (A).

2. What is the benefit afforded by non-steroidal anti-inflammatory drugs to the treatment of non-specific chronic low-back pain?

Non-steroidal anti-inflammatory drugs (NSAIDs) are used due to their antipyretic, analgesic, and anti-inflammatory effects. Those agents inhibit the cyclooxygenase (COX) enzyme, which exists in at least 2 isoforms, COX-1 and COX-2, and thus NSAIDs are classified according to their ability to inhibit 1 of the isoforms. The latest NSAIDs are predominantly selective COX-2 inhibitors, while the older ones are less selective4 (A).

Non-selective COX inhibitors
Indomethacin, given at a dose of 25 mg thrice-daily over six weeks, was similarly effective to piroxicam at a dose of 20 mg/day for the treatment of chronic low-back pain; these drugs
improved the patients’ mobility and ability to perform tasks, in addition to affording pain relief. The adverse events more commonly reported in association with piroxicam use include gastrointestinal irritation, weariness, diarrhoea, cardiovascular risk, constipation, and tongue pain1 (A).

Piroxicam beta-cyclodextrin at a dose of 20 mg was more efficacious than the same dose of piroxicam, inducing an average variation in the pain visual analogue scale (VAS, 0-100 mm) score of 3.07 ± 1.56 versus 1.75 ± 1.48 after 28 days of treatment8 (A).

Diclofenac, given at 150 mg/day over 4 weeks, effectively alleviated pain and improved the physical capacity of individuals with chronic low-back pain9 (A).

Naproxen, given at 550 mg twice daily for 14 days, proved effective in overall pain reduction and also alleviated nocturnal and motion-associated pain in individuals with chronic low-back pain. Diflunisal, given at 50 mg twice daily for 14 days, did not induce significant differences compared to a placebo. Naproxen and diflunisal were both similar to the use of diflunisal at 500 mg twice daily for four weeks was superior to acetaminophen at 1,000 mg four times per day at reducing pain and disability in individuals with chronic low-back pain11 (A).

Ketorolac tromethamine, given at 60 mg in a single daily dose (intramuscular injection), effectively treated low-back pain and induced a > 30% reduction in pain intensity in 63% of the cases. The main adverse events observed were nausea, paraesthesia, sleepiness, dry mouth, and pain at the injection site12 (A).

Selective COX-2 inhibitors

Nimesulide at 100 mg twice-daily effectively alleviated pain in individuals with low-back pain. Its main side effects are nausea, abdominal pain, headache, and vertigo13 (A).

Highly selective COX-2 inhibitors

Etoricoxib, at daily doses of 60 and 90 mg, effectively reduced the intensity of pain, with average VAS score variations of 12.94 ± 15.5 mm and 10.29 ± 13.3 mm, respectively, after four weeks of treatment and of 10.5 ± 12.2 mm and 7.5 ± 12.70 mm, respectively, after 12 weeks of treatment. Side effects were reported in 49% of the individuals in the placebo group, 64% in the 60 mg/day etoricoxib group, and 59% in the 90 mg/day etoricoxib group; the most common side effects were headache, nausea, diarrhoea, upper airway infection, pain aggravation, lower limb swelling, fatigue, dysgeusia, urinary tract infection, dizziness, abdominal pain, epigastric discomfort, and cough14,15 (A).

The efficacy of etoricoxib 60 mg/day with regard to pain relief and functional improvement is comparable to that of high-dose diclofenac9 (150 mg/day) (A).

Rofecoxib, at a dose of 25 or 50 mg/day, effectively reduced pain intensity, with average pain VAS score variations of 13.5 and 13.81 mm, respectively, compared to placebo, after 4 weeks of treatment [95% CI; relative risk (RR) = 39%; NNT = 5; p < 0.001]. Side effects were reported by 40.8% of the individuals in the placebo group, 48.1% in the 25 mg/day rofecoxib group, and 46.3% in the 50 mg/day rofecoxib group; the most common side effects were headache (10.1%, 8.2%, and 6.6%), diarrhoea (3.5%, 7.3%, and 4.8%), and upper airway infection (4.4%, 3.9%, and 5.7%) in the placebo, 25 mg/day rofecoxib, and 50 mg/day rofecoxib groups, respectively. Overall, rofecoxib at a dose of 50 mg/day did not exhibit advantages relative to rofecoxib at 25 mg/day16 (A).

Approximately two-thirds of rofecoxib-treated individuals reported significant pain reduction after two days of treatment, and this might have been felt as soon as 2 hours after the first dose17 (A).

Rofecoxib was recalled in 2004 due to its probable association with an increased risk of myocardial infarction or stroke following long-lasting continuous use 18 (A).

Valdecoxib, at a dose of 40 mg/day, effectively reduced pain intensity, with average pain VAS score variations of 41.9 mm versus 31.1 in the placebo group after 4 weeks of treatment (95% CI; RR = 16%; NNT = 6, p < 0.001). Side effects were reported by 25% of the individuals in the placebo group and 35% in the 40 mg/day valdecoxib group; the most common side effects were headache (6% and 9%), upper airway infection (4% and 5%), abdominal pain (< 1% and 4%), dyspepsia (< 1% and 3%), dizziness (0% and 3%), and diarrhoea (5% and 1%) in the placebo and 40 mg/day valdecoxib groups, respectively18 (A).

Valdecoxib was recalled in 2005 due to its probable association with an increased risk of thrombotic cardiovascular events following continuous use 19 (A).

Celecoxib, at a dose of 200 mg, given twice daily for six weeks, reduced pain intensity by at least 30% in approximately 65% of the individuals treated (95% CI; RR = 39%; NNT = 5). The most common side effects associated with its use are headache (5.8-7.2%), nausea (4.2-5.8%), sleepiness (3-4.5%), dizziness (4%), diarrhoea (3.7%), fatigue (2.7%), constipation (2%), itching (0.3-1.2%), dry mouth (1%) and vomiting (0-0.8%). Celecoxib, at a dose of 200 mg twice daily, was more effective and had fewer side effects than tramadol chloride (weak opiate) at a dose of 50 mg four times per day19 (A).

Additionally, the combination of celecoxib (approximately 3-6 mg/kg/day) and pregabalin (approximately 1 mg/kg/day) over 4 weeks effectively treated non-specific chronic low-back pain, with an average reduction in pain intensity of 38.2%20 (A).

Combination of non-steroidal anti-inflammatory drugs + steroid + muscle relaxant

The use of NSAIDs such as tiaprofenic acid (300 mg, twice daily), piroxicam (20 mg, once or twice daily), and meloxicam (7.5 mg, once daily) in combination with a steroidal agent (betamethasone) and a muscle relaxant (tetrazepam) effectively treated individuals with non-specific chronic low-back pain, with 5-6-point reductions in the pain VAS scores (0-10). The main adverse events associated with the use of this combination were epigastric pain and moon face21 (A).
Recommendation

Non-selective COX inhibitors can effectively manage pain in individuals with chronic low-back pain. The following agents are recommended for that purpose: indomethacin at 25 mg, thrice daily over six weeks; piroxicam at 20 mg/day; diclofenac at 150 mg/day over four weeks; or naproxen at 550 mg, twice daily over 14 days. Although non-selective NSAIDs are well tolerated, they might be associated with mild-to-severe gastrointestinal complications, usually after long periods of use17-19 (A).

Selective COX-2 inhibitors such as nimesulide at a twice-daily dose of 100 mg or meloxicam at 7.5 mg/day in combination with a steroid (betamethasone) and a muscle relaxant (tetrazepam) effectively alleviated low-back pain13,21 (A).

Highly selective COX-2 inhibitors such as celecoxib, at a twice-daily dose of 200 mg over six weeks, and etoricoxib at 60 mg/day can effectively manage chronic low-back pain8,14,15,19 (A).

Although the highly selective COX-2 inhibitors exhibit a lower incidence of adverse gastrointestinal events than non-selective COX-2 inhibitors, some studies have indicated an increased cardiovascular risk. Thus, it should be noted that the length of use is a determinant of this risk, as the increase in cardiovascular events occurs after 6 months of treatment22 (C).

Increased cardiovascular risk is also associated with advanced age, arterial hypertension, previous myocardial infarction, previous cardiovascular disease, rheumatoid arthritis, chronic kidney disease, and chronic obstructive pulmonary disease, among other factors23 (C).

3. What is the benefit afforded by opiates and derivatives to individuals with non-specific low-back pain, and when should these drugs be indicated? How long should they be used?

Opiates versus placebo

Tramadol combined with paracetamol versus placebo

The combined use of tramadol and paracetamol (T/P) induced improvements in pain, disability, and the quality-of-life related to moderate-to-severe non-specific chronic low-back pain (VAS ≥ 40 mm) after 90 days of treatment, with a satisfactory safety profile24 (A).

A study using 318 patients (161 T/P, 157 placebo) at an initial dose of 1-4 tablets (37.5/325 mg per tablet), increasing to a maximum of 8 tablets/day, in four daily doses with a 10-day titration period was performed. At the final assessment, pain had decreased by ≥ 30% on a VAS (0-100). At the end of treatment (90 days), the T/P group exhibited better results compared to the placebo group, with a relative risk reduction (RRR) = 23% (95% CI, 5-41%), an absolute risk reduction (ARR) = 13.7% (95% CI, 2.9-14.5%), and a NNT = 7 (95% CI, 4-35%). That effect was also observed relative to an outcome improvement ≥ 50% on the pain VAS over the same 90 days of treatment, with a RRR = 16% (95% CI, 0-32%), an ARR = 10.6% (95% CI), and a NNT = 9 (95% CI). T/P also induced improvements in the Roland Disability Questionnaire (RDQ) scores, with a reduction of 4.1 versus 2.6 (p < 0.023) for the placebo, as well as in the quality-of-life scores as assessed by the Short-Form McGill Pain Questionnaire (SF-MPQ), with a reduction of 8.4 versus 4.8 points for the placebo (p = 0.021). The occurrence of adverse effects was higher in the T/P group, compared to the placebo group (NNT = 5; 95% CI, 4-8).

The most common side effects of tramadol included nausea (13% versus 3.2% placebo; p = 0.001), sleepiness (12.4% versus 1.3% placebo; p < 0.001), and constipation (11.2% versus 5.1% placebo; p = 0.031), while no severe adverse effects occurred during the 90 days of treatment. The average tramadol dose was 4.2 tablets/day24 (A).

Tramadol monotherapy versus tramadol and paracetamol

T/P (37.5/325 mg) exhibited the same results as tramadol alone (50 mg), but with fewer side effects over 10 days of treatment for non-specific sub-acute (10-42 days’ duration) low-back pain25 (A).

The initial treatment was 4 daily intakes, with a titration period of 3 days, up to a maximum of 8 daily intakes of P/T (300/2,600 mg) and P (400 mg). The medication was administered over a 10-day period. The patients’ global satisfaction rates regarding the treatments after 10 days were 72.5% (P/T) and 72.9% (tramadol), and the final VAS scores were 27.9 (P/T) and 24.8 (tramadol), with no significant difference between the groups. Although it did not interfere with global satisfaction, the number of side effects was significantly lower in the P/T group than in the tramadol group (30/59 (50.8%) versus 44/60 (73.3%); p = 0.019). Two side effects were particularly significant: nausea, which occurred in 8 (13.6%) cases from the P/T group versus 21 (35.0%) from the tramadol group (p < 0.012); and dizziness/vertigo, which occurred in 3 (5.1%) cases from the P/T group versus 15 (25%) from the tramadol group (p < 0.006; 95% CI; RR = 16%; NNT = 5). No severe adverse effects were reported25 (A).

Buprenorphine transdermal system monotherapy

In individuals with chronic low-back pain, regardless of the cause (nociceptive or neuropathic), the use of a buprenorphine transdermal patch effectively controlled pain for a 4-week period, with a satisfactory safety profile26 (A).

Buprenorphine transdermal system (BTDS) at doses of 5, 10, and 20 µg/h, beginning at 5 µg/h with weekly titrations of 5 µg/h or 10 µg/h until appropriate analgesia is achieved, up to a maximum dose of 20 µg/h, reduced pain after 4 weeks of use (VAS scores, 37.6 ± 20.7 mm versus 43.6 ± 21.2 mm, p = 0.0487; pain ordinal scale24 (0-5: no pain, little pain, moderate pain, severe pain, excruciating pain; 1.7 ± 0.6 versus 2.0 ± 0.7, p = 0.0358) (A).

However, the functioning and quality-of-life scores did not differ between the groups. The following adverse effects were more frequent in the BTDS group compared to the placebo group: nausea (38.4% versus 16.9%, p < 0.0330) and sleepiness: (30.1% versus 6.2%, p < 0.0010), while no statistically significant differences were found in the occurrence of constipation, vomiting, itching, and dizziness. Severe adverse effects did not occur after the use of BTDS for four weeks26 (A).
Hydromorphone extended-release monotherapy

Individuals who used opiates for moderate-to-severe non-specific chronic low-back pain achieved satisfactory pain control with hydromorphone extended-release compared to a placebo\(^2\) (A).

Initially, hydromorphone (available in 4, 8, 16, and 32-mg doses) titration was performed, beginning with an initial single daily dose equivalent to the opioid in use, according to the ratio morphine/hydromorphone = 5:1. Titration was performed by increasing the amount up to 2 doses per week, to a maximum dosage of 64 mg/day (average, 37.2 mg/day). The baseline scores of the groups on a pain numerical scale after the initial drug titration were 3.1 and 3.2 units. The hydromorphone group exhibited less pain reduction (+0.2 score units) compared to the placebo group (+1.6; \(p < 0.001\)) at the end of the 12-week period. Approximately 60.6% of the patients in the hydromorphone group achieved at least a 30% reduction in their daily pain scale scores (0-10), versus 42.5% in the placebo group \((p = 0.01)\); while 42.4% of the individuals in the hydromorphone group and 24.1% in the placebo group achieved > 50% reductions in their daily pain scale scores \((p = 0.01)\).

Statistically significant changes were also observed on a 24-point disability scale, with average variations of 0.0 versus +1.0 in the hydromorphone and placebo groups, respectively \((p < 0.005)\) at the end of the 12-week period. The main adverse effects reported were constipation, nausea, vomiting, sleepiness, and headache; significant differences were observed between the groups with regard to constipation (7.5 versus 3.7%), joint pain (6.0% versus 2.2%), and sinusitis (4.5% versus 0.7%). One severe adverse effect occurred in the placebo group (vomiting with dehydration and kidney failure), which was attributed to abstinence syndrome during the opiate discontinuance stage\(^2\) (A).

Oxymorphone extended release monotherapy versus placebo

Oxymorphone extended release (ER) effectively treated low-back pain compared to a placebo in usual opiate users\(^8\) (A).

In that study, the initial once-daily dose of OPA (ER) was equivalent to that of the opiate in use (morphine/oxymorphone = 3:1). The dose was then titrated by 10-mg increases every 3-7 days until pain control was achieved (VAS ≤ 40 mm) over 3-5 days. That stage lasted for 4 weeks, and the average titrated dose was approximately 105 mg/day. Following stabilisation of the titration stage and up to the final assessment on week 12, the placebo group exhibited an increase of 31.6 mm in their VAS (0-100) scores, versus 8.7 in the OPA ER group \((p < 0.0001)\). The most common adverse effects were nausea, constipation, headache, and sleepiness; however, there were no statistically significant differences between the groups during the 12 weeks of treatment. During the 4-week titration stage, 49% of the volunteers exhibited nausea, 29% constipation, 29% headache, 28% sleepiness, 22% vomiting, and 19% itching\(^8\) (A).

Oxymorphone extended versus oxycodone controlled release versus placebo

The use of oxymorphone or oxycodone in equivalent doses was more effective in the control of chronic low-back pain than did a placebo and exhibited the same safety profile\(^9\) (A).

In a study, 213 individuals with moderate-to-intense non-specific low-back pain who used opiates for at least three days were allocated to three groups. One group was given oxymorphone ER, another, oxycodone controlled release (CR), and the third, a placebo. During the titration stage, which lasted 7-14 days, the volunteers were given oxycodone or hydromorphone every 12 hours, initially at a dose equivalent to the opiate in use. Pain control was monitored without using morphine sulphate rescue doses > 30 mg/day. In the hydromorphone group, titration involved daily 10-mg increases per dose to a maximum dose of 110 mg (average, 79.4 mg/day); in the oxycodone group, daily 20-mg increases were given to a maximum of 220 mg (average, 155 mg/day). The treatments were then maintained for 18 days. Oxymorphone ER and oxycodone CR were superior to the placebo with regard to changes in pain intensity (VAS 0-100), with changes of −18.21 (95% CI, −25.83 to −10.58; \(p < 0.0001\)) in the oxymorphone ER group and −18.55 (95% CI, −26.12 to −10.98; \(p < 0.0001\)) in the oxycodone CR group\(^2\) (A).

In the post-titration stage, only 2 adverse effects were significantly more frequent in the opiate-treated groups, constipation \((p < 0.01)\) and sedation \((p < 0.005)\); however, no statistically significant differences were found in the final scores among the three groups, and no serious adverse effects were reported. Conversely, in the titration stage, the occurrence of adverse effects was significantly higher in the two opiate-treated groups, compared to the placebo group, albeit with no difference between the two groups. Severe adverse effects were observed at that stage, including one case of reduced respiratory rate, one case of abdominal pain an increased creatine phosphokinase (CPK) level, and low-back pain aggravation in one volunteer\(^2\) (A).

Opiates versus non-steroidal anti-inflammatory drugs

Tramadol monotherapy versus celecoxib monotherapy

Celecoxib (200 mg, twice daily) was superior to tramadol (50 mg, four times daily) for the treatment of moderate-to-severe non-specific chronic mechanical low-back pain, and also induced fewer side effects\(^10\) (A).

Two parallel studies were conducted with different samples, in which successful responders were considered those who achieved improvements ≥ 30% on the Numerical Rating Scale of pain (NSR). In the first study, 63.2% of the celecoxib group versus 49.9% of the tramadol HCl group achieved a ≥ 30% reduction in their NSR scores (0-10) after six weeks \((p < 0.001)\). The second study found successful response rates of 64.1% in the celecoxib group versus 55.1% in the tramadol HCl group after six weeks \((p < 0.008)\). Among the celecoxib group, 31.1% and 30.6% of the volunteers in studies 1 and 2 reported at least one adverse effect (most commonly, headache, 7.2% and 5.8%; nausea, 4.2% and 5.8%; and dizziness, 4.0% and 4.0%, respectively). Among the tramadol groups, 45.8% and 46.7% of the volunteers in studies 1 and 2 exhibited adverse effects, respectively (most commonly, nausea, 19.5% and 15.7%; dizziness, 14.1% and 12.6%; and sleepiness, 10.9% and 9.5%, respectively; \(p < 0.0001\)) (A).
Naproxen versus oxycodone versus oxycodone + morphine extended-release

The combined use of extended-release and short-acting opiates was more beneficial to the treatment of non-specific mechanical low-back pain compared to controlled-release opiate alone and naproxen after 16 weeks of treatment31 (B).

The following three groups of volunteers were tested for 16 weeks: naproxen at 250 mg, four times daily (N); oxycodone at 10 mg, four times daily (O); and oxycodone + morphine extended-release (O/M), titrated according to the participants’ perception of pain to a maximum dose of 200 mg of opiate/day. The average pain VAS scores at the end of the 16-week experimental stage were lower in the O/M group compared to those of the O and N groups, with values of 65.5 (N), 59.8 (O), and 54.9 (O/M) (p < 0.001). Nevertheless, the groups’ disability scores did not differ. Among the side effects, the most frequent and less intense in the O/M group, compared to the other groups31 (B).

**Recommendations**

In randomised controlled trials, the individuals with non-specific chronic low-back pain who benefitted from opiate use were those with moderate-to-severe pain, defined as VAS scores ≥ 40 mm, despite the use of analgesics and anti-inflammatory agents, including opiates24-30 (A)31 (B).

Combined tramadol and paracetamol use (37.5/325 mg), given in 4–8 doses per day over 90 days, significantly improved pain, disability, and the quality-of-life related to non-specific chronic low-back pain25 (A).

Combined with tramadol and paracetamol (37.5/325 mg), given in 4–8 doses per day over 90 days, yielded the same results as tramadol alone (50 mg), but with fewer side effects after 10 days of treatment for non-specific subacute (10-42 days) low-back pain25 (A).

In individuals with chronic low-back pain, regardless of the cause (nociceptive or neuropathic), buprenorphine transdermal patches effectively controlled pain for 4 weeks of use, with a satisfactory safety profile26 (A).

Individuals who used opiates for moderate-to-severe non-specific chronic low-back pain for less than six months achieved satisfactory pain control over a 12-week period with hydromorphone extended-release compared to a placebo27 (A).

The use of oxymorphone extended-release for 4 weeks was efficacious and safe for the treatment of low-back pain compared to a placebo in usual opiate users28 (A).

The use of oxymorphone or oxycodone at equivalent doses for 18 days more effectively controlled of non-specific chronic low-back pain and induced fewer side effects30 (A).

Celecoxib use (200 mg, twice per day) for 6 weeks was superior to tramadol (50 mg, 4 times per day) for the treatment of moderate-to-severe non-specific chronic low-back pain and induced fewer side effects30 (A).

The combined use of long-release and short-acting opiates was more beneficial for the treatment of non-specific mechanical low-back pain compared to controlled-release opiate and naproxen during a 16-week treatment period31 (B).

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**4. Is antidepressant use efficacious for the treatment of non-specific chronic low-back pain?**

Duloxetine, a first-line agent32-35 (A) was efficacious at a dose of 60 mg/day for up to 12 weeks; this agent reduced the pain VAS scores by an average of 2-3 points. Additionally, duloxetine increased the frequency of an improvement in pain of ≥ 30% to 56% of individuals and of an improvement of ≥ 50% in 47% of individuals. Duloxetine at a dose of 12.0 mg/day exhibited the same beneficial effects for longer than three months32,34 (A).

All recommended doses of duloxetine induced variable and individual improvements in functioning and quality-of-life for > 3 months. Approximately 64% of the individuals who used duloxetine at doses of 20 mg/day, 36-67% at doses of 60 mg/day, and 73% at doses of 120 mg/day reported adverse events (95% CI; RR = 32%; NNT = 7; p < 0.001). Severe side effects that occurred with duloxetine use included asthma, myocardial infarction, dyspnoea, chest pain, transient ischaemic attack (TIA), toxic myopathy, muscle weakness, and vertigo; these were reported by 2.6% of the users. When used at a dose of 60 mg/day, the most common adverse effects were nausea in 7.3-22% of users; sleeplessness in 7.3-9%; headache in 4.8-10%, dry mouth in 9.7-11%, obstipation, in 2.4-9%; sleepiness in 7%, diarrhea in 2.4-11%; fatigue in 9%; and dizziness in 2.4-10%32-35 (A).

The results observed with escitalopram at a dose of 20 mg/day are similar to those observed with duloxetine. The side effects associated with both drugs appeared in 36% of the users, and the most common ones were dry mouth in 10.2% of users, sleeplessness in 7.6%, nausea in 5.1%, dizziness in 5.1%, headache in 2.5%, lack of appetite, and obstipation. The NNT could not be calculated because the pain intensity scale scores (a Likert scale ranging from 0-10), which were the primary outcome, were described in a general manner, such that only the average pain reductions in the duloxetine and escitalopram groups were reported35 (6.4 (1.4) and 6.3 (1.5), respectively) (A).

Nortriptyline, at a progressive dose of 25-100 mg/day, was efficacious at least 8 weeks, inducing an average reduction in pain of 22%. Its side effects included dry mouth in 82.1% of the individuals, sleeplessness in 71.4%, sedation in 60.7%, postural hypotension in 60.7%, constipation in 42.9%, sweating in 32.1%, and palpitations in 10.7%36 (A).

One study compared maprotiline, a norepinephrine reuptake inhibitor, and paroxetine, a serotonin reuptake inhibitor, for the improvement of non-specific chronic low-back pain. The authors concluded that maprotiline was efficacious at a maximum dose of 150 mg/day, as it reduced pain by 45% compared to 27% with placebo (p = 0.023) and 26% with paroxetine (30 mg/day over 8 weeks; p = 0.013). Side effects were manifested by 90% of the volunteers, the most frequent ones being dry mouth in 85%, sedation in 80%, sleeplessness in 70%, orthostatic hypotension in 50%, constipation in 50%, palpitations in 10%, and sweating in 5%37 (A).

Bupropion at a dose of 300 mg/day was ineffective, as were other selective serotonin reuptake inhibitors such as paroxetine in doses up to 30 mg/day36-38 (CI = 95%; RR = 32%, NNT = 17; p = 0.013) (A).
The main reason for patients to discontinue treatment was the occurrence of side effects; these were proportional to the dose used, as were the beneficial effects\textsuperscript{32-37} (A).

**Recommendation**

Antidepressants play a relevant role in the management of non-specific low-back pain, albeit with variable efficacy. Agents with associated adrenergic effects, such as tricyclic and dual antidepressants, exhibited better results when compared to selective serotonin reuptake inhibitors, most of which exhibited insufficient and doubtful results\textsuperscript{35-37} (A).

Duloxetine at doses of 20 or 60 mg/day over a 12-week period is recommended as a first-choice therapy\textsuperscript{32-35} (A).

Escitalopram at a dose of 20 mg/day for up to 12 weeks is a possible alternative because it induced results similar to those observed with duloxetine\textsuperscript{35} (A).

The use of these agents for > 3 months is not recommended, as the occurrence of side effects was observed after that period in all studies\textsuperscript{35-37} (A).

5. **What are the advantages of a combination of analgesics and muscle relaxants?**

Muscle relaxants represent an additional option for the treatment of non-specific chronic low-back pain and comprise antispastic and antispasmodic agents. The use of antispasmodic agents presents specific indications for the treatment of muscle disorders, and these agents are subdivided into benzodiazepines and non-benzodiazepines\textsuperscript{39} (A).

Several muscle relaxants are available, including carisoprodol, cyclobenzaprine, orphenadrine, and tizanidine among the non-benzodiazepines and diazepam and tetracepam among the benzodiazepines\textsuperscript{39} (A). With diazepam, muscle relaxation occurs as a rebound effect of central sedation\textsuperscript{39} (A).

Muscle relaxants exhibited better results than a placebo relative to an improvement in pain by the 8th day of treatment. Tizanidine (2 mg/day + diclofenac 50 mg/day over 8 days; p < 0.05) and cyclobenzaprine (5 mg/day over 7-10 days, p = 0.003) are the most widely investigated muscle relaxants for chronic low-back pain\textsuperscript{40,41} (B).

Tizanidine (2 mg/day + diclofenac 50 mg/days over 8 days; p < 0.05) and baclofen (30-80 mg/day over 14 days, p < 0.05) induced increased postural hypotension and increased the risk of falling in older adults; therefore, these agents must be used cautiously\textsuperscript{40} (B).

Cyclobenzaprine is a weak tricyclic antidepressant used as a muscle relaxant\textsuperscript{39} (A).

Nevertheless, no evidence indicates the superiority of any muscle relaxant over another for the treatment of non-specific chronic low-back pain. Two studies reported the superiority of tetracepam at a thrice-daily dose of 50 mg for 10-14 days over a placebo for non-specific chronic low-back pain, with a significant improvement in pain on days 7 and 8\textsuperscript{42} (RR = 2.04, 95% CI; p < 0.001) (B). However, that drug is no longer used as muscle relaxant, due to its sedative effects and the potential risk of addiction\textsuperscript{42} (B).

The adverse events associated with muscle relaxants include sedation, sleepiness, dizziness, blurred vision, nausea, and vomiting. Carisoprodol exhibited the potential for mental and physical addiction, which was associated with its active metabolite\textsuperscript{42} (RR = 2.04, 95% CI; p < 0.001) (B).

Cyclobenzaprine is contraindicated in cases with increased intraocular pressure or glaucoma. Caution is required in individuals with heart disease because, due to its tricyclic structure, this agent might induce severe arrhythmias and aggravate congestive heart conditions and the myocardial function in patients with infarction\textsuperscript{42} (B).

A review recommended NSAIDs and antidepressants as the first choices for the treatment of non-specific chronic low-back pain, due to the lack of adequate data supporting the indication of muscle relaxants\textsuperscript{40} (B).

The American Pain Society and the American College of Physicians do not recommend the use of muscle relaxants as first-choice agents. Instead, drugs such as acetaminophen and NSAIDs are recommended.

**Recommendation**

Muscle relaxants are not recommended as first-choice agents for the treatment of non-specific chronic low-back pain due to the lack of sound data in the medical literature regarding their beneficial effects on pain compared to their side effects.

**Non-pharmacological conservative treatments**

6. **What physical means are used?**

**Ultrasound**

Ultrasound (US) is a deep-heat modality that uses high-frequency acoustic vibrations above the human auditory range (above 17,000 Hz). The therapeutic frequencies vary from 0.8-1 MHz at a 0.15-cm wavelength\textsuperscript{13} (B).

The influence of US was investigated with regard to pain, trunk muscle strength, disability, walking performance, resistance, mobility, quality-of-life, and depression in patients with non-specific chronic low-back pain. That study compared the following groups of volunteers: group 1 (n = 20), who were subjected to electrical stimulation for 15 minutes with 4 electrodes on L2-L4 at 50 Hz and 50 ms, along with 45 minutes of supervised exercise; group 2 (n = 19), who were subjected to US for 10 minutes at a 1-MHz frequency, 1 W/cm\textsuperscript{2} of potency, and 5 cm\textsuperscript{2} of transducer area in slow circular motions on the lumbar paravertebral area, along with 45 minutes of supervised exercise; and group 3 (n = 20), who were subjected to the same exercise programme as the other 2 groups, with no further intervention. The interventions were applied to all 3 groups thrice weekly for 6 weeks. The results found a lack of statistically significant differences among the groups, as all of them exhibited improvements in pain,
functional capacity, and muscle strength, as well as positive depression and quality-of-life scores \(^{46} (p < 0.05) \) (B).

However, in that study, the quality-of-life scores from the Short Form-36 (SF-36) questionnaire showed improvements at the last assessment (after 6 weeks) from 44 (44-88) to 88 (66-99) in group 2 compared to group 3, the controls, which showed score improvements from 52 (44-88) to 77 \(^{49} (65-100; p = 0.001) \) (B).

In another study, group 1 was subjected to aerobic exercise and a home exercise programme, and exhibited statistically significant improvements in pain severity at a 1-month follow-up compared to the pre-treatment levels (VAS 0-100 mm = 57.05 ± 2.5 before intervention; 34.1 ± 27.6 at the 1-month assessment; \( p = 0.002 \)). Group 2 was subjected to surface warming of the lumbar region with hot packs for 15 minutes; continuous US at a 1-MHz frequency, 1.5-W/cm\(^2\) intensity, and a 5-cm transducer area in slow circular motions over the paravertebral area for 10 minutes; transcutaneous electrical nerve stimulation (TENS; 30-40 Hz via the conventional method) for 15 minutes, and conventional physical therapy thrice weekly for 6 weeks. That treatment regimen induced improvements in pain severity (VAS = 61.2 ± 20.5 before intervention versus 28.8 ± 28.1 at the 1-month assessment; \( p = 0.001 \)). Group 3 was subjected to home exercise alone and exhibited improvements in pain severity, with VAS scores of 56.0 ± 19.9 before intervention and 33.6 ± 24.3 at the 1-month assessment (\( p = 0.006 \)). Conclusively, no significant differences occurred among the 3 groups relative to pain intensity, disability, and the psychological state before and after treatment. Nevertheless, the group subjected to US and TENS exhibited a 47% greater improvement (\( p = 0.002 \)) compared to the other 2 groups at the 1-month assessment \(^{49} (B)\).

**Recommendation**

The use of continuous US is recommended at a 1-MHz frequency, 1-W/cm\(^2\) potency, and 5-cm\(^2\) transducer area, administered by performing slow circular motions on the lumbar paravertebral region for 10 minutes, together with a supervised exercise programme that focuses on the abdominal and lumbar muscles, is preceded by a 5-minute warm-up, and is followed by 5 minutes of stretching, thrice weekly for 6 weeks as a treatment for non-specific chronic low-back pain \(^{44,45} (B)\).

US is contraindicated in cases with the risk of gaseous fluid cavitation, such as in the eyeball and pregnant uterus, as well as on plastic endoprosthesis components, methacrylate, and the heart, in which it might cause turbulence in addition to cavitation. US is further contraindicated on epiphyseal plates, areas with damaged skin, patients with cognitive and intellectual deficit, as well as on tumours due to the risk of proliferation. US should be avoided on anaesthetic areas and joint facets close to regions where the spinal cord is exposed, as in laminectomy \(^{45} (B)\).

**Thermal water**

A randomised controlled double-blind study was conducted by Ágata Kulisch et al. that included 71 individuals with non-specific chronic low-back pain from both genders, aged 25-70 years. The participants were subjected to 20-minute daily treatment sessions with medicinal water or tap water, both at a temperature of 34 °C, on 21 occasions, and both groups underwent additional adjunctive electrotherapy. The study parameters were assessed at the baseline, immediately after treatment, and after 15 weeks; pain was assessed according to a VAS \(^{46} (0-100 \text{ mm}) \) (B).

After treatment, there were significant improvements in all parameters in the thermal water group. These improvements remained evident after 15 weeks. A comparison between the intervention and control groups revealed significant differences in the VAS scores. At the end of 3 weeks of treatment, the patients treated with thermal water exhibited significant therapeutic responses, manifested by the VAS scores, when compared to the control group (\(-14.8 \ (95\% \ CI, -18.9 \to -10.7) \) versus \(-8.2 \ (95\% \ CI, -14.1 \to -2.4), p < 0.05\)). Fifteen weeks after the end of treatment, the difference in the VAS score relative to the baseline was significantly higher in the group treated with thermal water (\(-17.6 \ (95\% \ CI, -22.9 \to -12.4) \) versus \(-5.246 \ (95\% \ CI, -13.9 \to 3.4), p < 0.05) \) (B).

**Recommendation**

Immersion in medicinal or tap water at a temperature of 34 °C for 20 minutes/day over a 3-week period is recommended for the treatment of non-specific chronic low-back pain.

**Shortwave diathermy**

A prospective randomised study of 97 individuals from both genders, aged 20-80 years old, with complaints of chronic low-back pain applied a shortwave diathermy protocol. The individuals in the intervention group (group A) underwent shortwave diathermy on the lumbar region thrice weekly for 15 minutes over a 6-week period and were prescribed meloxicam at a dose of 15 mg/day, PO \(^{47} (B)\).

A significant difference was observed between the groups by the end of the third week, but in most volunteers, improvements could only be detected at the end of week 6; these manifested as score reductions on the scales used, including a VAS (combined total score range, 0-34). The pre-treatment combined scores were 20.44 ± 3.02 for group A and 20.10 ± 3.51 for group B. At the end of week 6, the scores were 6.44 ± 3.06 for group A and 13.38 ± 3.10 for group B \(^{47} (p = 0) \) (B).

**Recommendation**

Shortwave diathermy is recommended on the lumbar region thrice-weekly for 15 minutes per session over a 6-week period for the treatment of non-specific chronic low-back pain \(^{47} (B)\).

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7. **What is the role of electrical stimulation in non-specific chronic low-back pain?**

The main electrical stimulation modalities used to induce analgesia are TENS and percutaneous electrical nerve stimulation \(^{48} \) (PENS) (A).
TENS can be applied at high frequencies (= 50 HZ) and with sub-threshold intensities to induce muscle contraction, which is known as sensory stimulation, or at low frequencies (< 10 HZ) and intensities fit to induce muscle contraction\(^\text{46}\) (A).

PENS comprises a combination of acupuncture and electrical stimulation\(^\text{48}\) (A). It is believed that PENS should be considered an analgesic modality that facilitates the exercise performance by individuals with non-specific chronic low-back pain\(^\text{49}\) (A).

PENS is contraindicated in pacemaker users, except when authorised by a cardiologist, as well as in individuals with epilepsy, heart problems, or cognitive impairments. Its use should be avoided during the first 3 months of pregnancy, especially on the lumbar and abdominal areas. Individuals with stroke sequelae should not undergo PENS on the face and neck\(^\text{49}\) (A).

A literature review of original articles published in English that reported prospective randomised, controlled, double-blinded studies observed a substantial superiority of analgesic interventions, based on the use of electrical stimulation over placebo or multimodal exercise programmes\(^\text{50}\) (A).

One prospective study randomly allocated 41 individuals with chronic low-back pain to 2 groups, group 1 (n = 21), which was subjected to a programme that included TENS and exercise, and group 2 (n = 20), which was subjected to exercise only and considered the control. Both outpatient programmes involved 3 sessions per week over an 8-week period\(^\text{50}\) (A).

Electrical stimulation was applied for 15 minutes with the patient in a prone position and for 15 minutes in a supine position. In the prone position, the electrodes were placed from L2 to L4 along the motor points for the paraspinal muscles and in the supine position, on the motor points for the abdominal external oblique muscles. A biphasic symmetrical wave was applied at a frequency of 50 Hz and a phase speed of 50 ms. The current intensity was adjusted for each individual volunteer until apparent muscle contraction was achieved (70-120 mA). The stimulus was applied to induce 10 seconds of contraction and 10 seconds of relaxation\(^\text{50}\) (A).

All pain parameters exhibited significant improvements in both groups after treatment, albeit these were greater in the intervention group (p < 0.001). The Oswestry Disability Questionnaire (ODQ) scores measured in the group 1 were 36.66 ± 9.53 at baseline and 6.57 ± 5.53 at the end of treatment. The corresponding scores in group 2 were 37.22 ± 17.04 and 19.22 ± 13.99 (p = 0.001). For the Pain Disability Index (PDI), the group 1 scores decreased from 19 (10-45) to 4 (0-23), while those of group 2 decreased from 22 (12-64) to 9.5\(^\text{50}\) (0-48) (p < 0.001) (A).

Another randomised clinical trial selected 200 individuals from both genders who were older than 65 years old and had chronic low-back pain to assess the efficacy of PENS, with or without general conditioning and aerobic exercise (GCAE), for reducing pain and improving physical functioning. The participants were randomised to receive either PENS, control-PENS (brief electrical stimulation to control for treatment expectancy), PENS + GCAE, control-PENS + GCAE twice weekly for 6 weeks. The needles in the intervention groups were placed bilaterally at levels corresponding to T12, L3, L5, and S2, as well as the motor point of the piriformis muscle. Electrical stimulation was applied for 30 minutes only at the T12-level. The GCAE programme was performed onsite for 60 minutes and included both general conditioning (strength and flexibility) and aerobic components. The home exercise programme comprised flexibility exercises and graded walking as the aerobic component. All 4 groups exhibited significant reductions in pain (range −2.3 to −4.1 on the McGill Pain Questionnaire short form) that were sustained at 6 months. The GCAE groups experienced significantly fewer fear-avoidance beliefs immediately post-intervention and at 6 months than did the non-GCAE groups\(^\text{51}\) (A).

A comparison of the various analgesic modalities showed that PENS was superior to TENS, while the latter was comparable to other therapies such as deep diathermy via US\(^\text{51}\) (A).

### Transcutaneous electric nerve stimulation versus ultrasound

One study compared the effects of electrical stimulation (ES) and US on pain, trunk muscle strength, disability, walking performance, spinal mobility, quality-of-life, and depression in individuals with non-specific chronic low-back pain. A total of 59 volunteers were randomly allocated to 3 groups: group 1 (n = 20), which underwent a programme comprising ES and exercise; group 2 (n = 19), which underwent US and exercise treatment; and group 3 (n = 19), which acted as the control and performed some conventional exercises. All the programmes were conducted thrice weekly for 6 weeks. The results indicated improvements in quality-of-life and pain, as assessed by SF-36 and by comparing the results at the beginning and end of the intervention. An intergroup comparison found similar improvements (p < 0.001) in the groups that received ES and US\(^\text{54}\) (SF-36 scores increased from 49 (11-77) to 88 (55-100) and from 44 (44-88) to 88 (66-99), respectively) (B).

Another study randomised 60 individuals to 3 groups. Group 1 performed an aerobic programme and home exercise, group 2 was subjected to physical therapy (hot packs, US, and TENS) and home exercise, and group 3 performed home exercise only. All 3 approaches reduced pain and increased the aerobic capacity; however, the combination of physical therapy and home exercise proved more effective when psychological features were considered\(^\text{52}\) (A).

### Transcutaneous electric nerve stimulation versus massage

The first appropriately randomised clinical trials compared TENS and massage via negative pressure. A gentle massage was produced by placing 4 suction cups on the skin; these were kept in place by mild negative pressure within each cup. A specially constructed apparatus produced slowly varying changes in pressure so that a constant, gentle massage was applied to the skin. Electrical stimulation was applied by an active electrode that was placed securely at the centre of the painful area of the back, and a second electrode was placed on the lateral aspect of a thigh. The output frequency was set at 4-8 Hz, and the current intensity was raised until the patient reported that it was unpleasant. The intensity was
then reduced to a level that the patient reported tolerable. Adjustments to the intensity were made during the session to maintain the same tolerable level. The intervention was applied twice weekly for 30 minutes per session until improvement or the completion of 20 sessions. All patients received the same standard exercises for low-back pain at the conclusion of each stimulation session. The results showed improvements in pain > 50% in 85% of the volunteers subjected to TENS versus 38% of the participants subjected to massage53 (A).

**Transcutaneous electric nerve stimulation versus percutaneous electrical nerve stimulation**

One study sought to establish the number of PENS sessions needed to alleviate chronic low-back pain and for how long analgesia is sustained. Individuals with peak pain intensities < 40 on a VAS (0-100) were subjected to twice-weekly interventions for eight weeks. Group A (n = 18) received PENS for eight weeks, group B (n = 17) received PENS for the first four weeks and TENS for the second four weeks, and group C (n = 18) received TENS for eight weeks. The pain level, degree of physical impairment, and daily NSAID intake were assessed before and 3 days after the first treatment, during weeks 2, 4, and 8 of treatment, and at 1 and 2 months after the sessions54 (A).

During PENS, the pain level decreased significantly after week 2 in group A (VAS score: from 55 ± 11 to 37 ± 10) and group B (from 56 ± 9 to 36 ± 13) (p < 0.05 or 0.01), and physical impairments and required NSAID intake decreased significantly after week 4 in group A (p < 0.05 or 0.01), but only at week 8 (p < 0.05 or 0.01) in group B. These effects were sustained until the 1-month follow-up (p < 0.01) in group A, but not in group B, while they were not observed at the 2-month follow-up even in group A. In group C, the pain level decreased significantly only at week 854 (p < 0.05) (A).

**Recommendation**

Electrical stimulation and the other physical means are thought to facilitate analgesia in the affected individuals in order to achieve physical rehabilitation through exercise programmes designed for non-specific chronic low-back pain; these programmes not only induce gains in but also maintain the range of motion by stimulating flexibility and strengthening the muscles that stabilise the trunk and the abdomen, in addition to the gluteal muscles.

Both TENS and PENS are recommended, albeit with some restrictions derived from their contraindications and side effects.

TENS involves the application of a biphasic symmetrical wave at a 50-Hz frequency and a 50-ms phase. The current intensity must be established on an individual basis until apparent muscle contraction is achieved (60-130 mA). Stimulation must be applied to induce contraction for 10 seconds and relaxation for 10 seconds55-57 (B). Bilateral placement of the electrodes at the level of L2 to L4 on the spinal erectors motor points51 is recommended (A).

The advantages of TENS include the possibility of home application without the need of a trained professional to place the electrodes, as the patient can be sufficiently trained and can understand the instructions given to ensure appropriate use, provided contraindications do not apply.

For PENS, it is recommended to bilaterally place the needles at the levels corresponding to T12, L3, L5, S2, and at the piriformis muscle motor point; stimulation must be applied for 30 minutes at T12 and for 15 minutes at the other sites twice weekly for eight weeks. Additionally, a 60-minute exercise programme should be indicated with the intent to promote strength and flexibility, along with an aerobic component.

It is worth observing that the use of TENS and PENS without a specific exercise programme does not suffice to maintain analgesia over a long period of time because those therapies merely facilitate the performance of specific rehabilitation exercises51 (A)58 (B).

**8. What is the benefit of exercise in the treatment of non-specific chronic low-back pain?**

Several models have been put forth for the treatment of non-specific chronic low-back pain, but none have proved more efficacious than the others59-63 (B).

Exercise programmes are used to provide relief to individuals with non-specific chronic low-back pain. Such programmes usually involve an aerobic component, strengthening and stretching, and orientation59-63 (B).

A general exercise program that included stretching, strengthening, and a warm-up induced pain reduction, and the positive effects were preserved for 5 years59 (p = 0.01) (B).

Programmes such as the back school induced improvements in pain intensity, functional capacity, and lumbar spine mobility compared to the controls60 (B).

Nevertheless, comparisons of various approaches such as intensive training, back school, and combinations of behavioural and physical therapy did not find significant differences61 (B).

A motor control exercise programme induced significant improvements when compared to general exercise and spinal manipulation/mobilisation after 8 weeks of treatment62 (B).

A study assessed rehabilitation programmes, including resistance training, and found that these exercise modalities improved musculoskeletal health, pain, and disability after 8 weeks and were safe and effective for the rehabilitation of individuals with non-specific chronic low-back pain63 (B).

One study of a 10-station exercise class that involved aerobic exercises, spinal stabilisation exercises, and manual therapy (spinal mobilisations) for 30 minutes per session over an 8-week period observed improvements in pain at 6 and 12-month assessments. According to some studies, such modalities are more beneficial when performed as 1-1 to 1 treatments than in a group. The parameters assessed in the abovementioned study included lumbar flexion, whereby while standing, the volunteers were asked to slide their hands down the front of their legs until they experienced the first point of pain or the first increase in pain. The distance from the end of the middle finger to the floor was measured with a standard tape measure, and the volunteers were then
requested to mark the intensity of pain on a pain VAS, where the left side represented no pain and the right side represented the worst pain imaginable. Additionally, the study measured lumbar extension, which was measured similarly with the volunteers sliding their hands down the posterior aspect of their legs; left and right-side flexion, which were measured in the same manner with the volunteers sliding their hands down the lateral aspects of their left and right legs, respectively; and the straight leg raise (SLR), while in a supine position, the ranges of left and right SLR were measured by placing an inclinometer (Isomed, Portland, OR) on the tibial tuberosity; the leg was passively elevated, and the angle at the first point of pain or first increase in pain was read from the inclinometer; the volunteers then marked the intensity of pain on the VAS (pain) line.

At 12 months after treatment, there were mean increases of 8.5 cm in the flexion range, 2 cm in the extension range, 2.5 cm in the left-side flexion range, 2.7 cm in the right-side flexion range, 12.6° in the left SLR range, and 10.5° in the right SLR range in the exercise group. The corresponding results for the individual treatment group were 12.5 cm (flexion), 1.5 cm (extension), 2.5 cm (left-side flexion), 1.3 cm (right-side flexion), 12.1° (left SLR), and 12.2° (right SLR); except for the left and right side flexion values, all results were superior in the individual group.

At 12 months, statistically significant decreases in the VAS (pain) scores were observed for all movements except left side flexion in the exercise group. At 12 months, 21 of 33 subjects (63.6%) who had participated in the exercise group felt that they had improved, and 12 of 33 (36.4%) felt that they remained the same as at the beginning of the study. The mean percentage improvement at 12 months was 62.9% (range, 20-100%). The corresponding data for the individual treatment group at 12 months were that 75.8% of the volunteers improved (range, 12-95%), while 7 of 29 (24.1%) remained the same.64 (B).

**Recommendation**

Exercise is indicated for the treatment of non-specific chronic low-back pain. However, several types of exercise have been reported in the literature, while most studies in fact combined with physical therapy to physical therapy alone in individuals treated with a combination of electroacupuncture and usual care, which included analgesics, NSAIDs, and physical therapy without TENS, compared to the group that continued their usual care only66 (B). Electroacupuncture was performed at 4-6 Hz with a pulse duration of 0.5 ms twice weekly for five weeks, for a total of 10 sessions. DeQi responses were achieved at all points, and 10-14 needles were used per session on acupoints BL23, BL24, BL25, BL28, Du3, and Du4, with up to 4 additional needles in cases with radiating leg pain on the following acupoints: BL 36, 54, 37, 40, GB 30, and 31. Each session lasted for 20 minutes. The group treated with acupuncture and usual care exhibited the following results compared to the group that continued their usual care only (control group): a decrease in the Roland Disability Questionnaire (RDQ; 0-18) score of 4.1 ± 3.9 at week 6 versus 0.7 ± 2.8 (control group; p = 0.001). This effect was maintained for up to 4 weeks after treatment (week 9), with a decrease in the RDQ score of 3.5 ± 4.4 from baseline compared to 0.43 ± 2.7 for the control group (p < 0.007). There was no significant change relative to the pain VAS (0-10) in the acupuncture group at week 6; however, by week 9, the individuals treated with acupuncture showed decreased pain scores (−0.2 ± 1.3) compared to the control group, which had a pain score increase of 0.7 ± 1.1; this difference between the groups was statistically significant66 (p < 0.02) (B).

The greatest benefit induced by the use of acupuncture combined with conservative orthopaedic treatments (COT) such as physical therapy, exercise, infrared heat therapy, back school, and mud packs compared to COT alone manifested 6 months after the onset of treatment, or 3 months after the last session65 (A).

One study performed 12 sessions of acupuncture, thrice weekly, and the needles were placed on the following points: BL 23, 25, GB 30, BL 40, 60, and GB 34; additionally, up to 4 “AhShi points” in the lumbar area were needled. Needle manipulation was mild to strong. DeQi was achieved for 30 minutes. Treatment with acupuncture + COT achieved a success rate (> 50% score reduction on a pain VAS from 0-100) of 67% (95% CI, 62-88%) at six months after the onset of treatment (three months after the last session) versus 14% (95% CI, 4-30%, p < 0.001) of those treated with COT alone66 (A).

One study compared traditional body and ear-acupuncture combined with physical therapy to physical therapy alone in individuals with non-specific mechanical low-back pain for at least 6 months. All volunteers received 26 sessions (30 minutes each) of standardised active physical therapy (PT) for 12 weeks, and the acupuncture group (AG) additionally received 20 sessions of combined traditional body and ear-acupuncture five times per week during the first two weeks of treatment and once per week for the next ten weeks. Acupuncture was found to be superior to the control treatment (CG) with regard to pain intensity and disability at the end of treatment, and this benefit was maintained at the 9-month follow-up66 (B). The DeQi sensation was elicited and the needles (0.3 × 40 mm) were left in place for 10-30 minutes. Twenty needles were used in body-acupuncture, at nine bilateral and two single points: BL23, BL25, BL31, BL32, BL40, BL60, GB34, SP6, GV3, and GV4, as well as six unilateral ear-points (os sacrum (38), parasympathicus (51), nervus ischiadicus in the group treated with a combination of electroacupuncture and usual care, which included analgesics, NSAIDs, and physical therapy without TENS, compared to the group that continued their usual care only66 (B).
(52), lumbosacrum (54), shenmen (55), and kidney (95)). The combination of acupuncture and PT (AG) was superior to PT alone (CG) after 12 weeks. On the last day of treatment, the change in the pain VAS (1-10) scores of the AG versus the CG group was −1.7 (95% CI −2.71 to −0.62; p < 0.000), and the change in the disability score (PDI, 0-70) was −11.3 (95% CI −17.01 to −5.44, p < 0.000). However, only the improvement in disability was maintained at the 9-month follow up, whereby the difference in within-group PDI score changes of the AG versus the CG group was −6.86 (95% CI, −12.57 to −0.96; p < 0.016) (B).

True versus sham acupuncture

There is controversy regarding the efficacy of true acupuncture (deep insertion of needles into acupoints) compared to sham acupuncture (a more superficial insertion of needles in sites distant from acupoints). Some studies found benefits of true versus sham acupuncture (A), while others found both techniques to be equivalent (B).

Nevertheless, it has been proven that acupuncture with sham insertion surface is not an inert procedure.

A study conducted by Brinkhaus et al. in 2006 with 298 volunteers found no benefit of deep acupuncture when compared to superficial (subcutaneous) acupuncture when needles were placed into the acupoints routinely used for chronic low-back pain at weeks 8, 26, and 52 (A). The volunteers were subjected to 12 sessions lasting 30 minutes each for 8 weeks, in which the needles (8) were bilaterally placed into at least 4 of the following points: BL20 to 34, BL 50 to 54, GB 30, and GV 3 to 5, and at least 2 distant points among the following: SI3, BL40, BL60, BL62, BL24, KI3, KI7, GB31, GB34, GB34, and GV14, and GV20. In the group that received subcutaneous acupuncture, 6-10 predefined non-acupuncture points were used. The lack of significance between the results of both groups was maintained at weeks 26 and 50 (A).

Another study found a benefit with the use of intramuscular versus subcutaneous acupuncture for the treatment of low-back pain (A). The selected points were Extra 19, VG6, GB34, BL54, BL62, and an additional four AhShi points, including needle stimulation, which comprised rotation in both directions at 2 Hz for 20 seconds during the first minute, and then every 5 minutes until the end of the sessions; the sessions lasted for 20 minutes and were performed eight times during one month. At the end of the treatment, pain reduction was greater in the group with deep acupuncture, although this difference was not significant. However, at the 3-month follow-up, a statistically significant difference existed between the groups, with better results in the group subjected to deep acupuncture, as determined by McGill Pain Questionnaire scores of 7.5 (± 12.94) versus 18 (± 17.16) (A).

One study of 186 volunteers found a benefit with the combined use of true acupuncture and conservative orthopaedic treatments (COT) such as physical therapy, exercise, infrared heat therapy, back school, and mud packs, compared with combined superficial acupuncture and COT, at a 3-month follow-up (A). The acupuncture involved 12 30-minute sessions, distributed thrice weekly, and the following points were needled: BL23, BL25, GB30, BL40, BL60, GB34, and up to four additional AhShi points in the lumbar region. The needle manipulation was mild to strong, and DeQi was achieved in all cases. The results were as follows: the success rate (> 50% reduction of scores on a pain VAS scale of 0-100 at three months after the end of treatment) was 77% (95% CI, 62-88%) in the group subjected to acupuncture, and 29% (95% CI, 16-46%) in the sham-acupuncture group; this difference was significant (p < 0.001). Immediately after the end of the treatment, the success rates were 65% in the acupuncture group (95% CI, 51-77%) and 34% in the sham-acupuncture group (95% CI, 22-49%). The difference between true and sham acupuncture at the 3-month follow-up was significant (p < 0.02) (A).

No difference in benefit was found between true and sham (superficial) acupuncture for the treatment of chronic low-back pain at 9 months after treatment (B).

True acupuncture versus placebo procedure versus transcutaneous electrical nerve stimulation

When considering the quality difference between the two studies mentioned in this document it can be said that acupuncture has greater efficacy versus TENS and placebo; in other words, the quality was higher in one of them (A) and in the other study, this was not stated (B).

One study that compared manual acupuncture or electroacupuncture to active placebo (TENS) for the treatment of non-specific mechanical low-back pain observed benefits with the investigated treatments. A total of 50 volunteers were allocated to three groups; two groups included the use of acupuncture, and one included inert TENS once weekly for eight weeks. In the acupuncture group, 14 points were used per session, including BL24, BL25, BL26, BL40, BL57, BL60, LI4, LI11, and EXJiajia. Each session lasted for 20 minutes, and the needles were manipulated until DeQi was achieved three times in the session. The same technique and points were used in the electroacupuncture group, which further included the application of a 2–15-Hz current at 2.5-second cycles on four needles, specifically one pair per side, again for 20 minutes. One, three, and six months after the end of treatment, greater benefits were observed in both groups treated with acupuncture compared to the placebo group (TENS), with VAS (0-100) score improvements of 13%, 23.5%, and 38.5%, respectively, in the acupuncture groups, compared to score declines of 28%, 24%, and 16%, respectively, in the placebo (TENS) group (p < 0.000, p < 0.001, and p < 0.001, respectively) (A).

Another study of 46 patients found no significant difference between the acupuncture and placebo groups (TENS), although this study was of poor quality (B). Both groups were treated weekly for 6 weeks, with each session lasting for 30 minutes. In the acupuncture group, 11 needles (0.3 × 50 mm) were placed at the following points: BL23, BL25, GB30, BL40, KI3, and GV4, and DeQi was achieved; the needles were manipulated 3 times per session at 10-minute intervals to maintain the DeQi sensation. In the TENS group, electrodes were placed on the lumbar region. No significant difference was observed between the groups at the 4-week and 6-month follow-up (B).
Simulated acupuncture versus true acupuncture

No benefit was found for true acupuncture when it was compared to simulated acupuncture, which did not involve the actual insertion of needles but instead a mere stimulation of the skin, in patients with chronic low-back pain (A). The following procedures were applied: individualised acupuncture (patient in a prone position with no constraints relative to the points used, insertion depth, or needle manipulation); standardised acupuncture (points Du3, B23, the low-back AhShi point, B40, and KI3 for 20 minutes with stimulation by twirling the needles at 10 and 20 minutes); and simulated acupuncture (no actual needle insertion). The sessions were performed twice weekly for six weeks and then weekly for four weeks (10 sessions in total). No statistically significant difference was found among the three acupuncture groups; however, a significant difference was found between these groups and a fourth group that received usual care only (A).

Acupuncture versus massage

After 10 weekly sessions, acupuncture was inferior to massage with respect to pain and disability in patients with non-specific chronic low-back pain. That effect was maintained from the end of treatment up to a 1-year follow-up (B). One study of 262 volunteers compared the following procedures performed in 10 weekly sessions: massage, performed by 12 therapists who freely applied commonly used therapies such as Swedish (71%); movement re-education (70%); moist heat or cold (51%); deep-tissue (65%), neuromuscular (45%), and trigger or pressure point (48%) techniques; and acupuncture, the technique of which was also freely selected by the acupuncturists and included basic traditional Chinese medicine (TCM) techniques, needle manipulation, and moxibustion. Massage proved to be superior to acupuncture at the end of the treatment, according to the modified Roland Disability Scale (RDS, 0-23) scores (6.3 versus 7.9, p < 0.01). At a 1-year follow-up, massage remained superior to acupuncture with respect to both the disability scores (6.29 versus 8.21; p < 0.05) and the symptoms scale (VAS, 0-100; 3.08 versus 4.74; p < 0.002) (B).

Acupuncture versus anaesthetic injection

Acupuncture proved to be more beneficial than local anaesthetic injections at the most painful palpation points in patients with low-back pain (B). Both acupuncture and anaesthetic injection were performed at 2-5 of the most painful palpation points on the lower back once weekly for 4 weeks. In the acupuncture group, 40 mm x 0.18 mm needles were inserted to a depth of 10-20 mm, using the bird pecking technique at 1 cycle per second for 20 seconds; in the local anaesthetic group, 5 mg of local anaesthetic were injected into the same points and at the same depth. Acupuncture proved superior to local anaesthetic for pain alleviation, with VAS score reductions of 49.4 ± 17.0 versus 19.5 ± 26.8 after 2 weeks and 51.8 ± 15.8 versus 22.1 ± 28.8 after four weeks of treatment; those differences were statistically significant (B).

Acupuncture and adverse effects

Minimal adverse effects were reported in all studies; the most common adverse effects were fleeting pain at the needle insertion site, local haematoma, mild local swelling, and short-term bleeding.

None of the analysed studies reported the occurrence of severe adverse effects.

Recommendation

Not enough studies of satisfactory quality have been found to enable a sound evidence-based recommendation regarding the use of acupuncture for the treatment of non-specific chronic mechanical low-back pain.

The combined use of acupuncture and conservative treatment modalities such as physical therapy, NSAIDs, analgesia, heat, self-care, and postural education was more beneficial than those same therapies alone for the treatment of non-specific chronic mechanical low-back pain. While some studies reported benefits with true acupuncture, others found both techniques to be equivalent (B). That controversy notwithstanding, sham acupuncture (superficial needle insertion) has been shown not to be an inert procedure. Additionally, one study found no benefit with the use of true acupuncture in individuals with chronic low-back pain compared to the use of simulated acupuncture (no actual needle insertion, but mere skin stimulation) (A).

Acupuncture proved more efficacious than a placebo (TENS) in 1 high-quality study (A), although this finding was not confirmed by another study (B); this discrepancy might be due to the differences in quality between the studies.

Acupuncture was found inferior to massage with respect to pain and disability after 10 weekly sessions for the treatment of non-specific chronic low-back pain. That difference was maintained at a 1-year follow-up (B).

Acupuncture proved to be more beneficial than local anaesthetic injection when both applied at the most painful palpation points for the treatment of chronic low-back pain (B).

Pain prevention

10. Is individual ergonomic orientation useful for preventing pain relapse?

The small number of available studies that address the application of ergonomics to relapse prevention in patients with non-specific chronic low-back pain does not yield any conclusive evidence in this regard (B).

A programme that included ergonomics and exercise for 15 1-hour sessions, conducted five days per week, was
not superior to individual physical therapy and spinal manipulation with respect to pain and disability. The results of the group subjected to the investigated programme, which included education in ergonomics at home and in different occupational settings, were poorer than those of the group subjected to spinal manipulation with respect to both pain and disability\(75\) (B).

Ergonomics did not show any effect when it was used to prevent the relapse of low-back pain\(76\) (B).

The ergonomical programme, which included an orientation about actions to reduce spinal loading, asymmetries, and unexpected loading related to nursing tasks, did not provide benefits with respect to the prevention of non-specific chronic low-back pain\(76\) (B).

**Recommendation**

No currently available evidence allows the characterisation of ergonomic interventions as beneficial for the reduction and prevention of non-specific chronic low-back pain relapses\(76\) (B).

**11. Does the maintenance of supervised aerobic exercise prevent pain relapse?**

Studies of individuals subjected to exercise programmes reported some benefits. However, neither these benefits nor their relevance to the overall state of health have been accurately investigated, as those studies included various confounding variables\(77\) (A).

The small number of studies that discussed whether the maintenance of supervised low-intensity exercise was useful for preventing pain relapse and their methodological limitations do not yield any conclusive evidence with regard to either the application of that treatment modality or its cost-effectiveness for non-specific low-back pain\(78-81\) (A).

Independently of its intensity and duration, exercise seems to be preferentially associated with the conditioning and wellbeing of individuals, particularly with regard to psychological features such as mood and self-confidence in the performance of the activities of daily life\(82-85\) (A).

Nevertheless, some studies that addressed the perceptions of individuals at 1 and 10 years after supervised physical training that involved static and dynamic exercise during twice-weekly 1-hour sessions for at least three weeks suggested that these sessions contributed with improvements in functional capacity and to the prevention of pain relapses\(86\) (A)\(87-89\) (B).

Pain reduction was observed in a study that applied a supervised exercise programme, divided into three phases of four weeks each. In the first phase (weeks 1-4), training therapy was performed twice weekly, with each session lasting for at least 1 hour and including static and dynamic exercises, using mainly pulleys and small weights. According to the individual's physical tolerance, the weight, number of repetitions, speed, and range of movement were adjusted and gradually increased during the first phase. In the next phase (weeks 5-8), the sessions were performed thrice weekly for 1 hour each, with a minimum of 2 × 15 repetitions per exercise.

The third phase (weeks 9-12) comprised two training sessions per week, for 1 hour per session. Each training session started with a warm-up procedure that included low-intensity aerobics and subsequent stretching\(86\) (A).

**Recommendation**

No currently available evidence allows the characterisation of exercise as a means for preventing pain relapse. The available studies show that independently of the type, time, duration, and intensity of exercise, its benefit for the prevention of future episodes of pain cannot be asserted\(86\) (A)\(87-89\) (B).

**Economic assessment**

**12. What is the cost-effectiveness of acupuncture for chronic low-back pain?**

Few studies that assessed the cost-effectiveness of acupuncture for chronic low-back pain could be located, and in the studies found, assessments were performed with incremental cost-effectiveness analyses based on gains in the estimated quality-adjusted life years (QALYs).

In the United Kingdom, for instance, a threshold of € 30,000 (pounds) per QALY is found to be consistent with decisions to adopt new technologies. In contrast, such a threshold does not exist in Germany and Brazil\(90\) (B).

One study conducted in Germany established a hypothetical threshold of € 50,000 (euro) per QALY. Both pain and quality-of-life were assessed at the baseline and at 3 and 6 months. The sample comprised 11,630 individuals (average age, 52.9 years old (standard deviation, 13.7); 59% female), of whom 1,549 were randomised to the acupuncture group and 1,544 to the control group, while 8,537 were included in the non-randomised acupuncture group. In the analysis after three months, back function improvements were more pronounced in the acupuncture group than in the control group, with mean HFAQ score increases of 12.1 (standard error (SE) 0.4) to 74.5 (SE, 0.4) points in the acupuncture groups and 2.7 (SE, 0.4) to 65.1 (SE, 0.4) points in the control group (difference, 9.4 points; 95% CI, 8.3-10.5; p < 0.001; control event rate = 0.631, experimental event rate = 0.426, RRR = 32%, ARR = 0.205, and NNT = 5).

The non-randomised volunteers exhibited more severe symptoms at baseline and function improvements similar to those of the randomised participants. The incremental cost-effectiveness ratio was estimated to be € 10,526 per QALY gained. Acupuncture in addition to routine care was associated with clinical improvements in the assessed population and was considered relatively cost-effective\(91\) (B).

Data analysis included the overall costs during the 3 months after randomisation, including costs not related to chronic low-back pain, as well as the diagnosis-specific costs (those due to chronic low-back pain and related conditions). The direct health-related costs included physician visits, hospital stays, medication, acupuncture treatment, and the number of sick-leave days\(91\) (B).
The acupuncture service was found to be cost-effective at 24 months; the estimated cost per QALY was £ 4,241 (95% CI, -£ 191 to £ 28,025), using the SF-6D scoring algorithm for responses to the SF-36 and £ 3,598 (95% CI, -£ 189 to £ 22,035), using the EQ-5D health status instrument91 (B).

The costs of acupuncture were higher than those of usual care, as the former involved an average of 8-10 sessions that lasted for 10-30 minutes per session, and 9.6 needles were used per treatment (range, 6-12). A total of 177 different acupoints were used, both unilaterally and bilaterally. The needles used were normally 25 or 40 mm long and 0.20-0.30 mm in diameter. Points from the bladder and the gallbladder channels were often used (38.4% and 14.9%, respectively), as was BL-23 (22.9%); the points selected were often combinations of local points (e.g., BL-23, BL-26, BL-53, BL-54, and GB-30, as well as minor lumbar points) and distal points (e.g., BL-40, BL-60, GB-34, and GB-40); the addition of the costs of medical visits, pain medication, physical therapy, and exercise resulted in a total mean cost higher in the acupuncture group (£ 471.10) than in the control group (£ 332.24); however, the quality-of-life was higher in the former, while the social cost, including lost productivity due to time taken off from work, was lower in the acupuncture group (£ 2,135.39) compared to the control group91 (£ 2,469.09) (B).

Recommendation

Although acupuncture for the treatment of non-specific low-back pain is associated with a cost increase, 10 sessions at a twice-weekly frequency are recommended, as these improve the patients' quality of life and reduce work absenteeism and thus reduce the individuals' social costs91 (B).

Acupuncture in addition to routine care induced relevant clinical benefits and was found to be cost-effective in patients with chronic low-back pain who were assisted at German primary care centres. Therefore, acupuncture should be considered as a feasible option for the management of patients with chronic low-back pain91 (B).

Conflicts of interest

M Imamura was paid a fee to give a lecture sponsored by Eli Lilly and Company. The other authors declare no conflicts of interest.

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