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# Scoping review for pain mitigation during intralesional injections of corticosteroid for hypertrophic scar and keloid treatment

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## ABSTRACT

**Background** Intralesional corticosteroid injection (ILCSI) has been proven to successfully treat hypertrophic scars (HTSs) and keloids and attain remission in 50% of keloids. Pain is a significant problem with ILCSI, which can affect treatment compliance and effectiveness. To date, many techniques involving ILCSI have been described and used to achieve scar treatment while reducing side effects. The injection technique remains the most widely available method in many healthcare centres.

**Objective** This scoping review explores strategies for alleviating pain while administering ILCSIs for hypertrophic scarring and keloid management. ILCSI is a second-line treatment for HTSs and a first-line treatment for keloids.

**Eligibility criteria** This scoping review included studies where HTSs and keloids were treated with ILCSI and considered diverse demographics and injection methods. This review excludes other methods of corticosteroid drug delivery where injection is not involved and where the pain assessed is unrelated to injection or infiltration of the scar.

**Sources of evidence** This review systematically searched critical databases from inception to December 2023, including ScienceDirect, PubMed and Web of Science, and handpicked articles traced from available review papers. Only English-language publications focused on pain management during ILCSIs for HTSs and keloids were included. All levels of scientific evidence were considered. An in-depth evaluation of the injection technique, type of analgesia or anaesthesia administered, effectiveness of pain management and overall treatment outcomes was conducted.

**Charting methods** Citations were compiled in an Excel spreadsheet, with three authors screening the titles and abstracts based on inclusion criteria. Decisions were finalised collaboratively, exclusions were documented and results were presented using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

**Results** 16 prospective studies, 2 retrospective studies, 1 case study and 15 journal articles were included. These studies examined ILCSI for hypertrophic scarring and keloid treatment. No differences in pain intensity between HTSs and keloids were reported. 11 studies systematically explored pain reduction methods such as topical analgesia, cryoanaesthesia, mixing triamcinolone acetonide with local analgesics, slow infiltration techniques, vibration analgesia and needle-free injectors.

**Conclusion** Pain can significantly impact patient compliance and treatment outcomes. This review offers a foundational reference for healthcare providers and researchers in the field of scar management, providing insights into current practices and highlighting areas for future research and development.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This scoping review did not include a critical appraisal of individual sources of evidence.
⇒ The search strategy was limited by the use of only a few databases, potentially leading to incomplete results.
⇒ The database search used different strategies, which may have affected consistency.
⇒ Overly specific terminology was used in the search strategy to make it feasible within time constraints.
⇒ The inclusion criteria for studies were subjective, which could influence the comprehensiveness of the review.

## INTRODUCTION

Pain and itching are prominent symptoms of hypertrophic scars (HTSs) and keloids and are often accompanied by allodynia. The central region of a keloid, where small nerve endings are concentrated, can be particularly prone to intense pain.[1] Uncontrolled pain and itch have been identified as risk factors for the development of major keloids.[2]

HTSs and keloids are pathological scars that can impact a person's physical function, contribute to psychological disturbances and affect their overall aesthetic appearance.[3] The process of wound healing can result in the formation of scars such as HTSs or keloids, a form of dermal fibroproliferative disorder.[4]

Several distinctions exist between HTSs and keloids, such as clinical presentation and histological characteristics.[5] Hypertrophic

scarring typically arises 4–8 weeks after skin injury. It rapidly grows for up to 6 months and gradually regresses over months to years, resulting in a flat, less conspicuous scar.[6] In contrast, keloids may develop years after minor injuries, even spontaneously, persisting without regression. Keloids are present as firm tumours with a shiny surface, telangiectasia and irregularly outlined borders. Thinned epithelium, focal ulceration, a colour range of pink to purple and hyperpigmentation may also be observed.[7] While HTSs share a similar appearance, they are typically linear, papular and nodular, following surgical or inflammatory lesions, respectively. Both lesions are commonly pruritic, with keloids potentially causing significant pain and hyperesthesia.[8]

Anatomical location plays a role, with hypertrophic scarring prevalent in areas with high tension, such as shoulders and knees. Moreover, keloids are predisposed to form on the anterior chest, shoulders, earlobes, upper arms and cheeks.[9] Regions such as the eyelids, cornea, palms, mucous membranes, genitalia and soles are less affected.[10] Keloids tend to recur after excision, whereas new HTS formation is infrequent after the original HTS is removed. The variation in pain and pruritus according to anatomical distribution has yet to be reported.

Histologically, HTSs primarily contain type III collagen, nodules with myofibroblasts, large collagen filaments and mucopolysaccharides. Keloid tissue, in contrast, consists of disorganised type I and III collagen, featuring pale-stained hypocellular collagen bundles without nodules or excess myofibroblasts. Both scar types exhibit overproduction of fibroblast proteins, suggesting pathological persistence of wound healing signals or a failure to appropriately downregulate wound-healing cells.

The distinctions between these two pathologies call for different management strategies, and interestingly, according to treatment guidelines from the International Scar Society (2014), intralesional corticosteroid injection (ILCSI) has been recommended as a second-line treatment for HTSs and a first-line treatment for keloids.[11]

The treatment of keloids with ILCSI began in 1951 and was effective in alleviating itching and pain despite the well-known ability of steroids to delay wound healing.[12] Corticosteroids mitigate abnormal scarring through their anti-inflammatory and immunosuppressive actions, inducing vasoconstriction and hindering the proliferation of fibroblasts and keratinocytes through their antimitotic effects.[13]

Since then, various methods of intralesional corticosteroid administration have been proposed; these methods include dosage variations, maximum dose considerations, the inclusion of local anaesthetic agents, treatment intervals, needle and syringe sizes, and injection levels.[14] The endpoint of injection is achieved by a specific dose per area or volume or by observing total pallor.

Remarkably, the application of steroids has evolved, incorporating innovative drug delivery methods such as topical formulations, tapes/plasters, chemical and biological transdermal permeation enhancers, physical transdermal drug delivery systems, laser-assisted approaches, nanocarriers and microneedle transdermal drug delivery systems.[15]

Despite the various available treatments for both keloids and HTSs, ILCSI remains a prevalent choice because of its proven effectiveness in achieving regression in 50%–100% of cases.[16] In addition, steroid therapy is compatible with combination therapy.[17]

Clinicians encounter a notable challenge during ILCSI, particularly with respect to pain. Various factors contribute to the discomfort experienced during these injections, such as needle penetration, direct tissue injury caused by inflamed and nerve-rich tissue, pressure buildup resulting in stretching sensations and differences in irritability among various corticosteroid formulations.

To date, numerous strategies have been implemented in clinical practice to address pain management. Sometimes, patients undergo general anaesthesia or sedation, whereas local or topical analgesia is used for minor scar lesions. In addition, the restriction of needle penetration, the use of a small-bore needle and slow infiltration with low-pressure administration are among the established techniques.

The impact of pain on the management of keloids and HTSs should not be underestimated. There is a question of how pain impacts patients seeking treatment, compliance and the effectiveness of the treatment.

This scoping review aims to explore and analyse the available literature describing pain control methods during ILCSI. This review will also investigate the effectiveness of pain control and scar treatment.

In 2023, a scoping review was conducted on the techniques of ILCSI for keloids.[14] While the study acknowledged the impact of local anaesthetics on injection pain, it did not thoroughly examine the available methods for pain control during the ILCSI. A preliminary search of databases, including MEDLINE, the Cochrane Database of Systematic Reviews and Joanna Briggs Institute (JBI) Evidence Synthesis, revealed no existing systematic reviews or scoping reviews on this topic.

In summary, this scoping review endeavours to address existing gaps in knowledge by comprehensively exploring and evaluating the effectiveness of pain management strategies used in the context of the ILCSI for treating keloids and HTSs. The overarching objective aligns with the core principles of the population, concept and context framework, which aims to provide a thorough understanding of the diverse methods employed for pain control in this specific therapeutic context.

## REVIEW QUESTION

This scoping review is designed with three objectives. First, it seeks to systematically map and analyse the literature on pain mitigation strategies during the ILCSI for HTSs and keloids. By examining a diverse array of sources, including clinical studies, peer-reviewed articles, clinical guidelines and expert opinions, this review aims

to comprehensively understand the methods employed for pain management in this specific intervention.

Second, the review aims to determine the identified gaps, controversies and challenges within the current body of knowledge. Research on HTSs and keloids, which focuses mainly on areas where more information is needed, where there is disagreement among experts, or where pain management during treatment is complex, will be conducted. Through this exploration, the review aspires to inform future research endeavours, guide clinical decision-making and contribute to enhance pain management protocols associated with the ILCSI.

Finally, in individuals with keloids and HTSs, what is the extent and quality of evidence concerning pain management during ILCSI? What are the available methods for mitigating pain and what are the effectiveness of these strategies? Furthermore, does pain management impact the efficacy of the ILCSI?

## ELIGIBILITY CRITERIA

### Participants

The target population included individuals diagnosed with HTSs or keloids. The inclusion criteria will encompass diverse demographics, age ranges, genders and races regardless of the number of treatments received to ensure a comprehensive representation. The exclusion criteria will consider individuals with contraindications to corticosteroids, pre-existing medical conditions interfering with treatment or a history of adverse reactions to the injection.

### Concept

This scoping review examined studies pertaining to HTSs, keloids and the ILCSI, with a focus on pain management. The investigation will encompass pain control methods across the preprocedure, during-procedure and postprocedure phases associated with the ILCSI. The exclusion criteria were as follows:

1. Studies that do not directly address the concept within the context of HTSs, keloids and ILCSI.
2. Research information on pain itself or pain control methods during the preprocedure, procedure or postprocedure phases is lacking.
3. Studies on which modes of steroid delivery for scars other than the intralesional injection technique are needed.

### Context

The context of the review is clinical settings in inpatient and outpatient clinics.

### Types of sources

This scoping review included primary and secondary research. The primary research was not limited to experimental studies. The secondary research included grey literature and handpicked articles that fulfilled the inclusion criteria.

## METHODS

This scoping review was conducted in accordance with the JBI's updated methodological guidance for conducting scoping reviews.[18] This review uses the guidelines and checklist for Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR; Tricco *et al*, 2018; see online supplemental appendix III).

Registration of the review protocol could not be performed in PROSPERO as this is a scoping review.

### Search strategy

A systematic search was performed on Science Direct, PubMed and Web of Science for articles from inception to 31 December 2023 by three authors MJ, AQS and SH. The search strategy involves a combination of relevant keywords. Medical Subject Headings (MeSH) terms and synonyms, Boolean operators and appropriate syntax wherever relevant. Initial searches were conducted to refine and test the search strategy to achieve inclusivity. The text words in the titles, abstracts and index terms were analysed to ensure the search captured the relevant literature. In the context of a scoping review, no explicit outcomes were stated in the search, aiming to capture all relevant papers, irrespective of the outcome measures used. Relevant research and articles were also identified from references from other publications. Only studies published in English were included. An example of the search strategy is provided in online supplemental appendix I.

### Study/source of evidence selection

Three authors (MJ, AQS and SH) evaluated titles and abstracts based on the specified inclusion criteria. After the search, all identified citations were gathered in a Microsoft Excel Spreadsheet in Google Forms (online supplemental appendix II). Records from the search were independently screened by lead authors MJ and ASH, and selected citations were compiled. Conflicts on articles to include and exclude were resolved by consensus and finalised by ASH and MJ. The outcomes of the search and the inclusion process are presented through a flow diagram, using the PRISMA-ScR flow diagram in figure 1[19]

### Data extraction

Data were extracted from papers included in the scoping review by the first author following data screening using data extraction tool by the reviewers. The tools were pilot tested in consultation with the coauthors and in accordance with the JBI methodology.[18]

The data extracted were divided into two categories: data from prospective, retrospective and case studies, and data from review articles and expert opinions. The extraction form was revised while data from each evidence source were extracted.

### Data analysis and presentation

The extracted data were divided into two categories: data from prospective, retrospective and case studies, and data

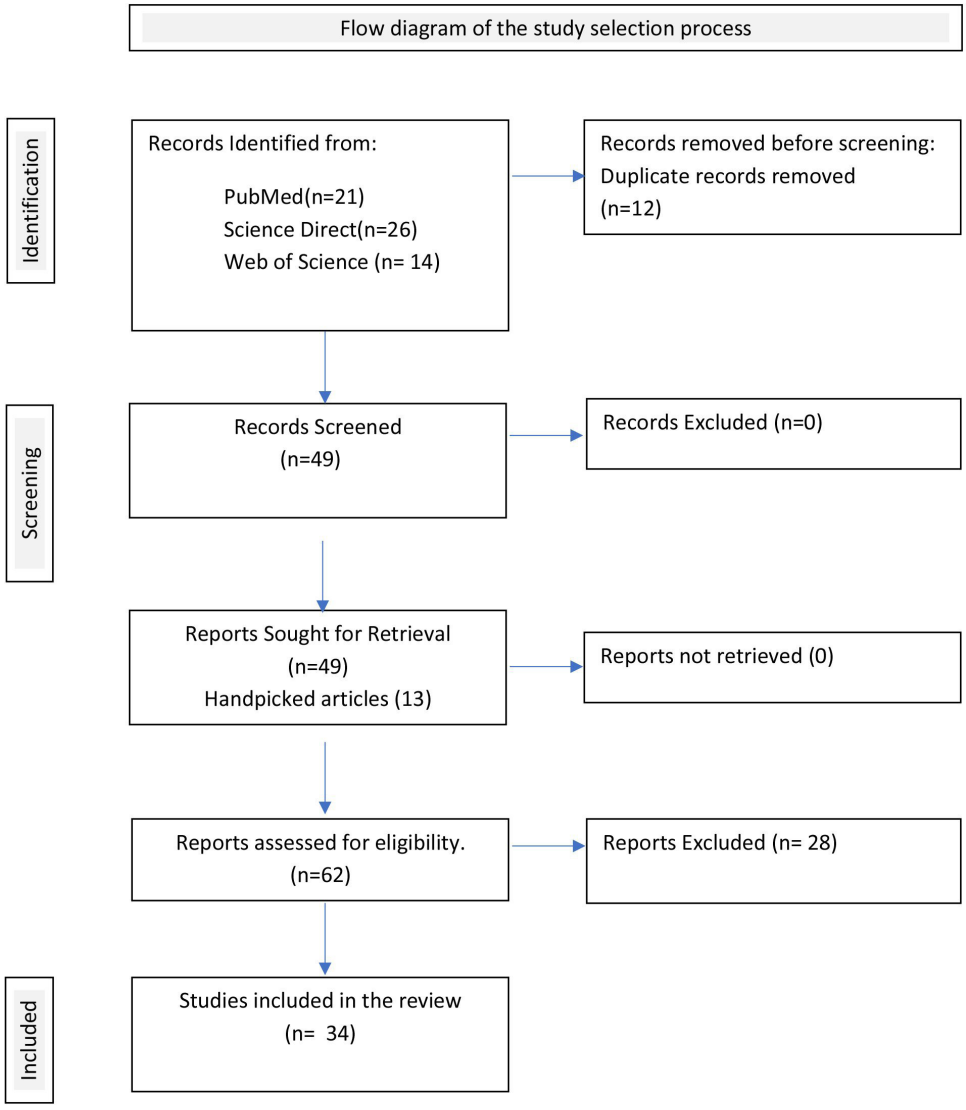


**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-analyses extension (PRISMA) flow diagram of the study selection process.

from journal articles, expert opinions and correspondences. This information was tabulated according to: (1) the country where the research was conducted and the patient population that received treatment, (2) the age of the population, (3) the number of patients and the number of scars that were treated with the ILCSI, (4) the location of the scar, (5) the type of corticosteroid, its concentration, dose and/or endpoint, if mentioned, (6) interval of treatment, including the session, (7) history of previous intralesional treatment, (8) anaesthesia method employed pre-, intra- and postinjection, (9) pain assessment tool and scar assessment tool used, (10) effectiveness of pain control, (11) effectiveness of scar treatment and (12) side effects and non-compliance. Data are presented in online supplemental tables S1 and S2.

Data from journal articles, expert opinions and correspondences are reported in a narrative summary. A narrative summary is also used to describe how the results relate to the review's questions.

## Patient and public involvement

Patients and/or the public were not involved in the design or conduct or reporting or dissemination plans of this research.

## RESULTS

The search yielded 61 articles, along with an additional 13 handpicked articles. 12 duplicate records were removed, and 28 reports were excluded. 34 articles were included for data extraction (shown in the flow chart in figure 1). There were 16 prospective studies, 2 retrospective studies, 1 case study and 15 journal articles, including expert opinions. All the prospective, retrospective and case studies included used triamcinolone acetonide (TAC) as a corticosteroid for hypertrophic scarring and keloid infiltration. No study has described any difference in the degree of HTS or keloid pain.

11 studies primarily investigated pain reduction with various anaesthetic methods, such as the use of topical analgesia,[20–23] cryoanaesthesia,[24] mixing TAC with analgesia,[20 25] slow infiltration,[26] vibration analgesia,[27] modified injection techniques[28] or needle-free injectors.[29–31] 10 studies evaluated the effectiveness of HTS and keloid treatment when specific anaesthetic methods were used, such as a modified injection technique, cryoanaesthesia before and after corticosteroid injection, a combination of TAC with local analgesia or a needle-free injector.[28–34] Four other studies compared pain during ILCSI for scars and verapamil injection or clobetasol propionate 0.05% cream[35–38] (online supplemental table S1).

### Patient population

16 studies included an adult population over 16 years of age, including four that also included patients from the teenage population. One prospective study explored the effectiveness of the ILCSI in children aged 1–14 years[34], and one retrospective study investigated pain control via needle-free injectors in patients aged 5–17 years[29] (online supplemental table S1).

Four studies had no prior intralesional TAC treatment for HTS/keloid,[20 24 36 38] and four studies excluded patients who had keloids treated for at least 3 months to 5 years before enrolment.[21 28 35 37] Five studies reported prior ILCSI, with two studies requiring patients who could not tolerate ILCSI pain or had needle phobia[22 26 29–31] (online supplemental table S1).

### Needle choice and injection rate for intralesional TAC treatment

The choice of needles was mentioned in 10 studies and ranged from 23 to 30 gauge, and 3 studies employed needleless injection. The extremely slow TAC infiltration rate is 3–6 mL/hour, whereas other studies mention a faster rate of 0.1 cc/(10–15) s and 0.5–1 cc/min[20 21 26] (online supplemental table S1). The rationale for the choice of needle and rate of injection is further explained with review articles and expert opinions.

### Anatomical location of HTSs or keloids in relation to pain and pain scores during keloid infiltration

No study has described the differences in pain between the anatomical locations of keloids and HTSs during steroid injection. One study reported a significantly greater Visual Analogue Scale (VAS) score during needle introduction for sternal keloids than for ear keloids[20] (online supplemental table S2).

### Preinjection analgesia

Pain during drug infiltration is consistently greater than pain during needle introduction into keloids, where pain during needle introduction improves with the use of eutectic mixture of local anesthetics (EMLA) with or without 1% lidocaine mixed with steroids.[20] Pain during needle introduction, however, can be greater than pain during drug injection when an extremely slow injection technique is employed.[26] Compared with topical EMLA, skin cooling can significantly improve pain during needle introduction[21] (online supplemental table S2).

One study examined the effect of the application of 60% lidocaine tape for 2 hours prior to the slow injection of steroids. Pain after steroid injection was compared with that before treatment, and the pain improved from a mean of 82.6 to 18.9 mm.[22] Pretreatment with cryotip resulted in significantly lower Verbal Descriptor Scale (VDS) and VAS scores[24] (online supplemental table S2).

Yosipovitch *et al* compared the combined effects of cryotherapy and TAC with those of steroid or cryotherapy alone.[33] The findings indicate that with combined therapy, keloid thickness and itchiness are reduced better than with TAC alone or cryotherapy alone. However, there was no difference in pain intensity between the treatment methods. Additionally, there was no keloid recurrence at the 8-month follow-up (online supplemental table S2).

In prospective, retrospective and case studies, sedation and general anaesthesia were not used.

### Mixed analgesia with steroids

Two studies focused primarily on pain management during intralesional TAC injections when mixed with local anaesthetics. In one study, the effectiveness of topical anaesthesia versus TAC combined with local anaesthesia was directly compared, showing similar pain levels whether EMLA cream was applied beforehand or when TAC was administered with lidocaine.[20] In a separate study, combining TAC with lidocaine resulted in superior pain relief. TAC with lidocaine was more effective than triamcinolone injection alone in reducing scar volume and improving pliability.[32] Recently, in 2023, a comparison of pain control between EMLA and 1% buffered lidocaine mixed with epinephrine (1:100 000) infiltration prior to intralesional TAC demonstrated that the Local anesthetics (LA) injection method relieved pain more significantly, with 63% of the patients studied preferring this method[23] (online supplemental table S2).

A study by a dermatological team investigated the ILCSI of keloids and other pathologies. It was concluded that triamcinolone, when mixed with lidocaine and epinephrine, has a significantly higher pain score.[25] The study included 6 patients with keloids, 5 of whom were treated with lidocaine mixed with TAC. This higher pain score is attributed to the acidic nature of the anaesthetic, which causes a burning sensation (online supplemental table S2).

### Other pain control methods during steroid injection

Extremely slow corticosteroid injection via an electrical syringe pump at a rate of 3–6 mL/hour over a duration of 10–20 min can achieve pain-free drug infiltration.[26] Xiao *et al*'s experiments on the one-third dose of TAC with 5-fluorouracil (5-FU) mixed with lidocaine given at the keloid base and the rest given after 5 min in a multipoint manner demonstrated that the pain intensity was lower than that of the conventional method.[28] The decrease in pain was attributed to collagen density being lower at

the keloid base, and with the effect of lidocaine at the base, little pain is experienced at the central part (online supplemental table S2).

Vibration anaesthesia using a vibrating device set at 150–183 Hz during TAC injection can significantly improve the VAS score. This method, however, can cause severe pain when applied to the back[27] (online supplemental table S2).

A needle-free injector device was used for corticosteroid infiltration into keloids in the Netherlands for patients who did not show significant improvement after needle injection, had needle phobia or severe injection-related pain. Participants included both paediatric and adult populations, who tolerated and indicated a preference for this method. The Patient and Observer Scar Assessment Scale (POSAS) and Global Aesthetic Improvement Scale (GAIS) scores also improved with this method.[29 30] One case reported Numeric Pain Rating Scale (NPRS) of 1 with every needle-free injection of TAC and 5-FU for keloid treatment, with an improvement in the POSAS score[31] (online supplemental table S2).

One study compared the pain scores experienced during the treatment of HTSs and keloids with the use of TAC versus intralesional verapamil. A total of 42 (84%) patients reported pain and burning sensations during verapamil treatment, whereas in 8 (16%) patients who received intralesional TAC, there was no discernible difference in pain levels.[35] On the other hand, another two studies reported discomfort during injection as an adverse outcome. In one study, pain was reported in 2 out of 64 injections with TAC and 4 out of 113 injections with verapamil.[36] In another study, pain was observed with TAC, whereas no pain was observed with verapamil injection (online supplemental table S2).

### Postprocedure pain and analgesia

Usanakornkul reported that 89.68% of injections were pain-free within 2 min of needle removal and that the pain was entirely resolved within 10 min of injection. In another study, at 1 hour postprocedure, the degree of pain associated with the use of skin cooling, EMLA or no analgesia was similar.[21] There was no mention that additional oral analgesia was required or supplemented in any of the Randomized controlled trial (RCT) (online supplemental table S2).

### Pain assessment and effectiveness of pain control

In nine of the studies, a VAS was used for pain rating, including the use of the Wong-Baker Pain FACES. Other scales, such as the VDS pain thermometer, which rates pain intensity from 0 to 10, and the 11-point NPRS, are also used. Satisfaction levels, which were divided into five levels, were assessed in one study.[21] Further specific questions were asked, such as “Which technique would you recommend if you had to be injected again?” and “What is the preferred pretreatment method?”[21 26 38] In other studies, pain was secondarily assessed as an adverse effect of intralesional scar treatment (online supplemental table S2).

### Treatment effectiveness and side effects

When pain management during the ILCSI was the primary objective of the study, treatment effectiveness was not examined in eight studies.[20–27] Treatment effectiveness was evaluated with the use of a modified injection technique, cryoanaesthesia, cryotherapy, TAC mixed with lidocaine and a needle-free injector.[25 28–33] Moreover, while the effectiveness of intralesional TAC in children was studied and intralesional TAC was compared with verapamil, $CO_2$ lasers and clobetasol propionate cream, pain related to intralesional TAC was observed[34–38] (online supplemental table S2).

A study investigated the treatment effectiveness of the ILCSI in 21 children and reported treatment failure in one case, recurrence after 30 months in one case and one treatment withdrawal due to intolerable pain, although all other participants experienced pain. Nonetheless, no local anaesthetic was used for this study[34] (online supplemental table S2).

Cryoanaesthesia was assessed for its effectiveness in scar treatment and was found to be more effective when given intralesional keloid injection in terms of thickness. No recurrence was noted at the 8-month follow-up.[33] Those treated with cryotherapy alone did not improve and were continued with combined therapy. Hyperpigmentation was observed with cryotherapy (online supplemental table S2).

Taweepraditpol and Udkhamtiang demonstrated that TAC, when mixed with lidocaine, has greater efficacy in reducing scar volume and pliability.[32] In another study assessing pain when combined with lidocaine and epinephrine for mixed pathologies where six keloids were included, the side effects of infection, hypopigmentation and skin atrophy were observed[25] (online supplemental table S2).

Scar thickness and hardness were measured via a modified steroid injection technique on keloids where the one-third TAC was mixed with lidocaine, and the 5 FUs were administered preliminarily 5 min before the remaining drug was injected. The reduction in keloid thickness and hardness improved with increasing experimental methods[28] (online supplemental table S2).

Two retrospective studies and one case study examined the effectiveness of needle-free injectors of corticosteroids for HTSs and keloids and investigated the effectiveness of pain reduction, simultaneously improving the POSAS score in the population studied[29–31] (online supplemental table S2).

Three studies compared the Vancouver Scar Scale (VSS) between intralesional TAC and intralesional verapamil injection. In one study, three patients were excluded because of their response to verapamil. In the same survey, TAC reduced height and improved pliability and pigmentation. At the 18th week and 3 months of keloid treatment, the VSS score was the same.[35] Ahuja

and Chatterjee, in another study, reported greater improvements in scar height, vascularity and pliability.[36] In another report that also used fractional $CO_2$ laser treatment for keloid treatment, the efficacy showed a reduction in height, vascularity and pliability. Pigmentation did not improve with any of the treatments (online supplemental table S2).

### Review articles

The effectiveness of TAC injection can reach between 50 and 100%, with 9–50% of patients experiencing recurrence. However, excessive pain during injections can result in non-compliance with treatment.[39] To minimise pain during injection, TAC can be administered in combination with local anaesthesia.[40] For challenging scars, undiluted injections are recommended to provide a relatively high concentration of the drug. The frequency and dosage of the medication can be adjusted according to the therapeutic response.[41] With repeated injections, keloids and HTSs infiltrate more easily, resulting in less pain during subsequent injections.[42]

When treating sternal keloids, subkeloid analgesia should be administered prior to corticosteroid infiltration. For people who are afraid of needles, the use of $CO_2$-powered or spring-based mechanical injectors during infiltration can reduce pain. However, this approach may result in the waste of the steroid preparation.[42] In terms of drug delivery, such as intralesional penetration and distribution, the needle and syringe method is the most reliable, followed by the $CO_2$-powered needleless injector and then the spring-powered injector.[43]

Needle disengagement is avoided through dental intraligamentary syringes, a 1 mL glass syringe with fitted metal finger handles or a Luer-lock system. A mechanical advantage of the dental syringe is that it requires less effort to penetrate strong fibrous tissue. The method of injecting steroids that a physician chooses relies on the equipment that is available.[42]

In addition to technique, medication combinations also play a role in treatment success. Richard and Fitzpatrick examined 9 years of intralesional 5-FU treatment for HTSs and reported that a combination of 0.1 cc of Kenalog (10 mg/mL) and 0.9 mL of 5-FU in the same syringe was more effective and less uncomfortable.[44] The triple combination of 5-FU, TAC and hyaluronidase, introduced in 2014, has caused injection pain that lasts for up to 4 hours. The severity of the pain varies, ranging from mild to moderate. To manage this pain, analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) and cold therapy are often needed.[45]

Furthermore, proper anaesthetic techniques are crucial in managing pain associated with injections. Before injections can be administered, other anaesthetic techniques are indicated, such as general anaesthesia.[46] The ring block approach is another recommended strategy that yields optimal analgesia.[47] To reduce atrophy and depigmentation, the injection should be restricted to the scar site and periscar, avoiding normal tissue surrounding the incision.[48]

By making the fibrous tissue less dense, cryotherapy may help with injection, which allows the injection to enter the tissue more readily. It may also partially anaesthetise the area prior to infiltration.[42]

### Expert opinions

Reeves noted in a related article on the ILCSI review that his preferred injection system is a fused 1 cc insulin syringe with a 27-gauge needle. This setup offers the benefit of preventing sudden disconnections and allows for a titrated dose of up to 0.01 mL.[49]

Azad and Sacks addressed intralesional steroid injection for HTSs, and as keloids are painful, suggested a preliminary smidgen of Ametop or EMLA with a film dressing to a non-scarred area.[50] Two syringes are loaded: the first is loaded with mixed short- and long-acting local analgesia that is injected beneath the scar, and the second is an insulin syringe with steroids for the keloid or HTS. The advantages of this technique include alleviating scarring, making steroid injections to keloids and HTSs painless and easier to perform. There were concerns that a needle prick adjacent to the scar could give rise to another HTS or keloid in the vicinity, and a slow injection of lidocaine mixed with a corticosteroid via an electric pump was advocated.[51]

A year later, Nduka *et al* described the use of oral analgesia prior to treatment and cooling of the skin with frozen saline sachets wrapped with wet gauze for 10–15 min prior to steroid injection.[52] In comparison, ethyl chloride spray is not tolerated because of rapid temperature changes. This method is quick, safe and cost-effective and avoids additional injections.

In another discussion about painless steroid injections, it was explained that the perception of pain during injection can be influenced by factors such as the type of solution used, its pH and temperature, the tissue puncture, the fluid pressure and the solution's flow rate.[53] Controlled infiltration with a microprocessor injection device intended for local anaesthesia administration for dental phobia was repurposed for LA administration before steroid injection.

To prevent new keloid formation, Mishra recommended using a field block or preparatory mixed short- and long-acting local analgesia below the keloid, through which keloid tissue close to its edge should be used without pricking healthy skin.[54] After 3 min, the keloid was anaesthetised, and TAC was administered. The benefits of this technique include painless intralesional injection, extended postinjection analgesia and prevention of new keloid formation; nonetheless, the discomfort persists with keloid injection in the LA, although it is well tolerated.

In 2008, Chuang *et al* applied Poiseuille's law, which governs the laminar flow of fluid dynamics, to explain the

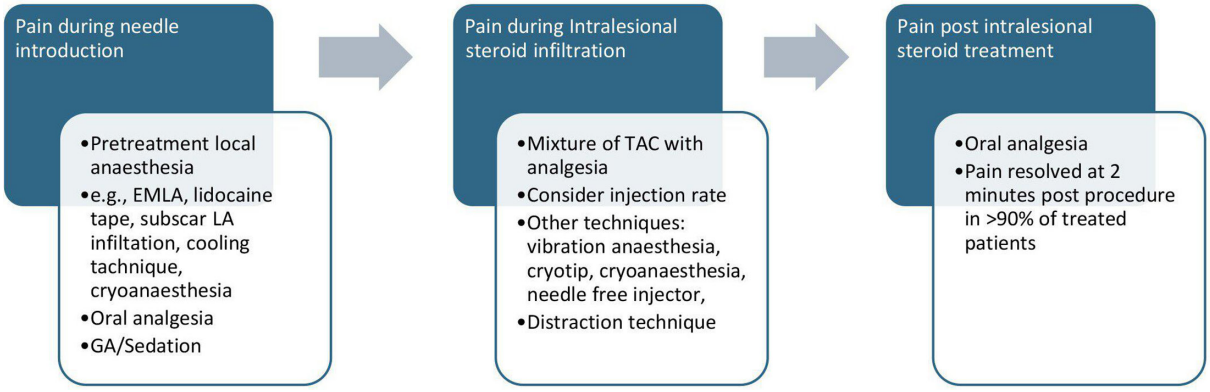


**Figure 2** Pain management strategies in intralesional steroid infiltration for hypertrophic scar (HTS) and keloid treatment.

limitations of using a 30-gauge needle for keloid treatment, $\text{Pgauge} = \frac{8\eta L(\text{flow rate})}{\pi R4}$ [55]

The inner radius that is raised to a power of four significantly influences the pressure rate, in which, at a given constant flow rate, a 30-gauge needle would be 27 times greater than that with a 23-gauge needle. This significant pressure difference explains why a 30-gauge needle may be ineffective for treating firm keloids. In this method, after local analgesia mixed with epinephrine is given below the keloid, the firm keloid is infiltrated with multiple longitudinal or cross-sectional passes with a large-bore needle to allow significant deposition of steroids. The needle tract side closes spontaneously and traps the steroid solution within the keloid. Chuang *et al* also advised using a Luer-lock syringe to prevent disengagement and ensure a safe and smooth injection process.

## DISCUSSION

This scoping review addressed pain issues related to the injection of HTSs or keloids with corticosteroids. It mapped out the available data from prospective, retrospective, case studies, journal articles and expert opinions.

The earliest described technique of triamcinolone injection involved the use of a 25-gauge needle and 1% lidocaine for local anaesthetic block. Injection initially encounters strong resistance, but as keloids soften, injection becomes less difficult.[6] To attain the lowest possible effective dosage and accommodate each person's unique sensitivity to corticosteroids, test doses of different strengths are advised.[48]

Pain during corticosteroid injection occurs in three phases: needle introduction, drug infiltration and post-injection.[20] Figure 1 illustrates details of the pain alleviation strategies. The drug infiltration phase is particularly painful and warrants special consideration. Pain tolerance varies among different age groups and anatomical locations of scars and has not been thoroughly investigated.

Patients with multiple keloids often prioritise specific scars for treatment on the basis of pain, itchiness or aesthetic concerns, although the criteria for such prioritisation have not been systematically established. Treatment endpoints also vary, with some studies using blanching as a marker, whereas others rely on corticosteroid dosage per scar volume or surface area. These differences impact pain levels, particularly due to pressure buildup in keloids during injection.

Various anaesthetic methods are available, including topical analgesia, local injections and innovative techniques such as vibration anaesthesia and needle-free injectors. General anaesthesia and sedation may be necessary for certain patients, but reviews on patient selection, cost implications and the comparative effectiveness of these methods versus local anaesthesia are lacking. The effective distraction technique is an understated method during the ILCSI.

Topical anaesthetic agents such as EMLA cream, lidocaine tape, skin cooling and cryoanaesthesia are effective for needle insertion but are not helpful during drug infiltration. Diluting TAC with local anaesthetics can greatly reduce its concentration and efficacy, as demonstrated in table 1, whereas its effect on pain during drug delivery may vary. However, it has the advantage of increasing the volume of injectable corticosteroids when the scars to be treated are numerous or large and when the dose of the injected steroids is limited.

**Table 1** Demonstrates the percentage (%) reduction of TAC reduction on dilution with a 1:1 ratio

| TAC concentration (mg/mL) | Dilution with local anaesthetic 1:1 (mg/mL) | Percentage concentration reduced from 40 mg/mL after dilution with local anaesthetic 1:1 (%) |
|---|---|---|
| 40 | 20 | 50 |
| 20 | 10 | 75 |
| 10 | 5 | 87.5 |

TAC, triamcinolone acetonide.

### Strengths and limitations of this study

The limitation of this scoping review is that it did not include research where analgesic methods are included but pain control is not observed, nor did it explore alternative corticosteroid delivery methods.

This review identifies several gaps in existing research, such as a lack of studies comparing different pain management techniques across diverse patient populations, including children and those with needle phobia. Additionally, many studies do not account for specific patient complaints, such as pain, itch symptoms or aesthetic concerns, which can influence the prioritisation and treatment of scars. The scars treated in research studies were often selected based on being previously untreated or having had a pause in treatment for a period of time.

Future research should aim to develop and validate standardised pain management protocols tailored to individual patient needs and clinical settings. Patient satisfaction and preference for pain control methods can be used to guide subsequent drug injections and further improve compliance and treatment outcomes. More rigorous and comprehensive studies are needed to explore the long-term outcomes of pain management strategies, including patient satisfaction, treatment compliance and overall quality of care.

## Conclusion

This scoping review is the first to address the pain related to the ILCSI for HTSs and keloids. This review illustrates that effective pain management can improve compliance and treatment outcomes. Pain associated with TAC injection can occur with needle introduction, drug infiltration and the postinjection phase. The available methods of pain control have varying degrees of success, and the effectiveness of pain control can be influenced by factors such as the patient's age, the anatomical location of the scar and previous treatment experiences. This information serves as a reference for clinicians to optimise pain management strategies and for future research in scar treatment.

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