

Adverse events associated with local anaesthetic use in musculoskeletal injection therapy: a scoping review

PALMER, Joe <<http://orcid.org/0000-0002-8185-8265>>, WANGIKAR, Manasi, NARSINGHANI, Omisha, BHOPALWALA, Sakina, RAI, Adithya and SANCHEZ BRACERO, Dario <<http://orcid.org/0009-0003-4992-5514>>

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ABSTRACT

Background:

Musculoskeletal disorders (MSDs) are a leading cause of disability worldwide and account for a substantial proportion of healthcare utilisation. Injection therapy combining corticosteroids with local anaesthetic (LA) is widely used for MSD management, including within physiotherapy practice. Despite widespread use, uncertainty remains regarding the safety profile of LAs and the potential risk of adverse events.

Objective:

To map the available evidence on adverse events and associated risk factors following local anaesthetic use in the management of musculoskeletal disorders.

Methods:

A scoping review was conducted following Joanna Briggs Institute methodology and reported according to PRISMA-ScR guidelines. MEDLINE, CINAHL, PubMed and Cochrane were searched from database inception to 2025, alongside targeted grey literature searching. Studies reporting adverse effects of LAs administered for musculoskeletal conditions within physiotherapy scope of practice were included. Data were extracted by multiple reviewers and synthesised thematically.

Results:

Thirty-nine sources were included. Cytotoxicity, particularly chondrotoxicity, was the most frequently reported adverse effect, appearing in 74% of included sources. Evidence indicated reduced chondrocyte viability, mitochondrial dysfunction and apoptosis following exposure to commonly used agents such as lidocaine and bupivacaine. Systemic toxicity, allergic reactions and psychogenic responses were reported less frequently. Key risk factors included higher dose or concentration, prolonged exposure duration, continuous intra-articular infusion, patient comorbidities and accidental intravascular injection.

Conclusion:

Evidence on adverse effects of LA use in MSD management is heterogeneous but consistently highlights cytotoxicity as a potential concern. Further clinical research is required to quantify risk and guide safer injection practices

1. Introduction

Musculoskeletal disorders (MSD), defined as diseases impacting the locomotor system involving bones, joints and soft tissues, are the leading cause of Years Lived with Disability worldwide and place a substantial burden on individuals and healthcare systems [1, 2]. In the United Kingdom, they account for around 30% of primary care consultations and are major contributors to work absence and persistent pain [3-5]. Clinical practice guidelines consistently recommend conservative, patient-centred management as first-line care for MSD [6]. However, the fluctuating and often persistent nature of these conditions means that symptoms frequently recur, and some patients ultimately progress to more invasive treatment options [6-8].

Injection therapy, commonly consisting of a combination of corticosteroid and local anaesthetic (LA), has been used in the treatment of MSD for over 70 years and has been within the scope of physiotherapy practice since 1997 [9, 10]. Recent years have seen a progressive increase in the number of physiotherapists performing injection therapy, likely due to the expansion of advanced practice and First Contact Physiotherapy roles [10, 11]. Although evidence regarding its effectiveness is mixed across a range of MSD such as tendinopathy, tenosynovitis and bursitis, injection therapy is recommended by NICE for the management of conditions such as osteoarthritis (OA) and for individuals with severe sciatica following unsuccessful conservative management [9, 12, 13].

Whilst the predominant driver for corticosteroid use in musculoskeletal injections can be attributed to its anti-inflammatory properties, rationale for LA inclusion appears to be more varied. Amide-type LA are most frequently administered in MSK practice in the form of Lidocaine and Bupivacaine. Their membrane stabilising effects reduce the propagation of action potentials by reversibly blocking sodium gated ion channels, thus limiting nerve conductivity. This makes them well placed to provide local pain relief and aid diagnosis during the clinical examination [9]. A recent survey of injection therapy practices amongst UK Physiotherapists found that 58.1% of respondents cited increased volume to aid steroid dispersal as the main justification for LA use, despite limited evidence of its benefit on outcomes [10, 14]. Emerging evidence has also suggested that LAs may possess anti-inflammatory, antimicrobial, and potential anticancer properties [15]. However, despite these suggested benefits, as with all medicines, LA use is not without risk [16].

Adverse events associated with LA use are well documented in the literature and range from mild allergic-type reactions to more serious complications, including anaphylaxis and local or systemic toxicity [17, 18]. However, despite these potential risks, questionable mechanisms, and limited evidence of benefit to longer-term outcomes, over 80% of UK physiotherapists practising injection therapy report including LA alongside corticosteroids for musculoskeletal conditions [10, 14, 19, 20]. This may be explained, in part, by the fragmented and inconclusive nature of the existing evidence.

The aim of this scoping review was to systematically collate, map, and present the available evidence on adverse events and risk factors of local anaesthetic use for MSD. By synthesising preclinical and clinical literature, this review will describe the range and severity of reported complications, including both frequent and rare events, as well as factors that may contribute to their occurrence. Consolidating the currently fragmented evidence base will help advance injection therapy as a treatment approach for MSD and identify future research priorities in the field.

2. Methods

2.1 Protocol and Framework

This scoping review was conducted following the Joanna Briggs Institute (JBI) methodology for scoping reviews, which provides a structured and rigorous approach to mapping complex and heterogeneous literature [21]. The review also adhered to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines to ensure transparency, reproducibility, and completeness in reporting [22]. The study protocol was not published prior to its undertaking. PRISMA-ScR methodology checklist can be found as supplementary materials 1.

2.2 Eligibility criteria

As per JBI recommendations, the inclusion/ exclusion criteria for this review followed the Population, Concept, Context concept [21].

The inclusion criteria for this scoping review were as follows: (1) studies involving human participants or human-derived cells in in-vitro designs; (2) studies reporting adverse effects of local anaesthetics administered for the treatment of musculoskeletal disorders within the

scope of physiotherapy practice [23]; and (3) studies conducted in any clinical setting or MSK-related specialism, using any study design, including randomised controlled trials, observational studies, case reports, and literature reviews. Exclusion criteria were as follows: (1) studies involving non-human participants; (2) studies in which the injection target was deemed to be outside the scope of physiotherapy practice [23]; (3) studies focused solely on dentistry, dermatology, or regional anaesthesia; and (4) studies not published in English.

2.3 Information Sources and Search Strategy

A comprehensive search strategy was developed in conjunction with the subject librarian at Sheffield Hallam University to capture relevant studies across multiple disciplines. The following electronic databases were screened due to their relevance to the research topic: Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE, Cochrane, and PubMed. A targeted Google Scholar search was conducted with the first 100 hits screened to capture grey literature sources such as unpublished theses, dissertations, conference papers and abstracts [22]. References of studies identified as suitable for inclusion were screened to identify additional relevant sources [21].

Keywords were categorised according to the Population–Exposure–Outcome framework: ("Local anaesthetic" OR "local anesthesia" OR "lignocaine" OR "lidocaine" OR "bupivacaine" OR "ropivacaine") AND ("injection" OR "intra-articular" OR "soft tissue injection" OR "periarticular injection") AND ("adverse effects" OR complications OR "side effects" OR toxicity OR "allergic reactions" OR "negative effects" OR "risks" OR "neurological effects" OR "cardiovascular effects" OR "adverse reactions") AND ("joint" OR "knee" OR "shoulder" OR "elbow" OR "hip" OR "tendon" OR "ligament" OR "bursa" OR "synovial tissue" OR "muscle" OR "soft tissue") NOT ("nerve block" OR "peripheral nerve block" OR "regional anaesthesia").

The search was performed in April 2025 from the inception of each included database.

2.4 Selection of Sources of Evidence

Following duplicate removal, titles and abstracts were independently screened by two reviewers, with any discrepancies resolved by a third independent reviewer. Full-text screening of all sources was subsequently undertaken independently by four reviewers, with disagreements resolved through consultation with the supervisory team.

2.5 Data extraction and synthesis

Data was extracted using a standardised table and checked by two members of the research team following a piloting exercise using one included study. This consisted of the following: author, title, study design, aim/purpose, study population, type of local anaesthetic, targeted tissue/joint, mode of administration, reported adverse effects, identified risk factors, and key findings. No formal quality appraisal was conducted, consistent with scoping review methodology, as the aim was to map the evidence base rather than evaluate intervention effectiveness [21].

2.6 Patient and public involvement

Patients and members of the public were not involved in the conceptualisation, design, analysis, interpretation, or dissemination of this study.

2.7 Equality, diversity and inclusion statement

The research team comprised six individuals from the United Kingdom (JP), India (MW/ ON/ SB/ AR) and Spain (DS) representing a breadth of cultural and ethnic backgrounds. The group was gender-balanced, with three males and three female researchers. Four authors (MW/ ON/ SB/ AR) completed this work as part of their postgraduate MSc studies at Sheffield Hallam University. The remaining two authors (JP and DS) are early career researchers.

To ensure comprehensive mapping of the existing evidence, no restrictions were placed on participant characteristics within the included sources. Our team hopes that these findings will support future researchers in identifying, exploring and addressing health inequalities within this field.

Results

A total of 4313 results were identified through the database search. Following the removal of duplicates, titles and abstracts of 3392 studies were screened. One hundred and eighty-seven articles were included for full-text screening, of which 158 were excluded for not meeting the inclusion criteria. Twenty-nine articles were identified through database searching, with an additional five studies retrieved via Google Scholar. One article was identified through

reference list screening, and four were included through hand searching. In total 39 studies [24-62] were included in the final scoping review and taken to data extraction (see figure 1).

Figure 1: PRISMA diagram

Sources were published between 1992 and 2024 and consisted of 12 (30.7%) experimental studies, 11 (28.2%) literature reviews, 5 (12.8%) systematic reviews, 3 (7.7%) case series, 2 (5.1%) cohort studies, 1 (2.6%) case report, 1 (2.6%) retrospective comparative study, 1 (2.6%) pilot study, 1 (2.6%) text and opinion, 1 (2.6%) book, and 1 (2.6%) editorial. All experimental studies were conducted in-vitro.

Following data extraction, the findings were organised into two main themes: Adverse effects (Figure 2) and Risk factors contributing to adverse effects (Figure 3). Each was further divided into subthemes reflecting common patterns and classifications across the included studies. Details of the studies contributing to the development of these themes are provided in Supplementary Materials 2.

Figure 2- Adverse events honey-comb chart

1.1 Cytotoxicity

Cytotoxicity was the most frequently reported adverse effect, appearing in 29 (74.3%) sources. Four sources described general cytotoxicity, including reduced cell viability, apoptosis and mitochondrial dysfunction. Chondrotoxicity was the predominant tissue-specific finding, reported in 25 of the 29 sources. It was most often associated with continuous intra-articular LA administration in the glenohumeral joint (n = 12), with a smaller number of reports involving the knee (n = 7). Lidocaine and bupivacaine were the most frequently implicated agents reported in 26 sources and were associated with decreased chondrocyte viability, impaired mitochondrial activity and apoptosis.

1.2 Systemic Toxicity

Systemic toxicity was documented in 6 studies (15.4%). Local Anaesthetic Systemic Toxicity (LAST), described as rare but potentially life-threatening, was reported in 6 of these. Central Nervous System (CNS) manifestations appeared in 6 studies, including agitation, seizures, tinnitus, dizziness, perioral numbness and loss of consciousness. Cardiovascular System (CVS) involvement was reported in 5 studies, with presentations such as hypotension, bradycardia, arrhythmias and cardiac arrest. Methemoglobinemia was identified in 3 studies, characterised by cyanosis, fatigue, headache and oxygen desaturation unresponsive to supplemental oxygen.

1.3 Allergic and Hypersensitivity Reactions

Allergic or hypersensitivity reactions were reported in five sources (12.8%). Anaphylaxis was the most frequently reported allergic/ hypersensitivity reaction, appearing in four studies. Of these, two were referenced with regards to IgE mediated type 1 hypersensitivity reactions, typically presenting with urticaria, angioedema, bronchospasm, and hypotension. Type IV delayed hypersensitivity was also noted in two sources, manifesting as contact dermatitis, erythema, oedema and pruritus. Two studies reported general allergic reactions without specifying type. Ester-type LAs were more commonly associated with allergic responses.

1.4 Other Adverse Effects

A range of other adverse effects not fitting the above categories were reported in eight sources (20.5%). Psychogenic reactions such as hyperventilation, dizziness, fainting and anxiety were reported in five studies. Vasovagal responses were reported in two studies, presenting with bradycardia, hypotension and transient loss of consciousness. Pseudo-allergic reactions were also reported in two sources, mimicking allergic responses in the absence of IgE mediation. General side effects such as nausea, vomiting, headache, urinary retention, and bruising appeared in one source. Malignant hyperthermia was reported in a single source.

2. Risk Factors

Figure 3- Risk factors funnel chart

2.1 Dose and Concentration

Dose or concentration-related toxicity was the most commonly suggested risk factor, reported in 20 sources (51.2%). Higher concentrations or cumulative doses of LAs were consistently suggested to be associated with increased risk of adverse effects. Bupivacaine and lidocaine were the drugs most frequently implicated with reported concentrations ranging from 0.031-2% (most commonly 0.5%) and 0.001-2% (most commonly 1%) respectively. Similar doses were reported for other amide-type anaesthetics such as ropivacaine, mepivacaine, levobupivacaine with concentration ranges from 0.031-2%.

The highest reported volume for a single bolus intra-articular LA injection was 40-60ml of 0.25% or 0.5% bupivacaine or 40-60ml 1% lidocaine which were performed following arthroscopic Anterior Cruciate Ligament Reconstruction (ACLR). Studies discussing prolonged exposure reported times ranging from 15 minutes in a single in vitro study to 65 Hours administered via pain pump. The sources reporting on the use of pain pumps typically involved infusion of 0.5% bupivacaine with volumes ranging from 100ml to 377ml and infusion rates of 2-3ml/hr (low-flow) to 4-5ml/hr (high-flow).

2.2 Patient-Specific Factors

Patient-specific risk factors were discussed in 14 sources (35.9%). Age was specifically referenced in five studies, often in relation to increased risk of adverse events in older people, with one of these making specific reference to LAST risk in 'infants' and another referencing 'younger' age groups in relation to chondrotoxicity risk. Osteoarthritis (n=5) and cardiovascular disease (n=4) were also frequently discussed. Hepatic or renal dysfunction (n=2), pregnancy (n=2), and heightened anxiety or needle phobia (n=2) were each identified in two studies. Other less commonly reported risk factors included low body weight (n=1), reduced muscle mass (n=1), and genetic enzyme deficiencies (n=1) (e.g., pseudocholinesterase deficiency).

2.3 Duration of Administration & Mode of Administration

Duration of LA exposure emerged as a commonly reported risk factor for adverse events, particularly when administered via continuous intra-articular infusion using a pain pump. This was identified in 13 sources (33.3%), 11 of which specifically related to chondrotoxicity, one systemic toxicity and one general cytotoxicity. Studies which provided specific time frames typically referenced administration periods of 30-60 minutes (n=6), with one study reporting 60-240 minutes.

Risk factors relating to injection technique and mode of administration were discussed in 14 sources (35.9%). Accidental intravascular injection was referenced in seven sources and was commonly discussed in relation to systemic toxicity.

2.4 Tissue Vascularity

Two sources (5.1%) suggested that tissue vascularity may act as a risk factor for adverse events, indicating that injections into highly vascular tissues may increase systemic absorption and potentially elevate the risk of CNS and CVS toxicity.

Discussion

This scoping review provides a comprehensive overview of the available evidence on adverse events following LA administration for MSD. Experimental designs constituted the majority of relevant sources, with narrative literature reviews being the second most common study design. Our synthesis gives the reader insight into the most frequently reported adverse events and risk factors associated with LA use.

Cytotoxicity, particularly chondrotoxicity, emerged as the most frequently reported adverse outcome across the included literature. Substantial LA-induced tissue damage was described in both cartilage and surrounding soft tissues, although study designs, models, and outcome measures varied considerably. Although some studies suggested that chondrotoxicity may disproportionately affect smaller joints, the glenohumeral and knee joints were the most frequently cited in reports of chondrotoxicity [52]. This must however be considered in light of the fact that these are amongst the most commonly injected joints in clinical practice [10]. Their prominence in the adverse event literature may therefore reflect exposure frequency and reporting patterns rather than an inherent size-dependent vulnerability.

Five included studies suggested OA to be a potential risk factor for LA-induced chondrolysis. Degenerative cartilage is characterised by structural disruption, including superficial layer compromise, chondrocyte depletion, and extracellular matrix degradation [60, 63]. These pathological features may increase cartilage tissue permeability and reduce resilience to chemical insult. When considered in light of the poor vascularity of chondral tissue, this could be further exacerbated by prolonged intra-articular exposure [60,64]. The same pathophysiological principles may partially explain the proposed association between smaller joints and increased cytotoxicity. Reduced synovial fluid extrusion in smaller or non-weight-bearing joints may prolong intra-articular retention of the anaesthetic [52]. Conversely, larger

compartmentalised joints such as the knee may permit greater dispersion and fluid exchange, potentially diluting the agent and limiting sustained focal exposure [35]. Taken together, these findings suggest that chondrotoxicity may not be governed by joint size in isolation, but by the interaction between degenerative pathology and site-specific pharmacokinetics. While mechanistic explanations are primarily derived from in vitro and animal models, the convergence of degenerative pathology and altered pharmacokinetics appears repeatedly in the literature and warrants further investigation in clinical populations.

LAs are frequently administered as intra-articular injections in the management of OA, often in combination with corticosteroids, which themselves have been suggested to exacerbate chondrotoxic effects [65]. Recent surveys of clinicians delivering injection therapy for MSD suggest that although most choose to include LA when administering intra-articular injections, only 10% consider chondrotoxicity when selecting pharmacological agents [10, 65]. This finding aligns with patterns identified across the mapped literature and highlights a potential gap between emerging experimental evidence and routine clinical decision-making. Osteoarthritic cartilage demonstrates structural compromise, including chondrocyte depletion and extracellular matrix degradation. The routine intra-articular use of LA agents with potential chondrotoxic potential presents a clear clinical paradox and may contribute to underreporting of adverse effects to chondral surfaces [52, 63, 66]. While NICE (2022) recommends intra-articular corticosteroid injections in specific circumstances, including when other treatments are ineffective or to facilitate therapeutic exercise, the balance between symptomatic benefit and potential structural risk remains incompletely understood [12].

Several procedural and pharmacological factors were repeatedly reported in relation to increased cytotoxic risk. Higher doses, elevated concentrations, prolonged exposure, continuous intra-articular infusion, and administration in the presence of compromised cartilage were commonly cited [36, 52, 54, 60, 62]. Although most injecting physiotherapists operate under a Patient-Group Direction (PGD) and are thus limited as to dosage and volume they can deliver, 30% of surveyed practitioners in 2024 were independent prescribers [10]. This increase in prescribing autonomy coupled with the apparent variation in injection therapy practices highlights the need for clear guidance as to what is considered a safe upper limit for concentration and volume of LA used in musculoskeletal injection therapy to reduce the risk of cytotoxicity [9, 10]. Intra-articular pain pumps were often suggested to contribute to chondrotoxicity and long-term joint damage, with nine included studies implicating continuous delivery systems in cumulative toxicity. Such findings were frequently reported within the literature since 2007 and has likely contributed to the apparent decline in intra-articular pain pump use in practice [32, 33, 55].

Agent-specific variation was also evident across the literature. Bupivacaine was most frequently referenced in relation to cytotoxic potential, with multiple studies reporting both apoptosis and chondrocyte necrosis [40, 60, 67]. Comparative analyses generally reported greater chondrotoxicity with bupivacaine than with lidocaine or ropivacaine, the latter often described as having a comparatively favourable safety profile [41, 45]. However, much of this evidence derives from in vitro or animal models, limiting direct clinical extrapolation. Notably, intra-articular administration of bupivacaine particularly via continuous infusion pain pumps was repeated repeatedly in adverse outcomes [32, 33, 62].

Systemic toxicity arises when circulating plasma concentrations of LA reach levels sufficient to exert effects beyond the intended site of action. This phenomenon, commonly referred to as LAST, most prominently affects the central nervous and cardiovascular systems [30, 68]. Mechanistically, toxicity is attributed to blockade of voltage-gated sodium channels, disrupting neuronal impulse transmission and myocardial conduction [69]. Early clinical features typically involve central nervous system excitation, including circumoral paraesthesia, tinnitus, agitation, and seizures, which may progress to central nervous system depression at higher concentrations [70]. Cardiovascular manifestations include conduction disturbances, arrhythmias, myocardial depression, and, in severe cases, cardiovascular collapse [71]. Our results found Bupivacaine to be more frequently cited in cases of severe cardiotoxicity, potentially related to its high affinity for cardiac sodium channels and slow dissociation kinetics. In contrast, lidocaine is more commonly associated with central nervous system symptoms, reflecting comparatively lower cardiotoxicity and faster channel binding dynamics [69, 70].

Inadvertent intravascular injection was reported in two studies as notable technical complications. Safe administration of injection therapy is central to recommendations for training programmes set out by the Chartered Society of Physiotherapy [72]. Procedural safeguards such as the performance of a safety aspiration prior to injection serve to reduce the likelihood of accidental intravascular injection are considered essential components of injection therapy training [9]. Despite this, severe adverse reactions following accidental intravascular injection are documented within the literature [57]. This is however complicated by findings within this review from two studies suggesting local tissue vascularity may contribute to the risk of increased systemic absorption [24, 25].

Broader patient specific factors and comorbidities were also suggested to be implicated in increased risk of systemic toxicity. Two included studies highlighted hepatic/ renal dysfunction in relation to worsened systemic toxicity, with plasma LA concentrations reported to be substantially higher in affected patients [24]. As most LA undergo primary hepatic metabolism, clearance depends on hepatic blood flow and extraction ratio, with only the unbound fraction

exerting pharmacological activity [24, 69]. Impaired liver or kidney function can slow drug metabolism and excretion, raising plasma concentrations and the risk of accumulation [18, 73]. Since age is a major risk factor for osteoarthritis, often treated with injections including local anaesthetics, age-related declines in renal and hepatic function may prolong exposure, lower toxicity thresholds, and increase the risk of systemic toxicity [4, 12, 18, 73-75].

Hypersensitivity reactions are arguably the most significant risk associated with administration of pharmacological agents such as LA due to their potential progression to life-threatening anaphylaxis [26, 30]. Our search identified four sources that discussed anaphylaxis in the context of LA use, all of which were narrative literature reviews. According to van Wicklin (2024), true allergic reactions following LA use are rare, accounting for <1% of associated adverse reactions; a figure consistently quoted across sources [25]. Another consistent finding with our results was the more frequent association of adverse events with the use of ester type LA in comparison to amide types [25, 30]. This is of particular interest as amide types are the most frequently used in musculoskeletal practice in the form of Lidocaine and Bupivacaine [9]. Critically however, a lack of evidence demonstrating additional benefit from the inclusion of LA as part of injection therapy for MSD raises questions as to whether this risk could be eliminated altogether through discontinued use of LA in practice [10, 14]. If increasing injection volume to aid medicine dispersion is a consideration for clinicians, particularly with intra-articular injections, exploring the effectiveness of using safer alternatives often used in placebo-controlled studies, such as saline, appears to be worthy of investigation [10, 76].

Strengths

This scoping review offers a comprehensive mapping of the available literature relating to adverse effects associated with local anaesthetic use in MSD. The inclusion of diverse study designs enabled broad exploration of both reported adverse outcomes and proposed risk factors. The structured thematic synthesis enhances transparency and highlights recurring patterns, particularly in relation to cytotoxicity and dose- and time-dependent toxicity. The focus on physiotherapy-relevant injection practice strengthens the contextual applicability of the findings.

Limitations

The exclusion of nerve block procedures, while intentional to maintain alignment with physiotherapy scope of practice, limits generalisability to the wider use of local anaesthetics. A substantial proportion of the evidence derives from in vitro and experimental models, which may not fully replicate in vivo human physiological conditions. The overall evidence base was

heterogeneous in design and reporting, and no formal risk of bias assessment was undertaken, consistent with scoping review methodology. As such, the findings should be interpreted as exploratory and hypothesis-generating rather than definitive guidance for clinical practice.

Recommendations for Future Research

The volume and consistency of literature discussing chondrotoxicity risk warrants a focused systematic review to evaluate the risk of chondrolysis following intra-articular LA administration. Future research should seek to quantify clinical risk and clarify the influence of modifiable factors, including dose, concentration, and exposure duration. Greater emphasis on prospective in-vivo monitoring and longitudinal outcome data is also required. Where local anaesthetic is used primarily to facilitate dispersion, comparative studies evaluating inert alternatives should be considered to determine whether potential risks may be mitigated.

Conclusion

This scoping review maps the breadth of available evidence regarding adverse effects and associated risk factors following local anaesthetic administration in musculoskeletal practice. Cytotoxicity, particularly chondrotoxicity, emerged as the most frequently reported adverse effect, with dose, concentration, exposure duration and continuous intra-articular infusion repeatedly implicated as contributory factors. Systemic toxicity, allergic reactions and technical complications were less frequently reported. Patient specific characteristics, choice of injectable, dosage, duration and method of administration were commonly reported risk factors for adverse events following LA. Further robust clinical research is required to clarify true risk magnitude, optimise safe dosing strategies, and inform evidence-based practice.

Competing Interests

The authors have no competing interests to declare.

Contributors

Prepared in line with the CRediT (Contributor Roles Taxonomy).

JP: Conceptualisation, Methodology, Validation, Writing (original draft and review & editing), Visualisation, Supervision, Project administration. **MW/ ON/ SB/ AR:** Methodology, Formal analysis, Investigation, Data curation, Writing (original draft and review & editing),

Visualisation. **DS:** Methodology, Validation, Writing (original draft and review & editing), Visualisation, Supervision, Project administration.

JP is the guarantor of the work.

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Ethics

Ethical approval was not required as this study involved secondary analysis of existing literature.

Data sharing statement

No additional data are available

What is already known?

1. MSD are the leading cause of disability worldwide
2. Injection therapy is a common intervention used in those with persistent/ recurring symptoms, most often consisting of a combination of corticosteroid and local anaesthetic
3. Commonly reported factors that influence clinicians' decision to offer LA as part of injection therapy for MSD are often not evidence based
4. The existing literature on potential adverse events associated with LA use in the management of MSD has not been comprehensively mapped or synthesised

What are the new findings?

1. Most of the studies investigating adverse events following LA use in-vitro experimental designs or non-systematic literature reviews
2. Cytotoxicity, specifically chondrotoxicity emerged as the most frequently reported adverse event and was often suggested to be exacerbated by prolonged exposure, higher dosages and the presence of osteoarthritis.
3. Other serious adverse events such as systemic toxicity and allergic reaction were less frequently reported
4. Despite being fragmented, the current evidence base is sufficiently developed to support a focussed systematic review on the risk of chondrotoxicity following intra-articular LA use

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