Joint and soft tissue Injection recommendations PCRMM

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The Primary Care Rheumatology and Musculoskeletal Medicine Society (PCRMM) comprises a group of GPs and allied health professionals interested in, and with expertise in musculoskeletal medicine. Most of our members work in primary care, but many also in intermediate and secondary care.

The following advice incorporates the minimum information that the PCRMM feels should be included in any set of guidelines on joint and soft tissue injections.

Please note the ultimate responsibility for the completeness and accuracy of the information provided to patients regarding joint and soft tissue injections rests with the individual clinician and the organisation employing them.

We have conducted a literature search of relevant evidence, searching under the broad headings listed within the guidance, or variations thereof, using the e–resources databases of the University of Bournemouth and East Lancs NHS Trust, and NHS Evidence. The searches concentrated on systemic reviews, meta- analyses, randomised controlled trials (RCTs), and controlled trials where available. We also made use of the expert opinions within the group where evidence was missing, contradictory or incomplete.

These recommendations focus primarily on steroid injections.

Introduction

Steroid Injections have been used widely for many years to help ease the discomfort and loss of function associated with joint and soft tissue disorders. Numerous studies and extensive clinical experience have established that such injections are generally a safe and effective treatment option[1], for example in knee osteoarthritis, an effect size of 1.27 vs placebo at 7 days has been demonstrated (> 0.8 is considered good effect size) [2].

There is apparently wide variability in clinical practice regarding exactly when and how joint and soft tissue injections are performed.

The PCRMM therefore decided to develop some recommendations regarding the safe and appropriate use of these injections which clinicians may find helpful.

The aim of this guidance is not to dictate how things should be done, or to replace clinical judgement. The PCRMM recognises that every patient and clinical presentation is unique, and the working environment is different for every practitioner. Many clinicians are obliged to work in highly time pressured environments and for this reason we have tried to keep this guidance concise. The intention is to provide a usable and safe framework which is appropriate for most clinical settings but can be modified according to individual requirements and as new evidence comes to light.

The PCRMM advises that any person carrying out injections must be adequately trained to do so. Arrangements should also be in place for ongoing staff development and clinical governance procedures to ensure continued safe and high-quality practice.

Full resuscitation equipment must be immediately available, and staff must be appropriately trained in its use.

As Joint and soft tissue injections involve exposure to body fluids, the practitioner must be protected by means of appropriate immunisation, the use of gloves, and safe sharps use and disposal.

Indications for joint and soft tissue injection include

- Arthritis
- capsulitis
- Bursitis
- Tendinopathy and tenosynovitis
- Enthesopathy
- Neuromas
- Ganglion cysts
- Entrapment and impingement syndromes of nerve and soft tissues
- Regional pain including back pain

Potential complications from injection include [2, 4]

- Hypersensitivity – local or systemic
- Tissue atrophy, nodule formation and skin hypopigmentation
- Tendon Rupture
- Infection, local or systemic
- Post injection flare of symptoms
- Facial flushing – usually 24-72 hours post injection and predominantly women.
- Menstrual irregularity
- Elevated blood sugar in diabetic patients
- Fainting
- Steroid induced osteonecrosis or arthropathy

Contraindications to injection include [2, 5]

- Allergy
- Local or systemic infection
- Active rash / broken skin at site of injection
- Uncontrolled Coagulopathy
- Fracture/unstable joint
- Tendon regions at high risk of rupture
- Injection into a prosthetic joint
- metalwork within the region of injection

Suggested approach to joint and soft tissue injection.

- Informed consent
- Supply patient with appropriate information leaflet
- Check INR on patients taking warfarin prior to the procedure
- Select the appropriate steroid preparation for the injection to be undertaken
- Use sterile alcohol swab to clean rubber seal on steroid vial if required
- Draw up local anaesthetic and steroid and discard needle(s)
- Attach new sterile needle(s)
- Mark skin injection site for example using plastic needle cover. If using skin pen avoid injecting through ink as this risks tattooing the skin.
- Clean area with appropriate topical antiseptic
- If using ultrasound guided technique, use sterile gel and sterile probe cover if contamination risk.
- Inject using aseptic no touch technique.
- Aspirate pre injection to ensure blood vessel not entered
- Cover site with sterile dressing
- The patient should be advised to remain in the department for 20 minutes post injection.
- Advise the patient to undertake relative rest for 24 to 48 hours after the injection particularly if the knee is injected.
- Advise the patient to avoid heavy, strenuous activities for 2 weeks post injection into a peri-tendinous region.

Background to guidance

Consent

Organisations require procedures in place relating to the dissemination of patient information and consent. The GMC updated its guidance on consent in November 2020 [10]. In addition, all relevant defence organisations for doctors and allied health professionals provide detailed information on consent processes on their respective websites[6,7,9].

There are three components to valid consent[6]:

• Capacity

• Information

• Voluntariness

Capacity indicates that a person can make a decision or take an action about their own care and treatment. A person who lacks capacity is unable to make a particular decision or take a particular action for themselves *at the time* the decision or action needs to be taken. Clinicians must start from the presumption that all adult patients have the capacity to make decisions about their treatment and care [60,10] A summary of The Mental Capacity Act Code of Practice, with respect to medical procedures can be found on the relevant defence organisation websites[6, 61,62]

Doctors must ensure that patients are aware of any "material risks" involved when undergoing a proposed treatment, and of reasonable alternatives. "*The test of materiality is whether, in the circumstances of the particular case, a reasonable person in the patient's position would be likely to attach significance to the risk, or the doctor is or should reasonably be aware that the particular patient would be likely to attach significance to it*."[6].

According to the GMC website [10, y]ou should usually include the following information when discussing benefits and harms.

a. *Recognised risks of harm that you believe anyone in the patient's position would want to know. You will know these already from your professional knowledge and experience.*
b. *The effect of the patient's individual clinical circumstances on the probability of a benefit or harm occurring. If you know the patient's medical history, you'll know some of what you need to share already, but the dialogue could reveal more.*
c. *Risks of harm and potential benefits that the patient would consider significant for any reason. These will be revealed during your discussion with the patient about what matters to them.*
d. *Any risk of serious harm, however unlikely it is to occur.*
e. *Expected harms, including common side effects and what to do if they occur.*

In the context of joint and soft tissue injections, the patient must be informed about the relevant risks and benefits of the injection. The clinician should document that such a discussion has taken place and that the patient has consented to the treatment. In England the patient is not required to sign a consent form[10] and this may in fact be less medico legally robust than clear and reasonable documentation of the discussion in the notes. However, employees should generally adhere to local policies with respect to when signed consent may be required [6]. This particularly applies to those clinicians working under patient group directions.

It is helpful for patient and clinician if the patient receives an information sheet to read prior to the procedure and to take away, detailing potential relevant adverse effects.

Infection risk

Infection is considered a rare complication of joint and soft tissue injection[1,11]. However the consequences can be catastrophic. Rates between 1:3000 and 1:50,000 are quoted in the literature [2,12]. However this rate may be higher in immunosuppressed patients i.e. in the region of 1:2000 [12].

Hand mediated transmission is the major factor contributing to healthcare associated infection (HCAI). Public Health England provides information regarding standard measures to reduce the risks of HCAI, including effective hand decontamination, the appropriate use of gloves, avoiding fomite contamination[13]. Clinicians should also follow an aseptic no touch technique for all injections, details of which will be locally available.

Patient skin preparation is generally recommended prior to surgical procedures to reduce skin bacteria numbers and thereby the risk of infection.

Prior to any procedure and skin preparation, the skin should obviously be free of visible dirt. The antiseptic preparation should be applied in concentrically enlarging circles beginning at the site of proposed injection[14]. All skin preparations should be used strictly in accordance with the manufacturer's instructions and within date. Consideration should be given to the use of single use skin preparations labelled as sterile [16]. Antiseptic contamination should be considered should infection occur post injection.

Commonly used products for surgical procedures include alcohol based, chlorhexidine based, and iodine based. These are all considered effective antimicrobial skin cleansers [17, 18, 19].

Alcohol for skin preparation is defined by the FDA as ethyl alcohol, 60% to 95% by volume in an aqueous solution, or isopropyl alcohol, 50% to 91.3% by volume in an aqueous solution. Alcohol is fast although short acting, has broad-spectrum antimicrobial activity (spores can

be resistant), and is inexpensive[15]. Flammability is an issue in the presence of electrical equipment. This is unlikely to be an issue in the context of office based joint injections. For skin disinfection, allow the alcohol to completely dry on the skin for 30 seconds [64].

One study in 2002 compared an isopropyle alcohol swab with chlorhexidine in spirit soaked cotton wool balls [20]. The discarded needles were cultured. No infections occurred during the study and there was no statistical difference between the groups regarding positive needle culture. However it was quicker and therefore cheaper to prepare the skin with alcohol. Both methods reduced the rate of positive culture compared to control (culture of needles from non-cleansed IM injections). No positive cultures grew pathogens typically associated with joint infection.

Bacterial resistance to chlorhexidine digluconate has been reported in Enterobacter spp., Pseudomonas spp., Proteus spp., Providencia spp. and Enterococcus spp. [21]. Recent studies suggest that alcohol-based solutions of chlorhexidine and iodine may have greater efficacy, easier application, extended durability, and better cost effectiveness when compared with aqueous-based solutions[17].

Dust covers on vials are not necessarily adequate to ensure sterility of the outside of the vial top. Therefore, swabbing with sterile alcohol swab is recommended for some medications [18]. Single use ampoules should be discarded after the required amount of drug is drawn up and not re-used for subsequent patients.

Tendon Rupture

There have been case reports of tendon rupture following steroid injection and ingestion[22,23,24]. Biopsy studies have demonstrated reduced cell viability and proliferation, reduced collagen synthesis and organisation, and reduced strength as a result of tendon exposure to steroid [25]. This effect has been shown to persist for 2 weeks in some studies, longer in others[26]. Yang et al 2014 cultured rat tenocytes with triamcinolone or lidocaine or both. They found in vitro evidence of a deleterious effect on tenocytes of both steroid and lidocaine and that the effect was synergistic when the tenocytes were exposed to triamcinolone and lidocaine together[27].

In general, it is therefore considered prudent to avoid injecting steroid into the body of a tendon, by using good injection technique. Unless there are compelling reasons to do so, avoid steroid injections in the vicinity of tendons at high risk of rupture due to pathology (severe tendinopathy) or anatomical location (achilles).

Osteonecrosis

The risk of osteonecrosis is highest with prolonged, high doses of exogenous steroids, particularly in the presence of other risk factors [28]. Short courses of steroids however have also been shown to increase the risk of this rare complication [29]. There have also been reported case studies of avascular necrosis temporally related to local intra-articular steroid administration [30]. It would seem wise to warn patients of this potential rare but devastating, complication prior to steroid injection, particularly in the presence of other risk factors for avascular necrosis.

Anti-coagulation and joint injection.

Patients taking anti-coagulants do so because of the risk of serious and potentially life-threatening thrombotic events. Any decisions around anti-coagulants in the context of a medical procedure must take that into account. Evidence suggests that necessary minor bleeding risk procedures can often be undertaken safely without anti-coagulant interruption [63,65,66].

The decision to undertake Joint and soft tissue injection in patients who are anti-coagulated requires careful consideration and alternative management strategies should be considered first line. However analgesic options are often limited in these patients.

For patients taking warfarin, provided the INR is within the therapeutic range i.e. less than 4.5, the risk of significant haemorrhage following joint or soft tissue injection appears very low [31, 32, 33]. Bashir et al 2015 reported no occurrences of significant haemorrhage following shoulder and knee injections in patients in whom the INR was 5.5 or less[34].

Many patients are now taking Direct Oral anticoagulants (DOACs). Dabigatran is an oral direct thrombin inhibitor. Rivaroxaban, Apixaban, Edoxaban and betrixaban are oral direct factor Xa inhibitors[35,66].

NICE oral anticoagulation guidance relating to anticoagulation with DOACS advises 'For most minor surgical procedures and those associated with a minor bleeding risk, it is recommended not to interrupt oral anticoagulation' and 'In general, these procedures can be performed 12–24 hours after the last dose of (DOAC) is taken'[66].

If bleeding should occur in patients taking DOACs, expert opinion suggests that in many instances, bleeding can be managed by withholding the DOAC and providing supportive care [38]. Therapeutic agents which may be administered in the event of uncontrolled bleeding in the context of DOAC administration include tranexamic acid, idarucizumab (dabigatran), prothrombin complex concentrate PCC (apixaban, edoxaban, rivaroxaban), andexanet alpha (apixaban, rivaroxaban) [63]

In summary Joint and soft tissue injections may be appropriate in managing patients who are anti-coagulated. Given that interrupting anticoagulation may precipitate life

threatening thrombosis, the benefits of continuing anticoagulation generally greatly outweigh the small risk of bleeding as a result of a joint injection. However the risks of haemorrhage and a management plan in the event of this complication should be discussed with the patient in advance.

Steroid type, dose and frequency

Common steroids used for joint and soft tissue injections in the UK include; hydrocortisone acetate, methylprednisolone and triamcinolone acetonide. Betamethasone, dexamethasone and triamcinolone hexacetonide are also licenced in the UK [40]. Of these, betamethasone and triamcinolone are the least soluble and are therefore considered the slowest to diffuse out of the joint and to give rise to the longest therapeutic action [41].

There is some evidence of chondro-protection by steroid indicated by a decrease in cartilage breakdown products in the circulation and joint fluid post injection [3, 41]. In humans and other primates, several studies have shown no definitive evidence of harm resulting from multiple steroid injections at the knee [5, 42]. Some animal studies however have suggested a toxic effect of steroid on articular cartilage. The ultimate effect may in part be dose dependent, with lower doses resulting in a reduction in the synthesis of proteolytic enzymes and an increased synthesis of proteoglycans, whilst higher doses may cause a decrease in type II collagen expression[43]. Occasional cases of apparent accelerated joint damage in humans post steroid injection have been documented 'steroid arthropathy'. However, analyses of some of these reported cases have suggested that factors other than steroid toxicity may have been responsible [41].

There seems to be little evidence regarding the optimum dose or frequency of steroid injection and routine practice appears to be based on experience rather than evidence [1]. A literature review of the evidence in this area carried out by Stevens et al 2008 ultimately concluded that 'The medication used, and the frequency of injection should be guided by the goal of the injection, the underlying musculoskeletal diagnosis, and clinical experience'

Similarly, Douglas' 2012 literature search regarding the frequency of joint injection in osteoarthritis concluded 'All published information concerning the frequency of intra articular corticosteroid injection appears to be based upon professional opinion - a search of the published medical literature failed to identify a study that had investigated how often intra articular corticosteroid can be injected into an osteoarthritic joint [41].

Systemic absorption of steroid has been shown to affect the hypothalamic- pituitary-adrenal (HPA) axis after steroid joint injections [44]. HPA-axis suppression can typically last up to four weeks after a single injection, occasionally longer, depending on the dose and frequency of injections [45]. This is incidentally also the same mechanism thought to affect menstruation. Rare cases of Cushing's syndrome have been reported but generally using unusually high doses and frequencies of joint injection. HIV patients on anti-retroviral medications may be

particularly susceptible to iatrogenic Cushing's syndrome [46]. Careful consideration should be given to this complication if multiple or repeat steroid injections are undertaken.

Soft tissue atrophy is an uncommon complication of steroid injection even in superficial dermatological procedures involving steroid injection. However, it may persist for years. It is thought to be due to persistence of steroid crystals in the tissues and is therefore less likely to occur with more soluble preparations [47, 48]. These are therefore preferred for soft tissue and superficial injections.

In summary, in the absence of convincing evidence to the contrary, it seems prudent to follow the manufacturer's instructions with regard to maximum dose and frequency for each steroid formulation. From speaking to PCRMM members these are actually higher than most practitioners would routinely use. The NHS website states that 'doctors usually recommend no more than 3 injections in the same area in the space of 12 months' [40].

There are many readily accessible textbooks, web sites and academic papers which give useful recommended doses for various steroid injections based on clinical experience [49, 50].

Hyperglycaemia

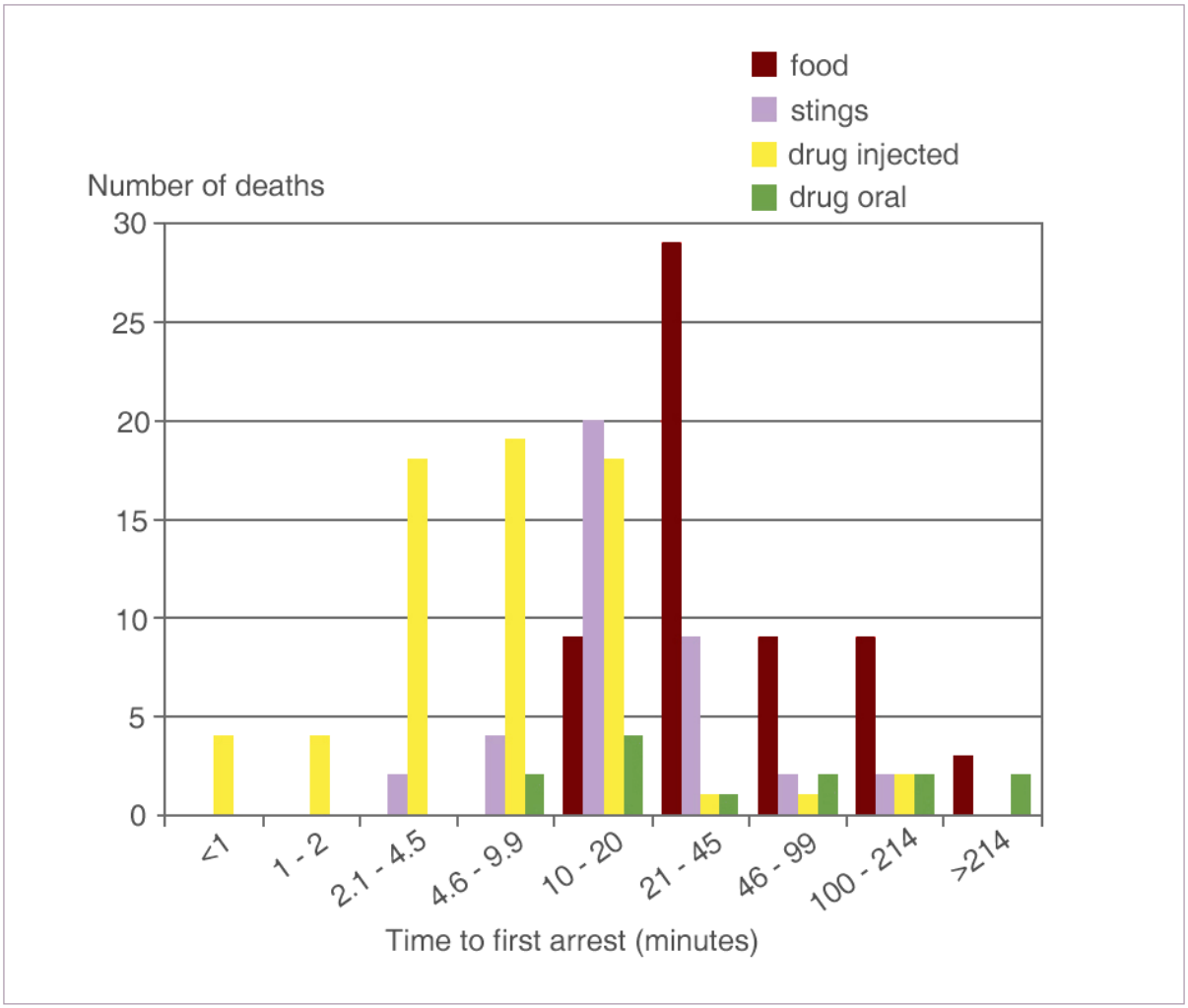
Intra articular and soft tissue steroid injections have been shown to elevate blood sugar in diabetic patients, commencing after a few hours and lasting for several days and occasionally longer [51]. Although these increases in glycaemia are statistically significant, for most patients they are generally not clinically significant [52, 53]. However diabetic patients should be warned of this effect and be given advice e.g., blood glucose testing and who to contact if unwell.

In 2018 PCRMM undertook a literature search of the available evidence regarding the risk of complications associated with joint injection on the background of an elevated HbA1c. We also consulted local rheumatology and diabetes specialists for their opinions. No association with adverse outcomes was found for joint and soft tissue steroid injections and HbA1c level. It was therefore felt inappropriate to recommend a cut off HbA1c level above which steroid injections could not be administered, rather to consider injection in diabetic patients on a case-by-case basis and encourage good diabetic control where needed.

Post injection advice

Anaphylaxis

According to the resuscitation council UK website, the time course for cardiopulmonary arrest resulting from injected medication predominantly occurs between 2 and 20 minute post injection. It would seem sensible therefore, that patients are asked to remain on site for the full 20 minutes [54].



1. Slide Reproduced with the kind permission of the Resuscitation Council (UK).

Rest

Rest following the injection is often advised. Reduced 'leakage 'of injected substances out of the rested joint compared to non-rested joints, has been demonstrated in inflammatory conditions [55]. The implication therefore, is that rest will result in a more prolonged therapeutic action of the injected substance. Some studies have shown prolonged symptom relief in inflammatory arthritis of the knee in rested compared to unrested joints [56]. Also Weitoft and Larsson 2005 demonstrated a greater fall in cartilage breakdown products in

those patients who had been allocated to bed rest for 24 hours post injection of 20 mg of triamcinolone hexacetonide [3].

However a study by Chatham et al found no evidence of symptomatic benefit for rest post steroid injection for inflammatory arthritis [57]. Also rest post injection may be detrimental at some joints e.g. at the wrist [55, 56].

Further research is required to determine if rest following injection is beneficial, particularly for degenerative conditions in non-weight bearing joints. This is pertinent given the accepted health risks associated with immobility.

At present however it would seem sensible to advise relative rest following injection of the knee joint particularly in the presence of inflammation for 24-48 hours.

For tendinous injections, or peri-tendinous injections, especially where there is a risk of inadvertent tendon injection, it may be advisable to recommend avoidance of strenuous activities for up to 2 weeks.

Steroid injections and immunisations

Current advice from ARMA is to avoid steroid injection within 2 weeks of Covid vaccination to minimise the risk of impaired immune response to vaccination [58].

Regarding inactivated influenza vaccination in adults and steroid injection, the PCRMM looked at the available evidence on this subject in detail and found no evidence that the steroid dose used in joint injections impairs the immune response to influenza vaccination[59]

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