Emergency department interventions for adult patients with low back pain: a systematic review of randomised controlled trials

Crystian B Oliveira ,[1,2] Hugo E Amorim,[3] Danielle M Coombs ,[3,4] Bethan Richards,[3,5] Marco Reedyk,[6] Chris G Maher,[3,4] Gustavo C Machado [3,4]

Handling editor David Metcalfe

For numbered affiliations see end of article.

Correspondence to
Dr Crystian B Oliveira, Department of Physical Therapy, Faculty of Science and Technology, Sao Paulo State University, Presidente Prudente, Sao Paulo, Brazil; crystianboliveira@gmail.com

CBO and HEA are joint first authors.

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ABSTRACT

Background Most low back pain trials have limited applicability to the emergency department (ED) because they provide treatment and measure outcomes after discharge from the ED. We investigated the efficacy and safety of pharmacological and non-pharmacological interventions delivered in the ED to patients with non-specific low back pain and/or sciatica on patient-relevant outcomes measured during the emergency visit.

Methods Literature searches were performed in MEDLINE, EMBASE and CINAHL from inception to week 1 February 2020. We included all randomised controlled trials investigating adult patients (≥18 years) with non-specific low back pain and/or sciatica presenting to ED. The primary outcome of interest was pain intensity. Two reviewers independently screened the full texts, extracted the data and assessed risk of bias of each trial using the Physiotherapy Evidence Database (PEDro) scale. The overall quality of evidence, or certainty, provided by a set of trials evaluating the same treatment was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which considers imprecision, inconsistency, indirectness and bias in the evidence.

Results Fifteen trials (1802 participants) were included with 12 of 15 at low risk of bias (ie, PEDro score >6). Based on results from individual trials and moderate quality evidence, ketoprofen gel was more effective than placebo for non-specific low back pain at 30 min (mean difference (MD) −15.0, 95% confidence interval (CI) −21.0 to −9.0). For those with sciatica (moderate quality evidence), intravenous paracetamol (acetaminophen) (MD −15.7, 95% CI −19.8 to −11.6) and intravenous morphine (MD −11.4, 95% CI −21.6 to −1.2) were both superior to placebo at 30 min. Based on moderate quality of evidence, corticosteroids showed no benefits against placebo at emergency discharge for non-specific low back pain (MD 9.0, 95% CI −0.71 to 18.7) or sciatica (MD −6.8, 95% CI −24.2 to 10.6). There were conflicting results from trials comparing different pharmacological options (moderate quality evidence) or investigating non-pharmacological treatments (low quality evidence).

Conclusion Ketoprofen gel for non-specific low back pain and intravenous paracetamol or morphine for sciatica were superior to placebo, whereas corticosteroids were ineffective for both conditions. There was conflicting evidence for comparisons of different pharmacological options and those involving non-pharmacological treatments. Additional trials measuring important patient-related outcomes to EDs are needed.

Key messages

What is already known on this subject

- Hundreds of trials have investigated interventions in people with low back pain or sciatica, although most have limited applicability to emergency care.
- There are few trials that enrol participants, provide treatment and measure outcomes in the emergency department.

What this study adds

- Ketoprofen gel for low back pain and intravenous paracetamol or morphine for sciatica were superior to placebo, whereas corticosteroids were ineffective for both conditions. There was conflicting evidence between different treatment options.
- The results derived from single trials, thus, additional trials measuring patient-reported outcomes and those relevant to the emergency department are needed.

BACKGROUND

Low back pain is the major contributor to years lived with disability worldwide,[1] generating huge burden to healthcare systems.[2] People with low back pain often present to emergency departments (EDs), ranking among the top 10 reasons for presentation in the USA, Canada and Australia.[3] Up to one-third of these patients are admitted to the hospital in Australia,[4] which imposes a high economic burden to the healthcare system. Overuse of opioid medicines is also common in patients with low back pain attending EDs in high-income countries,[5 6] despite potential serious consequences.[7]

There is conflicting evidence on how to manage low back pain in the ED. Although a number of trials have investigated the effectiveness of interventions in this setting,[8–13] most have limited applicability to emergency care. This is because many of these trials provide treatment and measure outcomes after ED discharge. For example, a previous trial in the ED showed that adding an opioid or a muscle relaxant to a nonsteroidal anti-inflammatory drug (NSAID) provided no additional benefits to NSAIDs alone for patients with acute low back pain.[10] However, in this trial, patients were recruited at the time of emergency discharge, provided with a 10-day

supply of the medicine with outcomes measured at emergency discharge, 1-week and 3-month follow-up.

There is evidence that emergency patients are different to those seen in primary care. Serious spinal pathologies, such as spinal abscess and vertebral fracture, are more frequently seen in EDs.[6] Emergency patients tend to report higher levels of anxiety and psychological distress which may influence their experience of pain.[14] Challenges related to the clinical environment, such as time constraints and overcrowding, may impede delivery of some care options in EDs.[15] The ED also has limited opportunity to establish relationships or follow-up when compared with primary care. Thus, a systematic review with a focus on EDs will have direct clinical implications and help guide emergency clinicians on the management of low back pain.

The aim of this systematic review, therefore, is to summarise the evidence from randomised controlled trials that enrolled patients with non-specific low back pain and/or sciatica presenting to EDs where the study intervention is administered, and patient-reported outcomes measured during an ED visit.

METHODS

This systematic review was prospectively registered in PROSPERO (CRD42019123821) and followed the reporting recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[16]

Searches

Literature searches were performed in MEDLINE, EMBASE and CINAHL from inception to week 1 February 2020. The searches used a combination of keywords related to the inclusion criteria of this review such as low back pain and sciatica, ED, and randomised controlled trial (online supplementary appendix 1). In addition, citation tracking was performed from included full-text articles and previous relevant systematic reviews. The searches were not restricted by language or date of publication. Study selection was performed by two independent reviewers (HA and CO) based on screening of titles and abstracts and then relevant full texts were assessed for eligibility. Any disagreements were resolved through consensus between the two reviewers.

Eligibility criteria

Study design

Only randomised controlled trials published in peer-reviewed journals were eligible.

Participants

We included trials investigating patients presenting to EDs with low back pain and/or sciatica. We did not restrict to any specific symptom severity or duration. Trials recruiting patients with spinal canal stenosis or those with serious pathologies (such as infection, vertebral fracture, malignancy, cauda equina syndrome or axial spondylarthritis) were excluded. Trials with mixed populations including other diseases such as rheumatoid arthritis or hip/knee osteoarthrosis were excluded unless they reported separated data or more than 75% of the population was diagnosed with non-specific low back pain and/or sciatica.

Intervention and comparison groups

Randomised controlled trials investigating any type of healthcare intervention delivered for adult patients ≥18 years with non-specific low back pain and/or sciatica during the ED presentation were considered eligible. Similarly, any type of comparison intervention was included in this review such as no treatment, placebo/sham procedures or another pharmacological or non-pharmacological intervention.

Outcomes

We included studies reporting at least two outcome measures from the time of arrival to the time of discharge from the ED. Thus, trials only reporting outcomes at endpoints collected after ED discharge were excluded. The primary outcome of this systematic review was pain intensity measured using a Visual Analogue Scale or Numerical Rating Scale. Secondary outcomes included: time to discharge (length of ED stay), functional measures (eg, ability to walk), adverse events (patients experiencing adverse events), and representation to the ED (proportion of patients representing to the ED within 48 hours).

Data extraction

Two authors (HA and CO) extracted the following information using a standardised data extraction form: sample characteristics (sample size, sex, age, symptoms duration) intervention and comparison groups and outcome data. Any disagreement was resolved through consensus. For pain intensity, point estimates (eg, means, medians) and measures of variability (eg, SD, 95% CIs) were extracted from each study arm for all relevant time points. When change from baseline and final measures were available, we extracted the change or effect estimates based on changes from baseline.[17] If needed, median and IQR were converted to mean and SD.[18] Pain scores were converted to a common 0–100 scale. For adverse events, we extracted the proportion of patients (numerator and denominator) reporting any or specific adverse events from each study arm before ED discharge. In case of missing data, we contacted authors to provide further information on participant's data. If data were not available, we estimated missing data following the recommendations provided in the Cochrane Handbook.[19]

Risk of bias and quality of evidence

Risk of bias was assessed using the Physiotherapy Evidence Database (PEDro) scale. The PEDro scale is a valid and reliable tool[20 21] containing 10 scored yes-or-no items for assessment of the internal validity of clinical trials investigating pharmacological and non-pharmacological interventions.[22] Two independent reviewers (HA and CO) assessed the risk of bias of all included studies and resolved any disagreement through consensus. Trials with scores greater than 6 were classified as having low risk of bias.

We assessed the overall quality of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[23 24] The overall quality of evidence was downgraded one level considering risk of bias (ie, trials classified as having high risk of bias, that is PEDro score <7) and imprecision (ie, trials reporting data for <400 participants). We did not assess inconsistency because the results of the comparisons were based on single trials.[23] Similarly, indirectness was also not assessed, because the inclusion criteria of this review considered population, intervention and outcome measures during an ED visit. The quality of evidence was rated from high to low.

Data analysis

Descriptive statistics were used to summarise demographic data and study characteristics. Mean differences (MD) and 95% CIs were obtained for all included studies. While we originally intended to pool trial results using meta-analysis, this was not appropriate due to substantial clinical heterogeneity related to

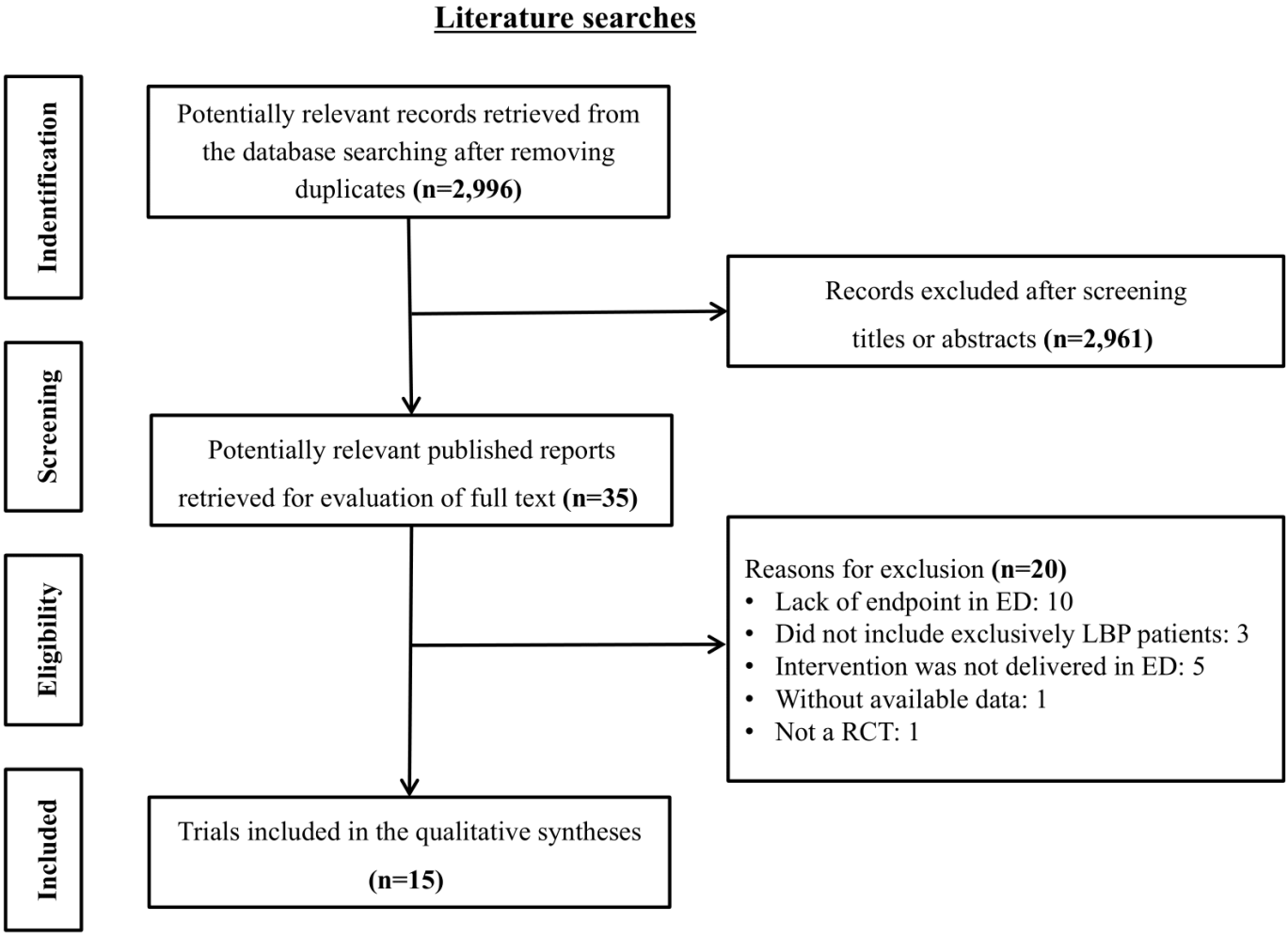

Figure 1 Study flow chart. ED, emergency department; LBP, low back pain; RCT, randomised controlled trial.

the experimental and control interventions. The closest we came to clinically homogeneous trials were three trials with a common control intervention (intravenous placebo), but the experimental interventions were very different (intravenous paracetamol, intravenous dexamethasone and intravenous morphine). We took the view that pooling across such different drugs would have limited clinical applicability for emergency physicians. As pooling would not be appropriate, the results were narratively described. The latest follow-up time reported by each trial was defined as the primary time point as this would be the closest to ED discharge and thus more relevant for emergency physicians. Since this time point varied between included trials, we also report effect sizes for all available time points in the tables and figures. Forest plots were created using Comprehensive Meta-analysis V.3.

RESULTS

Literature searches yielded 2975 records. Of these, 36 records were selected after title and abstracts screening as potentially eligible to be included in this review. Finally, 15 trials were considered eligible and were included.[8 13 25–37] Figure 1 describes the study selection process of this review. Fifteen trials[8 13 25–37] provided data for 1802 participants. Twelve trials[8 26–33 35–37] included patients with non-specific low back pain and three trials[13 25 34] included patients with sciatica. The sample size of the included trials ranged from 30 to 518 participants and the mean age ranged from 31.5 to 45.1 years.

Two trials tested paracetamol,[13 32] seven trials investigated NSAIDs,[28–32 34 37] two trials evaluated corticosteroids,[8 25] one trial investigated two formulations of a muscle relaxant,[35] five trials used opioid medicines,[13 26 28 31 32] one trial used a pharmacotherapy protocol[27] and one trial investigated a combination of thiocolchicoside, lidocaine and tenoxicam.[37] Four trials investigated non-pharmacological interventions including acupuncture,[27 33] a physiotherapy protocol[36] and trigger point injections of an anaesthetic.[29]

The included trials used as comparison interventions a placebo treatment,[28–31 34] NSAIDs,[37] usual ED care (ie, usual therapy provided at the discretion of the treating physician)[33] or walking training/aids.[36] Table 1 describes in detail the characteristics of the included trials, including drug dosages and regimens.

Risk of bias

Table 2 reports risk of bias of the 15 trials using the PEDro scale. Most included trials had low risk of bias; only three trials[27 29 33] had high risk of bias with a PEDro score <7. The most common methodological flaws identified were lack of concealment allocation,[26–29 34 35] and blinding of therapists.[26 27 29 33 36 37] A small proportion of trials did not blind participants or outcome assessors,[27–29 33 37] did not provide data for >85% of participants,[8 25 33] did not perform intention-to-treat analysis,[26 31 34] or did not report similar baseline characteristics.[27] All included trials reported appropriate random allocation, between group differences and variability measures.

Table 1 Characteristics of the included studies

Study name	Country	Source	Sample characteristics	Interventions	Outcomes and endpoint(s)
Akbas *et al*[37]	Turkey	ED of a tertiary care hospital	120 patients with acute LBP (duration of symptoms was not specified) **Group 1:** n=60 (45% female). Median age (IQR): 38.9 (28.3—44.8) **Group 2:** n=60 (48% female). Median age (IQR): 36.9 (27.5—45.0)	**Group 1:** mesotherapy (a minimum of 50 injections) of 2 mg intradermal thiocolchicoside, 16.2 mg lidocaine, and 5 mg tenoxicam **Group 2:** systemic therapy of 50 mg intravenous dexketoprofen for 5 min	Pain (0–10) Adverse events Endpoint: after 15, 30 and 60 min of the intervention
Balakrishnamoorthy *et al*[25]	Australia	EDs of two public hospitals	58 patients with sciatica **Group 1:** n=29 (58% female). Mean age (SD): 38.9 (9.1) **Group 2:** n=29 (44% female). Mean age (SD): 36.9 (9.9)	Both groups received a standardised regimen of regular analgesia (ie, paracetamol/codeine, ibuprofen and oral oxycodone as required), physiotherapy referral and education **Group 1:** single dose of 8 mg intravenous dexamethasone (corticosteroid) in 2 mL **Group 2:** 2 mL of a single dose of 0.9% intravenous sodium chloride	Pain (0–10) Length of stay (minutes) Adverse events Endpoint: at discharge
Behrbalk *et al*[26]	Israel	ED of the Tel-Aviv Sourasky Medical Center	59 patients with acute LBP (less than 3 weeks) **Group 1**: n=30 (53% female). Mean age (SD): 45.0 (11.0) **Group 2**: n=29 (65% female). Mean age (SD): 42.0 (12.0)	**Group 1:** single dose of 0.1 mg/kg (up to 10 mg) intravenous morphine administered in a 150 mL normal saline infusion for 30 min **Group 2:** single dose of 0.1 mg/kg (up to 10 mg) intravenous morphine with 25 mg promethazine administered similarly	Pain (0–100) Length of stay (minutes) Functional outcome (ability to walk) Adverse events Endpoint: after intervention
Cohen *et al*[27]	Australia	Four large EDs in Melbourne — two public and two private	518 patients with acute LBP (duration of symptoms was not specified) **Group 1**: n=174 (48% female). Mean age (SD): 42.1 (15.8) **Group 2**: n=178 (47% female). Mean age (SD): 40.5 (14.5) **Group 3**: n=166 (47% female). Mean age (SD): 40.3 (15.0)	**Group 1:** acupuncture with treatment protocols determined by a panel of specialist acupuncturists, provided predetermined points for each condition **Group 2:** pharmacotherapy according to a standardised protocol based on the relevant national guidelines of the National Institute of Clinical Studies and the National Health and Medical Research Council **Group 3:** combination of the acupuncture and pharmacotherapy treatments	Pain (0–10) Length of stay (hours) Adverse events Endpoint: after an hour
Eken *et al*[32]	Turkey	ED of a tertiary care university hospital	137 patients with acute LBP (starting over the last week), 39% female and mean age (SD) of 31.5 (9.5) **Group 1**: n=46 **Group 2**: n=45 **Group 3**: n=46	**Group 1**: single dose of 1 g intravenous paracetamol in 100 mL normal saline solution **Group 2**: single dose of 0.1 mg/kg intravenous morphine in 100 mL normal saline **Group 3**: single dose of 50 mg intravenous dexketoprofen in 100 mL normal saline solution	Pain (0–100) Adverse events Endpoint: after 15 and 30 min of the intervention
Ergun *et al*[35]	Turkey	ED of tertiary care university hospital	72 patients with LBP (duration of symptoms was not specified) **Group 1**: n=39 (33% female). Mean age (SD): 36.0 (10.0) **Group 2**: n=40 (27% female). Mean age (SD): 38.0 (11.0)	**Group 1**: 2 tablets of 400 mg oral phenyramidol plus 3 mL of intramuscular saline solution **Group 2**: single dose of 800 mg intramuscular phenyramidol plus placebo tablets	Pain (0–100) Adverse events
Eskin *et al*[8]	United States	A suburban ED with an annual patient census of 80 000 patients	79 patients with LBP (last 48 hours or acute exacerbation of chronic low back pain) **Group 1**: n=39 (33% female). Mean age (SD): 39.0 (8.0) **Group 2**: n=40 (27% female). Mean age (SD): 41.0 (9.0)	**Group 1**: single dose of 50 mg oral prednisone **Group 2**: The placebo group received the same regimen as the study group, using an inactive oral tablet	Pain (0–10) Endpoint: at discharge
Fox *et al*[33]	United States	ED of an urban academic medical centre	30 patients with acute and acute-on-chronic LBP **Group 1**: n=15 (53% female). Mean age: 43.0 **Group 2**: n=15 (60% female). Mean age: 38.0	**Group 1**: battlefield acupuncture (placement of indwelling semipermanent needles in up to five prespecified points on the ear, corresponding with established auricular acupuncture points) plus standard therapy **Group 2**: standard therapy provided at the discretion of the treating physician	Pain (0–10) Adverse events Endpoint: 30 min
Innes *et al*[28]	Canada	EDs of six university and community hospitals	113 patients with acute LBP (less than 72 hours) **Group 1**: n=55 (19% female). Mean age (SD): 33.1 (9.8) **Group 2**: n=58 (23% female). Mean age (SD): 36.0 (10.1)	**Group 1**: 10 mg oral ketorolac tromethamine. Then, 10 mg every 4 to 6 hours as needed, up to four doses in 24 hours **Group 2**: 600 mg paracetamol plus 60 mg codeine orally, in the same regimen	Pain (0–10) Adverse events Endpoint: after 30 min, 1, 2, 3, 4, 5, 6 hours of the intervention
Kocak *et al*[29]	Turkey	ED of a tertiary care university hospital	54 patients with acute LBP (less than 48 hours) **Group 1**: n=32 (47% female). Mean age (SD): 40.9 (13.2) **Group 2**: n=22 (36% female). Mean age (SD): 45.1 (13.0)	**Group 1**: single dose of 50 mg intravenous dexketoprofen in 100 cc isotonic solution over 5 min **Group 2**: trigger point injection of anaesthetic (2% lidocaine, 2.5-cc from 100 mg 5-cc of ampoule with 2.5-cc saline mixture). Then, the identified point was needled several times	Pain (0–10) Adverse events Endpoint: after 5, 15, 30 min, and an hour of the intervention
Lau *et al*[36]	Hong Kong	ED of a local acute hospital	110 patients with acute LBP (less than 24 hours) **Group 1**: n=55 (62% female). Mean age (SD): 52.0 (18.0) **Group 2**: n=55 (60% female). Mean age (SD): 49.0 (15.0)	**Group 1**: education session with a Back Care Booklet, mobility training in daily tasks (eg, sitting to standing), walking training and walking aids, and interferential therapy **Group 2:** control group including walking training and prescription of walking aids as indicated	Pain (0–10) Functional outcomes (RMDQ and Back Performance Scale) Endpoint: post-intervention but before discharge.

Continued

Table 1 Continued

Study name	Country	Source	Sample characteristics	Interventions	Outcomes and endpoint(s)
Serinken *et al*[13]	Turkey	ED of four tertiary care hospitals	300 patients with sciatica **Group 1**: n=100 (52% female). Mean age (SD): 44.6 (10.2) **Group 2**: n=100 (57% female). Mean age (SD): 43.7 (9.8) **Group 3**: n=100 (43% female). Mean age (SD): 40.3 (9.5)	**Group 1**: single dose of 0.1 mg/kg intravenous morphine in 100 mL of normal saline **Group 2**: single dose of 1 g intravenous paracetamol in 100 mL of normal saline (Perfalgan, Bristol Myers) **Group 3**: single dose of 100 mL intravenous normal saline	Pain (0–100) Adverse events Endpoint: after 15 and 30 min of the intervention
Serinken *et al*[30]	Turkey	EDs of three tertiary care hospitals	140 patients with acute LBP (less than 24 hours), 44% female and mean age (SD) of 35.0 (12.0) **Group 1**: n=70 **Group 2**: n=70	All the study patients received 50 mg intravenous dexketoprofen (Fastjel, ARVELES) **Group 1**: 2 g of 2.5% ketoprofen gel was administered over the area with pain and tenderness **Group 2**: placebo gel	Pain (0–100) Adverse events Endpoint: after 15 and 30 min of the intervention
Tanen *et al*[34]	United States	ED of a tertiary care medical centre that serves beneficiaries of active duty and retired military personnel	41 patients with acute sciatica **Group 1**: n=20 (36% female). Mean age (SD): 39.0 (12.0) **Group 2**: n=21 (50% female). Mean age (SD): 36.0 (10.0)	**Group 1**: single dose of 100 mg intravenous lidocaine over 2 min followed by a 10-cc normal saline flush **Group 2**: single dose of 30 mg intravenous ketorolac over 2 min also followed by a 10-cc normal saline flush	Pain (0–100) Endpoint: after an hour of the intervention
Veenema *et al*[31]	United States	ED of an urban university hospital	153 patients with LBP (duration of symptoms was not specified) **Group 1**: n=79 (40% female). Mean age (SD): 36.0 (12.1) **Group 2**: n=74 (37% female). Mean age (SD): 35.5 (12.8)	**Group 1**: single dose of 1 mg/kg intramuscular meperidine (pethidine) **Group 2**: single dose of 60 mg intramuscular ketorolac	Pain (0–100) Adverse events Endpoint: after an hour of the intervention

ED, emergency department; ID, intradermal; IM, intramuscular; LBP, low back pain; NSAIDs, non-steroidal anti-inflammatory drugs; ;RMDQ, Roland Morris Disability Questionnaire.

Quality of the evidence: GRADE ratings

The overall quality of evidence of the included interventions on pain intensity varied from low (downgraded for risk of bias or imprecision) to moderate (downgraded for imprecision). The sample size and risk of bias for secondary outcomes were similar to pain intensity, thus the quality of evidence for functional outcomes, length of ED stay and adverse events was also rated as low or moderate. Online supplementary appendix 2 describes the overall quality of evidence using the GRADE approach on pain intensity.

Pain intensity

Figures 2 and 3 detail the effects of the interventions on pain intensity in patients with non-specific low back pain and sciatica, respectively.

Paracetamol

For sciatica, 1 g intravenous paracetamol[13] was more effective than placebo (100 mL intravenous saline) at 15 and 30 min—for example, at 30 min MD was −15.7, 95% CI −19.8 to −11.6. The quality of evidence was moderate.

Non-steroidal anti-inflammatory drugs

For non-specific low back pain, 2 g of 2.5% ketoprofen gel[30] was more effective than placebo gel at 30 min (MD −15.0, 95% CI −21.0 to −9.0). We found that 60 mg intramuscular ketorolac or 1 mg/kg intramuscular meperidine had similar effects at 60 min.[31] There were no differences between 50 mg intravenous dexketoprofen and 1 g intravenous paracetamol at 15 and 30 min.[32] A combination of 2 mg intradermal thiocolchicoside, 16.2 mg lidocaine and 5 mg tenoxicam was more effective than 50 mg intravenous dexketoprofen at 15, 30 and 60 min.[37] These findings are summarised in figure 2.

For sciatica, 30 mg intravenous ketorolac[34] showed no advantage over 100 mg intravenous lidocaine at 60 min (figure 3). The quality of evidence for these comparisons was moderate.

Muscle relaxants

For non-specific low back pain, 800 mg intramuscular phenyramidol was not more effective than two tablets of 400 mg oral phenyramidol at 30, 60, 90 and 120 min (figure 2; moderate quality evidence).[35]

Corticosteroids

For non-specific low back pain, 50 mg oral prednisone[8] was not superior to oral placebo at ED discharge (figure 2). Time of discharge was not reported by the authors.

For sciatica, 8 mg intravenous dexamethasone[25] was not superior to placebo (0.9% intravenous sodium chloride) at emergency discharge (figure 3). The median length of stay ranged from 3.5 to 18.8 hours across both groups. The quality of evidence was moderate.

Opioids

For non-specific low back pain, 0.1 mg/kg intravenous morphine[32] was more effective than 1 g intravenous paracetamol at 15 min (MD −11.4, 95% CI −21.6 to −1.2), but not at 30 min. Similarly, 0.1 mg/kg intravenous morphine was superior to 50 mg intravenous dexketoprofen at 15 and 30 min.[32] We found that 600 mg oral paracetamol plus 60 mg codeine provided similar pain relief to 10 mg oral ketorolac trometh-amine at 30 min and at each hour until 6 hours after the intervention.[28] Similarly, there was no difference between 0.1 mg/kg intravenous morphine plus 25 mg promethazine and 0.1 mg/kg intravenous morphine alone shortly after the administration.[26] These findings are summarised in figure 2.

For sciatica, 0.1 mg/kg intravenous morphine[13] was more effective than placebo at 15 and 30 min—for example, at 30 minutes MD was −39.3, 95% CI −43.5 to −35.1. This same trial[13] showed that 0.1 mg/kg intravenous morphine was more effective than 1 g intravenous paracetamol at 15 and 30 min (figure 3). The quality of evidence was moderate.

Non-pharmacological treatments

For non-specific low back pain, auricular acupuncture plus usual ED care was more effective than usual ED care alone.[33] In another trial with three groups, however, acupuncture was not more effective than pharmacotherapy or acupuncture plus pharmacotherapy, nor was pharmacotherapy superior to acupuncture plus pharmacotherapy.[27] Trigger point injections showed

Table 2 Risk of bias of the included studies according to the PEDro scale

Studies	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	<15% dropout rate	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0–10)
Akbas *et al*[37]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Balakrishnamoorthy *et al*[25]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9
Behrbalk *et al*[26]	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7
Cohen *et al*[27]	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	5
Ergun *et al*[35]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Eken *et al*[32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Eskin *et al*[8]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9
Fox *et al*[33]	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	5
Innes *et al*[28]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Kocak *et al*[29]	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Lau *et al*[36]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Serinken *et al*[13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Serinken *et al*[30]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Tanen *et al*[34]	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	8
Veenema *et al*[31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9

PEDro, Physiotherapy Evidence Database.

superior pain relief than 50 mg intravenous dexketoprofen at 5, 10, 15, 30 and 60 min.[29] A physiotherapy protocol was not more effective than walking training/aids at ED discharge.[36] The quality of evidence was low.

Functional outcomes

Opioids

There was no difference between 0.1 mg/kg intravenous morphine alone and 0.1 mg/kg intravenous morphine plus 25 mg promethazine on the proportion of patients who were able to walk independently at discharge (percentage difference: −6.2%, 95% CI −13% to 25%), or assisted (percentage difference: −6.2%, 95% CI −13 to 25).[26] The quality of the evidence was moderate.

Non-pharmacological treatments

Physiotherapy was not superior to walking training/aids on disability measured using the Roland Morris Disability Questionnaire (MD −0.3 out of 24 points, 95% CI −2.8 to 2.2) or mobility measured by the Back Performance Scale (MD −0.6 out of 15 points, 95% CI −1.7 to 0.6).[36] The quality of the evidence was moderate.

Length of ED stay

Corticosteroids

We found that 8 mg intravenous dexamethasone vs placebo led to shorter ED stay for patients with sciatica (MD −15.3 min, 95% CI −18.4 to −12.2; moderate quality evidence).[25]

Opioids

Receiving 0.1 mg/kg intravenous morphine alone resulted in significantly shorter visits than taking 0.1 mg/kg intravenous morphine plus promethazine 25 mg in patients with non-specific low back pain (MD −78.0 min, 95% CI −140.0 to −16.0; moderate quality evidence).[26]

Non-pharmacological treatments

There was no statistically significant difference (p=0.87, low quality evidence) in the length of ED stay of patients with non-specific low back pain receiving acupuncture (median 3.8 hours, IQR 2.9–4.9), pharmacotherapy (median 3.9 hours, IQR 2.7–5.3) or acupuncture plus pharmacotherapy (median 3.7 hours, IQR 2.8–4.8).[27]

Adverse events

Table 3 shows adverse event data of 12 trials[13 25–33 35 37] including 1396 patients with non-specific low back pain and 358 patients with sciatica.

Non-steroidal anti-inflammatory drugs

One patient receiving 2 g of 2.5% of ketoprofen gel reported vertigo and another in the placebo group reported nausea (moderate quality evidence).[30]

Muscle relaxants

There was no difference (moderate quality evidence) in the number of patients reporting adverse events after receiving 800 mg intramuscular phenyramidol or 800 mg oral phenyramidol.[35]

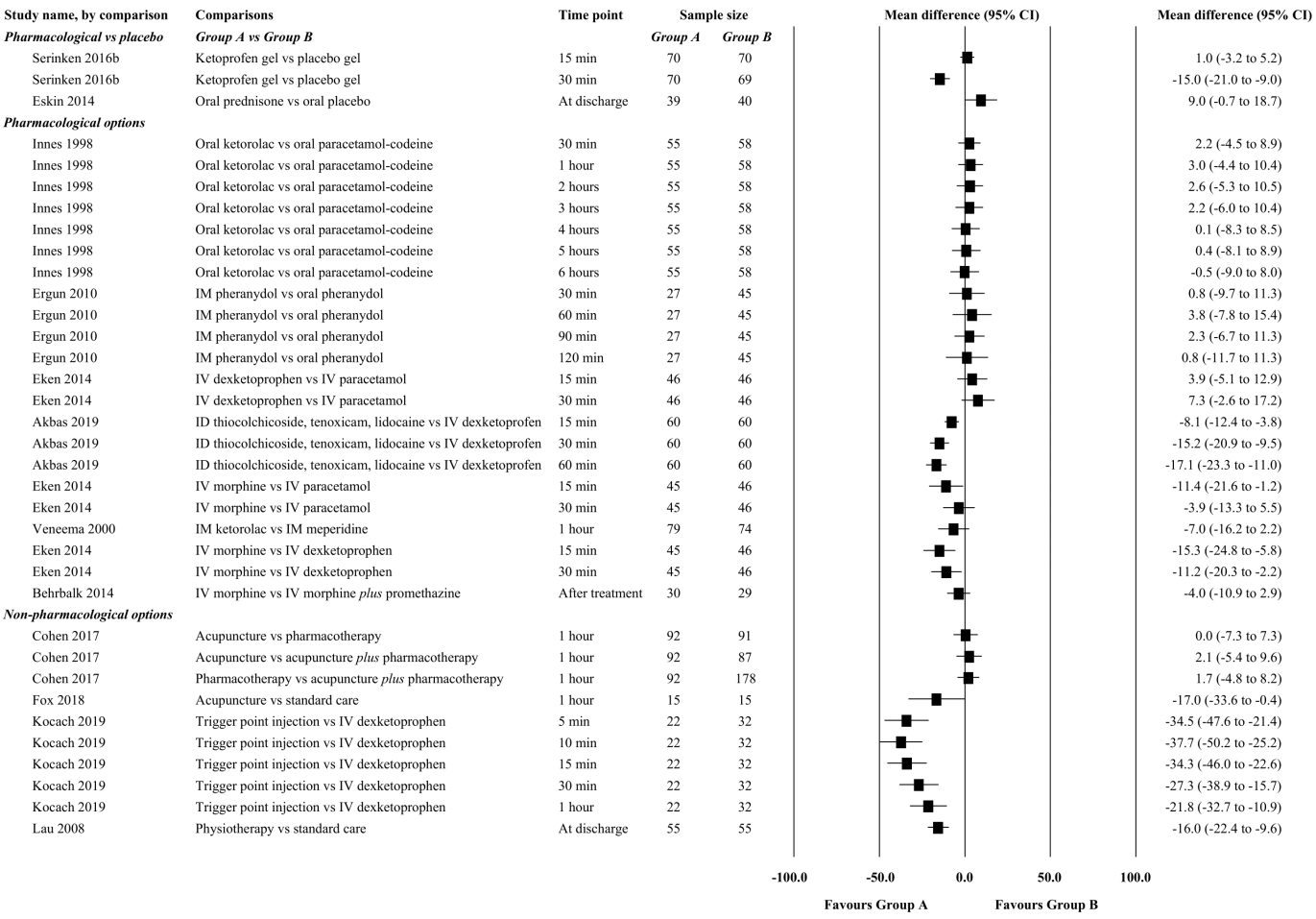

Figure 2 Effects of emergency department interventions on pain scores of patients with non-specific low back pain. ID, intradermal; IM, intramuscular; IV, intravenous.

Corticosteroids

There was no difference (moderate quality evidence) in adverse event rates between patients receiving 8 mg intravenous dexamethasone or placebo.[25]

Opioids

Receiving 0.1 mg/kg intravenous morphine plus 25 mg promethazine resulted in more patients reporting drowsiness and sedation than those receiving 0.1 mg/kg intravenous morphine alone (percentage difference 73%, 95% CI 50% to 85%), but no difference was found for nausea and vomiting (percentage difference 0.1%, 95% CI −13% to 14%).[26] Patients receiving 0.1 mg/kg intravenous morphine or 1 g intravenous paracetamol reported nausea and vertigo.[13] In addition, one patient receiving 0.1 mg/kg intravenous morphine reported hypotension whereas no patients in the placebo group reported adverse events.[13] Patients receiving 1 mg/kg intramuscular meperidine were 10.9 times more likely to experience adverse events (such as dizziness, nausea, sleepiness and dry mouth) compared with those receiving 60 mg intramuscular ketorolac (95% CI 4.6 to 25.7).[31] Similarly, patients receiving 600 mg oral paracetamol plus 60 mg oral codeine were 3.5 times more likely to experience at least one adverse event compared with those receiving 10 mg oral ketorolac tromethamine (95% CI 1.67 to 7.47).[28] There was no

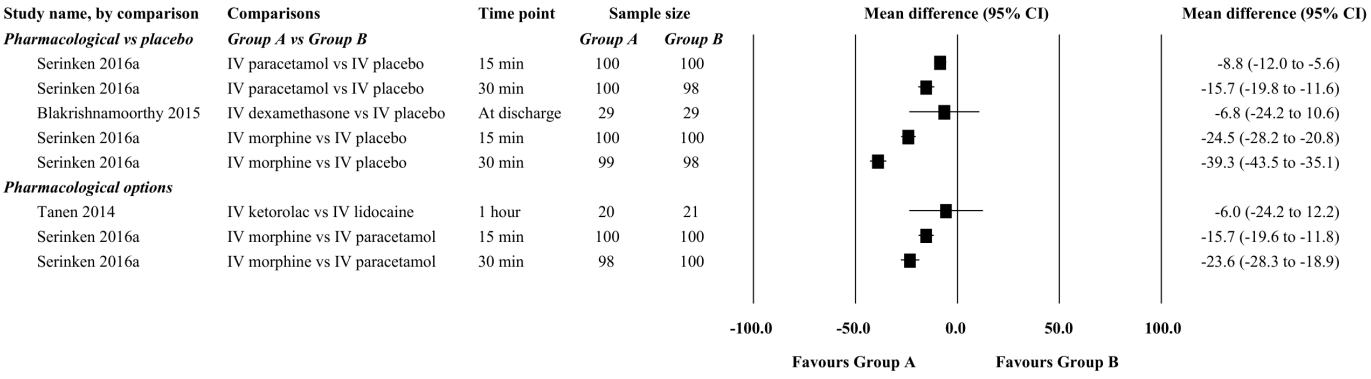

Figure 3 Effects of emergency department interventions on pain scores of patients with sciatica. ID, intradermal; IM, intramuscular; IV, intravenous.

Table 3 Details of the adverse events reported in the included studies

Study name	Group 1 (N of patients or adverse events)	Group 2 (N of patients or adverse events)	Group 3 (N of patients or adverse events)	Description of adverse events data
Balakrishnamoorthy *et al*[25]	8 mg intravenous dexamethasone (NS)	Placebo (NS)	N/A	Incidence of adverse events (ie, nausea, mild headache, light-headedness) but no distinction between the groups (18% vs 15%). One patient receiving intravenous dexamethasone reported peri-anal itching
Behrbalk *et al*[26]	0.1 mg/kg intravenous morphine (n=7)	0.1 mg/kg intravenous morphine plus 25 mg promethazine (n=30)	N/A	No of adverse events: drowsiness and sedation (n=33), nausea and vomiting (n=2), seizures/myoclonus (n=1), headache (n=1)
Cohen *et al*[27]	Acupuncture (n=73)	Pharmacotherapy (n=72)	Acupuncture plus pharmacotherapy (n=71)	No of patients reporting any adverse event
Eken *et al*[32]	1 g intravenous paracetamol (n=4)	0.1 mg/kg intravenous morphine (n=7)	50 mg intravenous dexketoprofen (n=4)	No of patients reporting allergic reactions (n=2), dizziness (n=3), dry mouth (n=2), vertigo (n=1), nausea and vomiting (n=5), mild sedation (n=1), hypotension (n=1)
Ergun *et al*[35]	800 mg intramuscular phenyramidol (n=3)	800 mg oral phenyramidol (n=5)	N/A	No of patients reporting headache, emesis, dry mouth or dizziness (n=8)
Fox *et al*[33]	Battlefield acupuncture (n=2)	Standard therapy (n=0)	N/A	No of patients reporting discomfort at needle insertion site (n=2)
Innes *et al*[28]	10 mg oral ketorolac tromethamine (n=21)	600 mg paracetamol plus 60 mg codeine (n=38)	N/A	No of patients reporting any adverse events per group: ketorolac (n=21) vs paracetamol-codeine (n=38) No of adverse events per group: ketorolac (n=31) vs paracetamol-codeine (n=76)
Serinken *et al*[13]	0.1 mg/kg intravenous morphine (n=4)	1 g intravenous parecetamol (n=3)	Placebo (n=0)	No of patients reporting nausea (n=4), vertigo (n=2), hypotension (n=1)
Serinken *et al*[30]	2 g of 2.5% ketoprofen gel (n=1)	Placebo gel (n=1)	N/A	No of patients reporting nausea (n=1), vertigo (n=1)
Veenema *et al*[31]	1 mg/kg intramuscular meperidine (n=41)	60 mg intramuscular ketorolac (n=8)	N/A	No of adverse events: dizziness (n=19), nausea (n=8), parathesias (n=4), sleepiness (n=11), dry mouth (n=4), hot (n=1), dyspnoea (n=1), pain at site (n=1)

N/A, not applicable; NS, not stated.

difference in the risk of adverse events between 0.1 mg/kg intravenous morphine versus 1 g intravenous paracetamol (RR 1.79, 95% CI 0.56 to 5.69), 0.1 mg/kg intravenous morphine versus 50 mg intravenous dexketoprofen (RR 1.79, 95% CI 0.56 to 5.69), or 1 g intravenous paracetamol versus 50 mg intravenous dexketoprofen (RR 1.00, 95% CI 0.27 to 3.76).[32] The quality of the evidence was moderate.

Non-pharmacological treatments

One study comparing trigger point injection with 50 mg intravenous dexketoprofen did not report any adverse event.[29] In addition, the proportion of patients reporting any adverse event was similar (p=0.84) between acupuncture, pharmacotherapy and acupuncture plus pharmacotherapy.[27] Two patients receiving auricular acupuncture reported discomfort at needle insertion site.[33] The quality of the evidence was low.

Representations

None of the included trials reported rates of representation to the ED within 48 hours.

DISCUSSION

Our review identified 15 randomised controlled trials investigating several interventions for non-specific low back pain and/or sciatica during an ED visit. Compared with placebo, ketoprofen gel showed significant effects in reducing pain intensity in patients with low back pain. Intravenous paracetamol and morphine were both more effective than placebo for sciatica. In contrast, corticosteroids were not effective for low back pain or sciatica. Trials comparing different pharmacological or non-pharmacological treatments showed conflicting results. There was limited evidence on functional outcomes, length of stay and representations. Opioids had an increased risk of transient adverse events compared with NSAIDs. The overall quality of evidence was low or moderate, suggesting that future studies are likely to change our estimates.

Our findings for ketoprofen gel[30] and oral prednisone[8] in patients with low back pain align with the available evidence from primary care.[38 39] The absence of significant differences between some pharmacological treatments has also been observed in trials conducted outside the ED.[9–11 40] Two trials conducted in Turkey found large effect sizes that are rarely seen in low back pain trials.[34 37] Similarly, two high risk of bias trials investigating auricular acupuncture[33] and trigger point injections[29] for low back pain showed surprisingly large effects across all time points. The lack of efficacy of corticosteroids for sciatica[25] also aligns with findings in another systematic review that mainly included primary care data.[41] Some comparisons included in our review (eg, intravenous paracetamol vs intravenous morphine vs placebo for sciatica[13]; ketorolac vs lidocaine for low back pain)[34] have not been investigated in other clinical settings.

None of the trials investigating functional outcomes reported statistically significant differences. The lack of reporting on functional outcomes might reflect the difficulties in collecting these measures in the busy ED setting. Some items of the instruments used measure functional outcomes[42] would not be responsive to change in a short ED visit (eg, 'I got dressed more slowly than usual because of my back pain'). Other instruments that have been shown to be responsive to change over a short period of time, such as the Back Performance Scale,[43] might be more appropriate in ED settings. Another finding from our review was the significant shorter stays for patients with sciatica receiving dexamethasone[25]. Although the use of opioids was associated with an increased risk of adverse events,[13 26 31] most of these events were considered to be minor and transient.

The lack of supporting evidence in the ED is clearer when we look at longer-term outpatient studies. For example, there are numerous trials conducted in community settings showing no additional benefits of muscle relaxants to NSAIDs for acute low back pain,[9 10] yet in the ED there is only one trial of muscle relaxants, which compared two forms of the drug.[35] Nevertheless, a search for trials on the WHO International Clinical

Trials Registry identified 10 ongoing trials investigating several interventions, including acupuncture, patient education, chamomile oil, spinal braces, NSAIDs, exercise, cannabidiol, lidocaine patches and implementation of a model of care. Although some of these ongoing trials may contribute to more definitive conclusions, more trials should be conducted to investigate interventions commonly used in EDs to manage low back pain and sciatica and include patient-reported outcomes (eg, physical function) and specific measures to the ED that are often routinely collected (eg, lenght of stay and representations).

This review was prospectively registered,[44] followed PRISMA reporting guidelines[16] and Cochrane recommendations.[17] We performed a comprehensive search to identify potentially eligible trials and focused on studies measuring outcomes during an ED visit. However, we found great variability across trials, which did not allow us to pool the data. While some trials had a common control intervention, the experimental interventions were markedly different—for example, intravenous morphine versus intravenous dexketoprofen[32] and trigger point injection versus intravenous dexketoprofen.[29] Clinical practice guidelines distinguish between different classes of medicines and types of non-pharmacological treatments, so pooling different medicines would not be helpful to ED physicians who provide care informed by clinical guidelines. Our findings are based on single trials, which may restrict generalisability. Also, the medications tested in the trials might not be readily available in some countries. For example, phenyramidol was the only muscle relaxant investigated in the included trials,[35] but baclofen and orphenadrine are more frequently used in Australia. In addition, replicating these trials could lead to different results. For example, the beneficial effects of antibiotics for patients with chronic low back pain and Modic changes[45] have been disputed after a recent replication trial.[46]

Emergency physicians often use strong pain medicines, such as opioids. For example, a recent study in Australia showed that nearly 70% of patients with low back pain receive an opioid medicine while in the ED.[6] There is, however, limited evidence conducted in ED settings to evaluate the benefits and harms of this practice. The evidence base on the benefits and the dose–response relationship of opioids in this population is weak and there is clear evidence of an increased risk for harms.[7] If emergency physicians are to initiate opioids for low back pain, they should, therefore, follow current primary care guidelines and trial NSAIDs and weak opioids first.[47] Since many emergency patients have contraindications to NSAIDs, primary care guidelines can offer helpful evidence for non-pharmacological options. For instance, educating patients on staying active, providing information to self-manage the condition, and using heat therapy for pain relief are common recommendations in primary care guidelines[47] that emergency physicians should feel comfortable advocating.

CONCLUSION

Our systematic review identified that ketoprofen gel was superior to placebo for patients with non-specific low back pain. Intravenous paracetamol and morphine were both superior to placebo in reducing pain related to sciatica. In contrast, corticosteroids were ineffective for non-specific low back pain or sciatica. Trials investigating different medicines or non-pharmacological treatments revealed conflicting findings. There is a research gap on the effects of interventions on functional outcomes, length of stay and representations. Opioids showed an increased risk of transient adverse events. The overall quality of evidence was low or moderate, thus, additional large high quality trials are needed to better guide emergency physicians in the management of non-specific low back pain and sciatica.

Author affiliations
[1]Department of Physical Therapy, Faculty of Science and Technology, Sao Paulo State University, Presidente Prudente, Sao Paulo, Brazil
[2]University of Western São Paulo (Unoeste), Presidente Prudente, Sao Paulo, Brazil
[3]Institute for Musculoskeletal Health, The University of Sydney and Sydney Local Health District, Sydney, New South Wales, Australia
[4]School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia
[5]Rheumatology Department, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia
[6]Emergency Department, Concord Repatriation General Hospital, Sydney, New South Wales, Australia

Twitter Crystian B Oliveira @crystianbso and Gustavo C Machado @gustavocmachado

Contributors CBO, HEA, DMC, BR, MR, CGM and GCM were involved in the design of the review. CBO, HEA and DC developed the search strategy, and performed study selection, data extraction and risk of bias from included studies. CBO, CGM and GCM were involved in the data analysis. All authors were involved in interpretation and discussion of results, drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication.

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ORCID iDs
Crystian B Oliveira http://orcid.org/0000-0002-6911-7018
Danielle M Coombs http://orcid.org/0000-0003-0005-7851
Gustavo C Machado http://orcid.org/0000-0002-8544-0448

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