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Rotator Cuff–Related Shoulder Pain: To Inject or Not to Inject?

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The shoulder is the third most common site of musculoskeletal pain, and each year approximately 1% of adults over the age of 45 years present to their primary care provider with a new episode of shoulder pain.[4,9] The most common source of shoulder pain is thought to involve the tendons of the rotator cuff and associated structures around the subacromial space.[30,59] Clinically, the ability to accurately differentiate between the rotator cuff tendons and other related tissues is limited.[22,26] As with other musculoskeletal conditions of no specific structural cause, a more generic diagnostic term has been suggested, *rotator cuff–related shoulder pain* (RCRSP),[34] which is an overarching clinical term that includes a number of conditions, such as subacromial impingement syndrome,[42] subacromial pain syndrome,[13] and rotator cuff tendinopathy.[35,36]

The management of RCRSP may include exercise, surgery,[40] or injection therapy (commonly involving corticosteroids).[59] Up to 96% of musculoskeletal clinicians consider subacromial corticosteroid injection an efficacious treatment for RCRSP.[29] Approximately 22% of those who report shoulder pain to their general practitioner receive an injection during the initial consultation.[59] Furthermore, it has been suggested that diagnostic injections have a potential role in helping diagnosis by way of determining whether symptoms arise from a specific structure.[8] A wide range of health professionals across various disciplines, including physical therapists, perform injections in the management of musculoskeletal conditions. Those who perform or recommend injection therapy for RCRSP have a duty of care to provide advice on the expected benefits and outcomes, as well as the potential risks and associated harms. Clinicians also need to consider what medication to inject, where to inject it, and how to inject it. The aim of this Viewpoint is to discuss these issues.

What to Inject?

Corticosteroid and Local Anesthetic Injections Corticosteroid medications (alone and in combination with local anesthetic) have been used in the management of various musculoskeletal disorders for the last 60 years and are the most common form of drug used for injection therapy.[52] A recently published meta-analysis assessed short-term outcomes and concluded that corticosteroid injections provide, at best, minimal pain relief in a small number of patients with RCRSP, with a number needed to treat of 5.[38] These findings are consistent with those of previous reviews suggesting that the benefits of corticosteroid injections for RCRSP are inconsistent[14] and short lasting (up to 8 weeks).[2,7,12,14,20] Furthermore, there is equivocal evidence for the use of corticosteroid injections for RCRSP in the medium term and long term.[2,7,12,14,20] This is due, in part, to a limited number of well-designed studies assessing outcomes at medium- and long-term follow-up.[12]

There are also concerns about the safety of corticosteroid injections. Although adverse events are rare,[6,14] there is evidence of corticosteroid injections having potentially negative effects on rotator cuff tissue.[15,16,43,44] One prospective study[44] reported a 17% incidence of full-thickness

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rotator cuff tears at 12-week follow-up in patients who received a corticosteroid injection. Because this study did not include a group that did not receive an injection, it could not identify a causal relationship between the injury and the injection. In addition, the findings of this study were not replicated in a similar case-control study.[4] Despite concerns, there is no definitive consensus on the possible negative effects of corticosteroid injection therapy on rotator cuff tissue.

Local Anesthetic Injections Alone In light of the potentially deleterious effects of corticosteroids on tendon tissue, it has been suggested that local anesthetic injections alone (albeit not without risk) may be a safer alternative.[12,34] Local anesthetics such as lidocaine and bupivacaine may have a therapeutic effect by reducing tenocyte numbers[9,53] and altering collagen organization in tendons.[28] Increased cellularity has been associated with tendinopathy,[54] and, if elevated, reducing tenocyte numbers may be a possible mechanism by which local anesthetic injections contribute to the restoration of tendon homeostasis.

To date, there have been no randomized controlled trials comparing local anesthetic injections with an established sham injection in the treatment of RCRSP. There is evidence that local anesthetic injections have less favorable outcomes in comparison to corticosteroid injections (in combination or alone) in the short term.[12] However, there is no evidence to suggest that local anesthetic injections are any less or more effective than corticosteroids (in combination or alone) in the mid to long term.[12]

Sodium Chloride (Saline) Injections There is a paucity of research comparing saline to other forms of injection for the treatment of RCRSP.[12] It appears that only 2 previous studies have been conducted that compare corticosteroid with saline-only injections.[47,61] Neither study reported a significant difference in pain outcomes between groups in the short term. Due to methodological limitations, both of these studies appear to have a high risk of bias, and conclusions must be interpreted with caution. There is clearly a need for future high-quality research to establish whether saline injections are an efficacious treatment option in the management of RCRSP.

Platelet-Rich Plasma Injections There are conflicting opinions regarding the use of platelet-rich plasma for various musculoskeletal pathologies.[17,19] A recent systematic review[37] identified 3 studies that met inclusion criteria for RCRSP.[32,46,56] All 3 studies included small sample sizes and were thus underpowered, meaning the researchers were unable to detect clinically meaningful effects.[37] The reviewers concluded that for the treatment of RCRSP, platelet-rich plasma injections demonstrate negligible to small mean effect sizes across the 3 included studies (0.32).[37] This finding is not surprising, as it is documented that pain is often poorly correlated with tissue pathology.[21,48] The decision to use a treatment designed specifically to target tissue healing, such as platelet-rich plasma, may be based on flawed reasoning. In summary, there is a lack of evidence to make any clear suggestions of any benefit of platelet-rich plasma for the treatment of RCRSP.

Prolotherapy Prolotherapy involves injecting specific concentrations of hypertonic dextrose solution around pathological tissue in an attempt to encourage collagen synthesis and tissue healing. Although prolotherapy is used by some clinicians in the management of RCRSP, the exact mechanism of supposed therapeutic action has not been clearly identified.[55] One recent randomized clinical trial, in which patients and evaluators were blinded to treatment selection, reported favorable outcomes for prolotherapy compared to saline injections at 9-month follow-up.[3] Interestingly, this benefit could not be attributed to the treatment's proposed regenerative effects on tendinopathic tissue. Further research suggests favorable outcomes when compared with nonsurgical management[33] and exercise[55] at 1-year follow-up. The conclusions of these latter 2 studies need to be considered cautiously, as neither study included a sham control group, and thus favorable results may be attributed to contextual (placebo) effects. It is clear that further high-quality research comparing prolotherapy with other types of injection therapy is needed, as well as a better understanding of its mechanisms of action.

Where to Inject?

Research investigating the importance of the location of the injection has solely focused on corticosteroid injections. It is established that intratendon corticosteroid injection may lead to significant structural disorganization and even necrosis of tendon tissue.[25,31,60] Evidence suggests superior outcomes for subacromial corticosteroid injection over a combined approach of subacromial and intratendon injections.[27] Therefore, the preferred location of injection for RCRSP is into the subacromial-subdeltoid bursa or subacromial space.[39]

Studies investigating the systemic effects of corticosteroid injections have suggested no significant difference in outcomes for RCRSP between subacromial and intramuscular (buttock) injections. Both injection locations provided significantly better outcomes compared to an intramuscular saline injection designed as a placebo.[58] A more recent study compared a treatment group that received both subacromial corticosteroid and intramuscular (buttock) local anesthetic injections, with a control group that received subacromial local anesthetic and intramuscular corticosteroid injections. The study reported no significant difference between local and systemic corticosteroid injections.[18] This conclusion needs to be considered cautiously, as the benefits reported in this study's[18] control group may be a result of the possible aforementioned effects of the subacromial local anesthetic injection. Future research is needed to explore this area.

How to Inject?

Historically, musculoskeletal injection therapy has relied on clinical knowledge

of specific anatomical landmarks to guide needle placement. Researchers have previously attributed poor outcomes of injection therapy to inaccurate needle placement, assuming that an accurate needle placement should improve clinical outcomes.[27,50] Evidence is contradictory as to the accuracy of landmark-guided injections into the subacromial space, with a previous systematic review and meta-analysis suggesting that landmark- and ultrasound-guided injections are equally accurate.[1] In contrast, other evidence suggests accuracy ranging between 30% and 80% for landmark-guided injections.[24] Despite this uncertainty, the use of musculoskeletal ultrasound to guide needle placement continues to gain popularity.[18,23,41]

To date, 5 systematic reviews have compared the efficacy of landmark- and ultrasound-guided injections for the treatment of RCRSP. Despite the inclusion of the same trials within several reviews, conclusions are somewhat contradictory.[1,5,51,57,62] The lack of consensus within the literature has led to a degree of confusion as to the role of ultrasound to guide injections. However, researchers are in agreement that there is a paucity of well-designed studies comparing these injection methods. In general, studies mostly assess short-term outcomes in smaller samples, and are often nonrandomized and therefore subject to selection bias. Furthermore, studies are at risk of performance bias, as participants have often not been blinded to their treatment group. This raises the question of whether any observed advantages of ultrasound-guided injections are related to contextual effects, perhaps highlighting the clinical importance of the "treatment act" as opposed to the treatment itself. For these reasons, conclusions from this body of research should be interpreted with caution.

Future Research

Recent advances in the understanding of tendon-related disorders like RCRSP have focused on the assessment and treatment of load capacity.[10] Critics of injection therapy may argue that it seems contradictory to treat a condition that is defined by a lack of tolerance to load (capacity) with a treatment that is known to cause structural changes that may reduce tissue capacity. Perhaps it is of no surprise that the role of injectable substances such as corticosteroid (known both for potent anti-inflammatory and potentially deleterious structural effects) and their mechanism of action remain uncertain. Our understanding of what causes tendon-related conditions to be associated with the experience of pain is still limited,[48] as is our understanding of the relationship between tendon pain and structure.[21,48] Furthermore, the importance and role of inflammation in tendon pain are still debated,[11,45] and these are all areas of much-needed future research.

In relation to injection therapy research, future studies should aim to reduce performance bias by including validated sham control groups, thus ensuring sufficient participant blinding. To evaluate the success of blinding, researchers should ask participants whether they believe they received the active treatment. There must also be transparency within the reporting of participants' perceptions of the different treatment options and whether these perceptions affected their outcomes. Once these factors have been controlled for, the various injection types and techniques can be more accurately compared. As with other fields of musculoskeletal medicine, comparisons should also be made with other conventional treatment options, for example, the "wait and see" approach or exercise therapy. Long-term follow-up should be used, and researchers should assess baseline and follow-up psychosocial and pain-related measurements to identify patient characteristics that may help predict outcome.

The conclusions of this Viewpoint are in agreement with a recent systematic review that compared treatments for multiple musculoskeletal pain presentations that may be treated with pharmacological injections.[2] This Viewpoint argues that current evidence is equivocal with respect to the optimal procedure, frequency, dose, and active component of the injection, and that injections may be no more effective than nonpharmacological interventions such as exercise.[2] The continued use of injection therapy in the treatment of RCRSP has been attributed by some to force of habit and an underappreciation of the placebo effect.[38] Furthermore, its cost-effectiveness has also been questioned.[12] Currently, clinicians and those considering undergoing a shoulder injection for RCRSP should remain cautious due to the poor quality of research evidence.

Key Points

- As a result of a paucity of high-quality research in this area, it is not possible to make strong recommendations regarding the type, location, and technique of injection therapy in the management of RCRSP.
- There is no clear consensus on the possible negative effects of corticosteroid injections on rotator cuff tissue.
- When compared to local anesthetic injections alone, corticosteroid injections may provide mild short-term pain relief for some patients with RCRSP. There is no evidence to suggest a difference between injection types in the mid to long term. ◉

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