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REVIEW

The use of skeletal muscle relaxants in musculoskeletal injuries: what is the evidence?

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Abstract

Skeletal muscle relaxants (SMRs) consist of a heterogeneous group of medications with a side effect profile of concern. The aim of this paper was to review the evidence of use of SMRs in the treatment of sports injuries. A literature search between 2005 – 2018 (Ovid MEDLINE, SPORTDiscus and SCOPUS) were conducted. In addition, citations within articles were searched, and the most commonly prescribed SMRs in South Africa were also used to explore the literature for additional publications. Relevant studies that met the inclusion criteria were selected. Clinical recommendations for general practitioners are given based on the Strength of Recommendation Taxonomy (SORT) level of evidence. Combination drugs rather than single agents are mostly used, however the effectiveness of SMR agents, single and in combination, as well as its significance as opposed to analgesics and non-steroidal anti-inflammatory drugs, still has to be evaluated. Evidence suggest SMRs to be probably effective for use in non-specific lower back pain (acute and chronic lower back muscle strains, ligament sprains, soft tissue contusions), as well as for whiplash associated disorder, mechanical neck disorders, piriformis syndrome, lateral epicondylosis, and plantar fasciitis. It does not appear if there is a role for SMRs as part of combination management for acute cervical strains, post-exercise muscle soreness or myofacial pain syndrome. However, substantial evidence to confirm the use of SMRs in the treatment of sports injuries have not been adequately investigated and is currently largely based on case reports and general reviews.

Keywords: muscle relaxant, sports injuries, musculoskeletal injuries, management, exercise, athlete

Introduction

The escalation and interest in the range of elite and recreational sports participation over the last years lead to the number and variety of injuries sustained to increase concomitantly.[1-3] Regardless of increased emphasis on injury prevention in sports by way of awareness, better conditioning and specific preventative measures, injury occurrence remains a problem.[4] The focus of treatment of such an injury is to facilitate the safe return to sports, reducing the risk of re-occurrence of an injury while alleviating psychological stress and promoting health.[4]

The treatment of a sports injury aims to reduce pain, swelling, inflammation, and muscle spasm associated with injury, as well as facilitating restoration of function and return to sports.[4]

Treatment modalities that may affect tissue healing include *non-pharmacological* procedures such as the POLICE principle (Protect, Optimal Load, Ice, Compress, Elevate) and physiotherapy modalities, as well as *pharmacological* management (analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and skeletal muscle relaxants). The choice of the preferred modality used may differ when treating an acute injury as opposed to a chronic injury. Some of these modalities are established and have been used widely, but many novel treatment modalities are gaining favour (Table 1).

Table 1: Established and novel treatment modalities for soft tissue injuries

Established:
1. POLICE[5]
2. Analgesics[6]
3. Anti-inflammatory agents (NSAIDs[7-8], COX-2 inhibitors[9], Corticosteriods[10-14]
4. Physiotherapy modalities[15-17]

Novel treatment modalities:
1. Skeletal muscle relaxants (focus of this article)
2. Other modalities (experimental)
   a. Platelet rich plasma (PRP)[18-19]
   b. Prolotherapy (anti-fibrotic agents e.g. Aprotinin)[20-21]
   c. Basic Fibroblastic Growth Factor (b-FGF)[22-23]
   d. Relaxin (inhibitor of fibrotic cytokines)[24-25]
   e. Glyceryl trinitrate[26-28]

An in-depth discussion of each of these modalities is beyond the scope of this review. Our focus is on the potential use of skeletal muscle relaxants in sports injuries. As most of these drugs have little to no direct action on striated skeletal muscle's contractile mechanism, the term *muscle relaxants* is actually a misnomer.[29] Therefore, for the purpose of this review, drugs that have been approved to treat muscular pain or spasms from musculoskeletal conditions, will be referred to as skeletal muscle relaxants (SMRs). Limited information is available on the prescription and application of SMRs in the sports environment. Therefore,

the aim of this paper is to review the role that SMRs play in the management of sports injuries.

Relevant Definitions

Spasticity vs. spasm:

Spasticity and spasms are two distinct aetiologies and responds differently to certain medications. Antispasmodics and antispasticity agents are generally not interchangeable. *Spasticity* is a motor neuron disorder that manifests as a continuous muscle spasm that results in increased muscle tone and stiffness. *Muscle spasms* are involuntary localised contractions of a muscle or muscle group that causes pain. The exact relationship between the pain and muscle spasm is not well understood and the cycle of pain-spasm-pain is not strongly supported by scientific evidence. Studies report that pain have a tendency to inhibit rather than facilitate voluntary reflex contractile function.[30-34]

Sports injury:

In the recent consensus statement on pain management in elite athletes by the International Olympic Committee, a sports injury is defined as a new or recurring musculoskeletal complaint incurred during competition or training that require medical attention, regardless of the potential absence from competition or training.[35] Engebretsen et al.[36] have previously suggested the definition of a sports injury should require restricted activity for at least one day.

Sports injuries can occur in very different ways and our understanding thereof has increased in recent years. *Acute injuries* occur as a result of a single-impact macrotrauma, such as a sudden ankle sprain, joint dislocation, or ruptured tendons caused by a single traumatic or forceful blow or event. *Overuse (also referred to as chronic) injuries* occur as a result of repetitive microtrauma caused by frequent, repeated injury of muscles, tendons, ligaments, joints, and bones. A persisting or constantly recurring injury that may involve a variety of tissues at a number of different sites. *Acute on chronic injury* is an acute exacerbation of a chronic condition. These basic mechanisms of injury or a combination thereof, can produce injury in any part of the body and are responsible for all sports injuries.[4]

Acute vs. chronic pain:

Pain associated with any sport injury is classified as *acute (*pain duration up to 6 weeks), *subacute* (pain duration between 6–12 weeks) or *chronic* (pain duration of 3 months or longer).[35,37] Acute and chronic pain are different clinical entities. *Acute pain* is provoked by a specific disease or injury, it serves a useful biologic purpose, is associated with skeletal muscle spasm and sympathetic nervous system activation and is self-limited. *Chronic pain*, in contrast, may be considered a disease state. It is pain that outlasts the normal time of healing, if associated with a disease or injury. Chronic pain may arise from psychological states, serves no biologic purpose, and has no recognizable end-point.[38]

Sprain vs. strain:

A *sprain* is a stretch, or a tear of a ligament caused by direct or indirect trauma. A *strain* is a pull or a tear of a muscle or tendon caused by direct, forceful contact, excessive muscle contraction or overstretching (acute), or monotonous repetitive movement (chronic).[39]

Background information on management of musculoskeletal injuries

Wellbeing is a patient's main concern, however a culture of risk is deeply embedded in sports tradition. It is well recognised that in the management of acute pain in those athletes restricted from same-day return to play (RTP), medications should not be prescribed as a stand-alone treatment. It remains essential to identify the injury and the cause of pain and to include other non-pharmacological measures.[35] Therefore, the treatment of sports injuries should include both non-pharmacological and pharmacological management.

Non-pharmacologic modalities include the POLICE principle (Protect, Optimal Load, Ice, Compress, Elevate)[5] Traditionally, the healing approach was RICE (Rest, Ice, Compress and Elevate), however inappropriate amounts of resting an injury may cause further tissue damage as it does not allow the body to remodel necessary bony, musculoskeletal or collagenous structures at appropriate times throughout the healing phases, and promoting inactivity as a form of treatment, will result in the body adapting for rest. The short-term use of ice (in combination with paracetamol) will provide an equivalent analgesic effect without serious side effects. Elements of the POLICE principle, and application thereof, may differ in chronic injury where exercise rehabilitation remains the cornerstone of management to regain function.[40]

Various physiotherapy modalities are used in the treatment of acute and chronic muscle stiffness and pain. Dry needling, transcutaneous electrical nerve stimulation (TENS), passive stretching, massage, trigger point release and myofascial release have shown to be effective in reducing pressure pain threshold and increase muscle flexibility.[15-17]

Pharmacologic modalities include the use of NSAIDs or COX-2 inhibitors (celecoxib, rofecoxib, valdecoxib), centrally acting agents (tramadol/acetaminophen), opioids, and oral SMRs. All these agents help to alleviate discomfort associated with pain and muscle spasm.[41-50]

There are few good studies available to guide the rationale for the use of medications in the treatment of acute musculoskeletal injuries. When examining clinical trials, a number of factors complicate evaluation of efficacy of one drug over another in the acute setting. Factors include: inconsistent and vague inclusion criteria, the use of subjective and different clinical end points, varying doses of study drugs, highly different placebo response rates, underpowered trials, poorly clarified non-pharmacologic interventions and inappropriate statistical procedures.[51-53] It is thus complicated to generalise the comparative effectiveness of distinctive agents and/or combinations thereof. Furthermore, the

majority of acute musculoskeletal conditions are self-limiting by nature, therefore experience in the long-term use of medications for musculoskeletal spasm and pain is quite limited.[53]

NSAIDs, COX-2 inhibitors, and muscle relaxants respectively, accounted for 16.3%, 10%, and 18.5% of total prescriptions for back pain in the United States in 2000. Among individual drugs, ibuprofen and naproxen accounted for most of the prescriptions for traditional NSAIDs (60%), whereas two thirds of the prescriptions for muscle relaxants were attributable to cyclobenzaprine, carisoprodol, and methocarbamol.[54]

There is some evidence that professional athletes use muscle relaxants and other medications with or without medical advice. Various surveys since 2000 on the trends and use of medication intake by elite male football players prior to international matches, have indicated muscle relaxant usage between second and fourth highest. In many instances various different preparations were taken simultaneously. The number of players taking muscle relaxants increased significantly over the four tournaments (2.2% in the 2000 FIFA Futsal World Cup to 14.3% in the 2012 FIFA Futsal World Cup, $p < 0.05$). This high consumption of medication use in international football raises the questions on whether medication is used for therapeutic reasons only.[55-58] The use of medication in elite female soccer players, however seems fewer than in adolescent male soccer players during global world contests.[59]

The prescription of medications should be consistent with established, recognised pharmacological and pharmacodynamic principles (i.e. the biochemical, physiologic, and molecular effects of drugs on the body). This include the time of onset of action, the effectiveness for pain relief, any potential side effects and complications as well as the route of administration.[35] Administration can be oral, intramuscular, intravenous and/or topical. Physicians, more often than not, recommend or prescribe oral medications for the treatment of acute musculoskeletal pain.[29] In general, acute pain medication should not be used for more than five days. Medication for more severe injuries associated with moderate to severe pain, should be re-evaluated if pain persists beyond 10 days.[35]

What is a skeletal muscle relaxant (SMR)?

SMRs consist a diverse group of medications, with structurally unrelated active ingredients, and with varied pharmacologic profiles and side effects.[34] These drugs have been approved to treat two different types of underlying conditions: spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions. Spasticity is not covered in this article. SMR drugs used for musculoskeletal injuries are presented in Table 2.

The goal of SMR administration is to reduce skeletal muscle spasm, to assist in pain relief and to increase mobility of affected muscles.[24,39] Pain relief can be affected by either muscle relaxation and/or sedation due to the muscle relaxants. Also more randomised control trials (RCTs) are needed to confirm effectiveness, but from a clinical perspective combination drugs (e.g. SMRs and NSAIDs or Cox-2 inhibitor / SMRs and tramadol or acetaminophen) seem to be more effective than single agents.[39]

Mechanism of action: SMRs generally depress spinal and supraspinal polysynaptic pathways with prominent non-specific sedative properties. SMRs do not appear to relax skeletal muscle directly or to depress muscle excitability, neuromuscular transmission or depression of neuronal conduction.[39]

Pharmacology: SMRs seem to have a similar onset of action, but vary substantially in duration of activity, elimination half-lives, pharmacokinetics and pharmacodynamics. Most SMRs are metabolised in the liver.[39]

Side-effects: The main common side-effect shared by SMRs is drowsiness and dizziness due to the effect on the central nervous system (CNS). Less common joint adverse events include nausea, vomiting, appetite loss and headache.[39] Specific side-effects of each drug are listed in Table 2.

Table 2: Most common muscle relaxants used in painful musculoskeletal conditions[29,34,39]

Active ingredients	Mechanism of action	Route of administration	Unique side effects*	Contra-indications	Drug interactions
Antispasmodics					
Carisoprodol (e.g. Vanadom)	Mechanism of action probably due to sedative effect. Meprobamate is its active metabolite. Interrupts interneuronal activity in the descending reticular formation and spinal cord.	Oral	Agitation, nervousness, tremor, irritability, fainting, seizures, depression, dependency.	Pregnancy, breastfeeding.	CYP2C19 inhibitors (e.g. celecoxib, chloramphenicol, fluoxetine, fluvoxamine, omeprazole may reduce elimination. CYP2C19 inducers (e.g. carbamazepine, norethisterone, rifampin) may increase elimination.
Chlorzoxazone† (e.g. Paraflex)	Acts primarily at the spinal cord and subcortical areas of the brain to inhibit multisynaptic reflex arc.	Oral	Malaise, urine discoloration. Hepatotoxicity with jaundice may be fatal.	Pregnancy/ lactation, known hypersensitivity to the drug.	CNS depressants Caution with alcohol

Cyclobenzaprine (e.g. Myprocam)	Derivative of tricyclic antidepressants, acting primarily at brain stem level. Reduces acceptability of alpha and gamma motor neurons.	Oral	Numbness dry mouth, fatigue Anticholinergic effects (dizziness, dry mouth, constipation, urinary retention, ocular hypertension), palpitations, sinus tachycardia, cardiac conduction disturbances.	Caution with Tramadol, barbiturates, alcohol & other CNS depressants, children under 12yrs. Possible hepatotoxicity.	Serotonergic agents. CNS depressants. CYP1A2 inhibitors (e.g. ciprofloxacin, fluvoxamine, oral contraceptives, verapamil) may reduce elimination. CYP1A2 inducers (e.g. tobacco) may increase elimination.
Metaxalone (e.g. Skelaxin)	Mechanism unknown, but is thought to cause myorelaxation via sedation.	Oral	Paradoxical muscle cramps and respiratory depression when used with opioids, benzodiazepines, or barbiturates. Rare in haemolytic anaemia, leukopenia, jaundice.	Severe renal & liver impairment, children, pregnancy & lactation, hepatic impairment.	CNS depressants Caution with alcohol
Methocarbamol (e.g. Robaxin)	Unknown mechanism but is thought to cause myorelaxation via sedation. Carbamate derivative of guaifenesin.	Oral	Hypotension, syncope, thrombophlebitis, amnesia, confusion, diplopia, mild muscular incoordination, nystagmus, seizures, vertigo, blurred vision, conjunctivitis, nasal congestion, metallic taste.	Alcohol, pregnancy, other CNS depressants. Hypersensitivity to methocarbamol. Caution in renal & hepatic insufficiency and if using dangerous machinery.	CNS depressants
Orphenadrine (e.g. Norflex)	Anticholinergic receptor antagonist. H1 receptor antagonist. NMDA receptor antagonist	Oral Intramuscular	Confusion, urinary retention, dry mouth, dry eyes, weakness, nasal congestion. Ataxia, excitement, easy bruising, nose bleeds, sore throat, fever, dyspnoea. Rare in aplastic anaemia.	Pregnancy/lactation, glaucoma, myasthenia gravis, enlarged prostate.	CNS depressants.
Thiocolchicoside (e.g. Neoflax)	Anti-inflammatory and analgesic properties. Acts as a competitive $GABA_A$ receptor antagonist, and glycine receptor antagonist with similar potency and nicotinic acetylcholine receptors to a much lesser extent.	Oral Intramuscular Topical	Allergy, vasovagal reactions, hepatotoxicity in systemic routes.	Powerful convulsing properties. Contra-indicated in individuals prone to seizures. Teratogenic and decreased fertility in men.	CNS depressants. Anticonvulsants. Antibiotics e.g. Amikacin, Clindamycin.
Tolperisone (e.g. Myotop SR)	Centrally acting SMR that acts at the reticular formation in the brain stem by blocking voltage-gated sodium and calcium channels.	Oral	Muscle weakness, arterial hypotension, dry mouth.	Myasthenia gravis, pregnancy & lactation.	Other centrally acting muscle relaxants. Benzodiazepines or NSAIDs may need reduced dosage.
Antispasticity drugs					
Benzodiazepines (e.g. Vallium)	$GABA_A$ receptor agonist that results in presynaptic inhibition in the spinal cord.	Oral Intramuscular Intravenous	Antegrade amnesia, hangover effect. Cardiac or pulmonary arrest with IV administration. Potential for dependence /abuse, cognitive impairment, withdrawal symptoms with discontinuation.	Pregnancy, allergy, glaucoma. Severe hepatic impairment.	Some herbal supplements. Grapefruit. Drugs e.g. fluconazole, ritonavir- use lower dose. CNS depressants.
Botulinum A (e.g. Botox)	A neurotoxin that inhibits release of acetylcholine at the neuromuscular junction.	Sub-cutaneous	Flu-like symptoms, rash and muscle weakness at injection site.	Pregnancy, lactation, allergy to other botulinum species.	–

CNS: Central Nervous System
CYP: Cytochrome P450
*Common side effects shared by all Skeletal Muscle Relaxants are listed in the text.
†Recently discontinued
$GABA_A$: γ-Aminobutyric acid
IV: Intravenous
NMDA: N-Methyl-D-aspartate
NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

Abuse potential: Although there is a potential, addiction and social recreational use seldom occur in those patients that use SMRs responsibly. Literature indicates that SMRs are not commonly the primary drugs of abuse.[60]

Method of Grading of Evidence

An electronic literature search for peer-reviewed publications on SMR use in sport was conducted in June 2018 using the keywords:[a] *'muscle relaxant' AND 'athlete OR sport OR exercise'*. Subject keywords were used in isolation and combination within each data source to identify relevant publications. The initial data sources included Ovid MEDLINE, SPORTDiscus and SCOPUS and search results were limited to full text, English language and human-only studies from peer reviewed journals published 2005 – 2018. The bibliographies of the most relevant articles were pearled for additional, relevant sources that fitted within the scope of the study focus and were reviewed for inclusion in the review (these included publications prior to 2005). Additionally, a shortlist of the most commonly prescribed SMRs in South Africa was compiled and used to explore the literature for additional publications. Articles were only included if they matched the criteria set out in Table 3 and at least two of the three reviewers (DJvR, AJvR, CV) deemed its content appropriate to the review.

Table 3: Criteria for study selection

Inclusion criteria:	Exclusion criteria:
• English language	• Non-peer reviewed
• Human studies	• Animal studies
• Peer-reviewed	• Contextually irrelevant
• Publication date 1997 – 2018 (including pearled additions)	• Spasticity
	• Spinal cord injuries
• Contextually focused on SMRs	• Joint dislocations
	• Fractures

The Strength of Recommendation Taxonomy (SORT) grading system was used to grade the level of evidence of each research article. As a grading system, SORT offers a more patient-centred approach, focussing on "patient-oriented outcomes that measure changes in morbidity or mortality".[61]

Results

The use of SMRs and the specific outcome of the literature review, evidence rating and clinical recommendations for general practitioners are summarised in Table 4.

Discussion

The aim of this paper was to review evidence for the possible use of SMRs in the treatment of sports injuries. The main findings are that limited original research studies are available,[117] and it appears that the current use of SMRs is mainly based on case reports and reviews that were not done systematically. Also, studies mostly make use of combination drugs rather than single agents. This complicate drawing conclusions on efficacy of SMRs specifically.[117]

Regarding specific conditions, many of the studies use vague terminology and did not confirm a specific diagnosis. From our findings there are some evidence that SMRs can be effective in non-specific lower back pain (acute and chronic lower back muscle strains, ligament sprains, soft tissue contusions)[67,69-71,74-77], as well as for whiplash associated disorder[82-84], mechanical neck disorders[84], piriformis syndrome[91-93], lateral epicondylosis[97-102], and plantar fasciitis.[103-106]

An interesting finding points toward the use of SMRs (specifically BotA) in the management of recalcitrant anterior knee pain. Current evidence is promising, but only one RCT in highly selected and refractory cases of anterior knee pain that exhibit muscle imbalance (vastus medialis and vastus lateralis) has been conducted, which shows reduced pain and improved function in conjunction with exercise rehabilitation.[95] Therefore more research is required.[94-96]

It does not appear if there is a role for SMRs as part of combination management for acute cervical strains[80-81], post-exercise muscle soreness[87-88], or myofascial pain syndrome [110-116] but again more research is required.[117]

Conclusion

SMRs consist of a heterogeneous group of medications with a side effect profile of concern. The use of SMRs in the treatment of sports injuries has not been adequately investigated and current recommendations are largely based on case reports and general reviews. Validated and well described randomised clinical trials of SMRs that measure important clinical outcomes are essential. The effectiveness of SMR agents, single and in combination, as well as its significance as opposed to analgesics and NSAIDs, still has to be evaluated. This review highlights the gaps in the current literature, but also provides practical clinical guidelines on the possible use of SMRs in the treatment of sports injuries.

Keypoints

1. Literature comprises mainly of case studies and general reviews, i.e. lack of good evidence
2. Non-specific diagnosis used in most studies
3. Response to oral skeletal muscle relaxants is best for acute conditions; there is very limited clinical experience for chronic conditions
4. Combination drugs seem to be superior compared to single agents
5. Side-effect profile is a concern

a. In cases where the search results were either too broad or restricted or may have been non-satisfactory in focus the keywords 'neuromuscular blocking agent', 'nondepolarizing agent', 'pain', 'anti-spasmolytic' and 'analgesic' were also employed.

Table 4: Clinical recommendations for general practitioners based on SORT (Strength of Recommendation Taxonomy[61])

A: consistent, good-quality patient-oriented evidence
B: inconsistent or limited-quality patient-oriented evidence
C: consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Type of Injury	Evidence	Evidence Rating		Clinical Recommendations for General Practitioners
Lumbar				
Youth				
Lumbar disc herniation	RC[62]; GR[63]	C	-	Limited evidence, side effect profile is a concern, rather opt for other drug choice e.g. analgesics and NSAIDs, specialist referral advised
Spondylolysis and spondylolisthesis	GR[64]	C		
Adult				
Spondylolysis	GR[65]	C	-	Evidence based on a general review (expert opinion). Consider use if muscle spasm is part of the symptom / sign complex, in combination with analgesics and NSAIDs in the short-term
Disc herniation	GR[65]	C		
Degenerative disc disease	GR[65]	C		
Radiculopathy	GR[66]	C		
Non-specific LBP*	SR[67-72]; GR[73]; RCT[74-77]	B	-	Fair evidence, however non-specific diagnosis i.e. short-term use an option if muscle spasm is part of the symptom / sign complex, but re-evaluate and refer for specific diagnosis if weak response
Cervical				
Entrapment/Radiculopathy	GR[78-79]	C	-	Limited evidence, short-term use if muscle spasm is part of the symptom / sign complex
Combination therapy for acute strain	RCT[80]; GR[81]	B (not effective)	-	Non-specific diagnosis. The use is supported by a general review, however a RCT did not support it, cautious use is advised.
Combination therapy for acute sprain	GR[81]	C	-	Non-specific diagnosis. Limited evidence, cautious use is advised.
Whiplash associated disorder	CLC[82]; GR[83]; SR[84]	B	-	Limited evidence with unclear benefits as supported by a systematic review.
Combination therapy for acute discherniation	GR[85]	C	-	Limited evidence to support combination therapy, including rest, activity modification and NSAIDs
Mechanical neck disorders	SR[84]	B	-	Limited evidence with unclear benefits as supported by a systematic review.
Thoracic				
Multiple spinous fractures	RC[86]	C	-	Referral to specialist
Post exercise muscle soreness	OS[87]; RCT[88]	B (not effective)	-	Not recommended
Piriformis syndrome	EO[89]; CR[90]; RCT[91-93]	B	-	Limited evidence, combination therapy advocated. BotA injections show good results for pain improvement, but should only be administered by a specialist.
Patellofemoral pain syndrome	GR[94]; RCT[95]; CC[96]	C	-	Although promising only one very small RCT in highly selected resistant cases was reported, BotA injections should be administered by a specialist, further research required
Lateral epicondylosis	GR[97]; RCT[98-102]	B	-	Evidence based on level B evidence, further research required. BotA injections should be administered by a specialist, patients should be selected carefully. A common finding after BotA injection is weakness of finger extension.
Plantar fasciitis	RCT[103-106]	B	-	Conservative management with other modalities e.g. night splint, physical therapy, insoles before considerations of BotA injections. BotA injections should be administered by a specialist, patients should be selected carefully.
Neurogenic thoracic outlet syndrome	GR[107]	C	-	Limited evidence, but use can be considered, in combination with NSAIDs rest and physical therapy.
Stiff limb syndrome	RC[108]	C	-	Rare disorder, management by specialist
Rectus femoris haematoma	RC[109]	C	-	Treatment with SMRs may be an option, however better studies are required
Myofascial pain	GR[110]; RCT[111-116]	C	-	Limited evidence, with the injection of BotA not supported by available research studies. Combination therapy can be used with caution.

* Non-specific LBP: Acute and chronic muscle strains, ligament sprains, soft tissue contusions
Combination therapy: rest, activity modification, physical therapy, variety of medication (NSAIDs, analgesics, anti-depressants). Not BotA injections.
SR: Systematic Review RCT: Randomised Control Trial OS: Observational Study CR: Case Review CC: Case Control
RC: Reported Case GR: General Review EO: Expert Opinion CLC: Clinical Commentary

Contributorship:

Dina C Janse van Rensburg (DJvR): responsible for the overall content, review concept, manuscript planning, search strategy, search and review of identified literature, data interpretation, manuscript (first draft), manuscript editing, and facilitating funding

Audrey Jansen van Rensburg (AJvR): manuscript planning, search and review of identified literature, data interpretation, manuscript (first draft), manuscript editing

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