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Hyaluronidase to Reduce Pain from Local Anaesthetic Infiltration for Carpal Tunnel Decompression

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1. Abstract

Aims: The aim of this prospective cohort study is to investigate the effect of hyaluronidase on pain experienced during local anaesthetic infiltration for carpal tunnel decompression.

Methods: Two cohorts of twenty consecutive patients each underwent carpal tunnel release by a single surgeon over a five-month period. The first twenty patients received a local anaesthetic solution of lignocaine and adrenaline whilst the second group received a mixture of lignocaine, adrenaline and hyaluronidase (Hyalase®). All consecutive patients booked for simple open carpal tunnel decompression under local anaesthesia were included. Patients with other compressive neuropathies, generalized neuropathies or other concomitant hand pathologies were excluded from the study. The primary outcome measurement was pain experienced during local anaesthetic infiltration. Patients were asked to indicate the level of pain felt using a visual analogue scale (VAS) between 0 (no pain) to 10 (maximum pain they can imagine). Secondary outcome measures were operating time, measured as tourniquet time and early complication rates.

Results: Patients administered local anaesthesia with hyaluronidase experienced significantly less pain on infiltration of the proximal palm ($p < 0.05$) and distal palm ($p < 0.05$) compared to those that did not receive hyaluronidase. Infiltration of the palm was the most painful part of the procedure for both groups. There was no statistically significant difference in pain reported on initial needle insertion ($p = 0.95$) or on infiltration of the distal forearm ($p = 0.10$). No patients in either group required additional local anaesthetic. The mean tourniquet time for the group receiving local anaesthesia without hyaluronidase was 3.79 minutes (range 3 to 5 minutes, SD 0.71) versus to 3.65 minutes (range 3 to 5 minutes, SD 0.67) for the hyaluronidase group. There was therefore no significant difference in operating time between the two cohorts ($p = 0.53$). No early complications were observed in either groups.

Conclusion: This study finds that hyaluronidase is effective at reducing pain during local anaesthetic infiltration for carpal tunnel release. We therefore recommend its routine use.

2. Keywords: Hyaluronidase; Hyalase; Infiltration; Injection; Pain; Local anaesthesia

3. Introduction

Carpal tunnel syndrome is the most common

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peripheral nerve entrapment, accounting for 90% of nerve compressions [1]. An estimated one in ten people develop symptoms during their life [2]. Symptoms include paranesthesia, pain and paresis in the distribution of the median nerve of the distal upper limb. This can cause significant functional impairment for patients [3,4].

Management of carpal tunnel syndrome includes conservative options such as patient education, minimizing movements that exacerbate symptoms, avoiding heavy lifting, ergonomic aids at work, splinting at night, massage, mobilization and exercise and local corticosteroid injection. The gold standard treatment for carpal tunnel syndrome, particularly for long term relief, is surgical decompression [2]. Carpal tunnel release is amongst the commonest procedures in hand surgery [5].

Median nerve decompression is performed by dividing the transverse carpal ligament (flexor retinaculum) which acts as the roof of the carpal tunnel. Patients often also have compression from the distal portion of the antebrachial fascia (deep fascia of the forearm) so this is also usually released. The procedure can be achieved through an open incision or endoscopically. While there is continuing debate over the comparative safety and efficacy of these techniques, both appear to be equally effective [6]. Both procedures are generally performed under local anaesthesia with tourniquet control, though other options are available such as general anaesthesia, regional block or wide-awake local anaesthesia no tourniquet technique (WALANT) [7,8].

The most painful part of carpal tunnel release is thought to be the initial infiltration of the local anaesthetic, as the proximal palmar skin over the carpal tunnel area is particularly sensitive [9]. The senior author (AL) has tried a number of techniques to reduce this injection pain. In our experience, the most successful technique is adding hyaluronidase to the local anaesthetic mixture of lignocaine and adrenaline.

Hyaluronidase is a naturally occurring enzyme that degrades hyaluronic acid. It therefore temporarily disrupts extracellular matrix, promoting diffusion of substances through tissues [10]. This “spreading effect”, first noted almost 100 years ago, is used in a range of applications from ophthalmic surgery to subcutaneous drug and fluid administration [11-13]. Hyaluronidase is also used in the field of plastic surgery, most often to manage dermal filler related complications [14].

Hyaluronidase has also been used in carpal tunnel surgery as an adjunct to local anaesthetic infiltration. A prospective, double-blind, randomized controlled trial of 70 patients found that post-operative visual analogue scale (VAS) pain scores were significantly lower in patients administered local anaesthetic with hyaluronidase compared to those administered local anaesthetic alone. Operation times were also significantly shorter in the hyaluronidase group, perhaps due to the enzyme separating tissue planes, aiding surgical dissection. The pre-operative pain scores taken immediately after local anaesthetic infiltration were not significantly different between the two groups [15]. However, there is limited evidence investigating the effect of hyaluronidase at reducing pain during local anaesthetic infiltration, particularly during carpal tunnel release surgery. Hyaluronidase does appear to be effective at reducing infusion pressures and pain when infusing fluids into skin using microneedles [16]. Conversely, a prospective, double-blind, randomized controlled trial of 25 participants found that adding hyaluronidase to 1% lignocaine significantly increases pain on injection compared to injecting lignocaine alone. Although hyaluronidase was found to be useful for increasing the area of anaesthetized skin and reducing tissue distortion [17].

The aim of this prospective cohort study is to investigate the effect of hyaluronidase on pain experienced during local anaesthetic injection for carpal tunnel release surgery. We present a

comparison between two cohorts of consecutive patients, one with addition of hyaluronidase, one without.

4. Methods

Study Design and Setting

This prospective study consisted of two cohorts of twenty consecutive patients each undergoing carpal tunnel release performed by a single surgeon (AL) over a five-month period. The first twenty patients received the usual local anaesthetic mixture of lignocaine and adrenaline whilst the second group received a solution of lignocaine, adrenaline and hyaluronidase (Hyalase®).

Participants

All consecutive patients booked for simple open carpal tunnel decompression under local anaesthesia were included. Patients with other compressive neuropathies, for example cubital tunnel syndrome, generalized neuropathies or other concomitant hand pathologies were excluded.

Procedure

The local anaesthetic infiltration technique used was identical in both groups of patients. However, the first group of twenty patients received a local anaesthetic mixture of 10mls of 1% lignocaine and 1:80000 adrenaline whilst the second group received 10 ml of 1% lignocaine, 1:80000 adrenaline and 1500 IU of hyaluronidase (Hyalase®). The needle was inserted just proximal to the proximal wrist crease, raising a bleb by injecting approximately 2 ml of the local anaesthetic mixture. After approximately 20 seconds the needle was then advanced in a distal direction in the subcutaneous plane, in an antegrade technique, injecting the rest of the local anaesthetic solution to cover the length of the planned incision. During the injection, increasing turgor in the subcutaneous plane was confirmed both visually and by palpation to avoid any deeper injection and inadvertent injury to the median nerve.

After confirming anaesthesia over the entire length of the incision, release of the flexor retinaculum and distal portion of the antebrachial fascia was carried out under an upper arm tourniquet control. The same surgical procedure was performed for patients in both cohorts.

Outcome Measurements

The primary outcome measurement was pain experienced during local anaesthetic infiltration. Patients were asked to indicate the level of pain felt using a visual analogue scale (VAS) between 0 (no pain) to 10 (maximum pain they can imagine). Figure 1 depicts the VAS provided to study participants. An independent assessor recorded the pain scores.

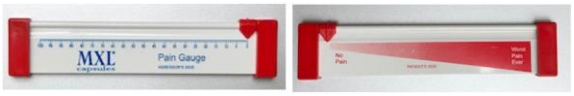

Figure 1: Visual Analogue Scales Provided to Patients to Report Level of Pain Experienced.

The points of pain assessment were chosen based on the senior author's (AL) experience of when patients typically report pain during the infiltration of local anaesthesia. Figure 2 depicts the points of pain assessment. These were on initial needle insertion into the distal forearm, raising the subcutaneous bleb in the distal forearm, local anaesthetic infiltration in the proximal palm under the proximal half of the planned incision and on infiltration under the distal half of the planned incision.

Figure 2: Points of Pain Score Measurement During Local Anaesthetic Infiltration.

1. At the time of needle insertion into the distal forearm
2. Raising the subcutaneous bleb in the distal forearm

3. Local anaesthetic infiltration in the proximal palm under the proximal half of the planned incision
4. Infiltration under the distal half of the planned incision.

Secondary outcome measures were operating time, measured as tourniquet time and complication rates.

5. Data Analysis

Data was collected and inputted into a Microsoft® Excel spreadsheet. Mean VAS pain scores and standard deviations were calculated for each cohort at the four assessment points.

A two-tailed, unequal variance T-test was calculated to assess for statistically significant differences in pain scores and operating time between the two cohorts.

Statistical significance was taken as a p-value less than 0.05. Analyses were done using the SPSS 26.0 software package (IBM Corporation, Chicago, IL). Graphs were created with Microsoft® Excel for Mac Version 16.37.

6. Results

Patient Demographics

A total of 40 patients were included in this prospective cohort study; 20 patients received local anaesthetic alone and 20 patients received local anaesthetic with hyaluronidase.

The mean age of the non-hyaluronidase group was 60 years old (SD 11.6) while the mean age of the hyaluronidase group was 56 years (SD 10.6). The number of males to females in the non-hyaluronidase cohort was 6:14 and 4:16 in the hyaluronidase cohort.

Pain Assessment

Patients administered local anaesthesia with hyaluronidase experienced significantly less pain on infiltration of the proximal palm ($p < 0.05$) and distal palm ($p < 0.05$) compared to those that did not receive hyaluronidase.

Infiltration of the palm was the most painful part of the procedure for both groups. There was no statistically significant difference in reported pain during initial needle insertion ($p = 0.95$) or on infiltration of the distal forearm ($p = 0.10$). No patients in either group required additional local anaesthetic. See Table 1 and Figure 3 for the mean VAS pain scores.

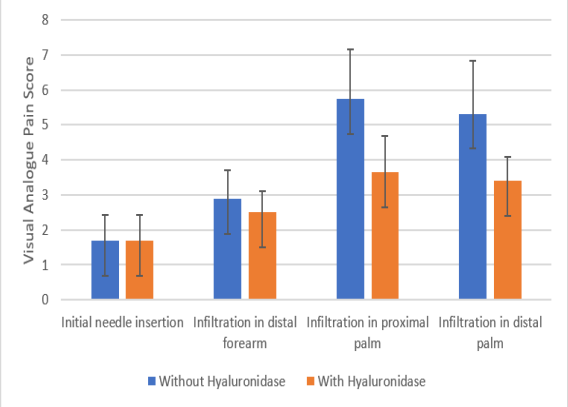

Figure 3: Bar Chart of Mean Visual Analogue Pain Scores During Local Anaesthetic Infiltration with and without Hyaluronidase.

Table 1: Visual Analogue Pain Scores Reported During Local Anaesthetic Infiltration with and without Hyaluronidase.

Mean VAS Score at Points of Pain Assessment	Local anaesthetic mixture without hyaluronidase	Local anaesthetic mixture with hyaluronidase	p value
On initial needle insertion (range)	1.68 (1-3)	1.70 (1-3)	0.95
On infiltration in distal forearm (range)	2.89 (2-4)	2.50 (1-3)	0.10
On infiltration in proximal palm (range)	5.73 (3-8)	3.65 (2-5)	<0.05
On infiltration in distal palm (range)	5.31 (3-7)	3.40 (2-4)	<0.05

Secondary Outcome Measures

The mean tourniquet time for the group receiving local anaesthesia without hyaluronidase was 3.79 minutes (range 3-5 minutes, SD 0.71) versus to 3.65 minutes (range 3-5 minutes, SD 0.67) for the hyaluronidase group.

There was therefore no significant difference in operating time between the two cohorts ($p = 0.53$). All

procedures were carried out uneventfully and no complications were observed in either groups.

7. Discussion

Hyaluronidase is an enzyme that naturally degrades hyaluronic acid present in body tissues. It has been used therapeutically for decades due to its ability to increase tissue permeability and thus promote diffusion of substances [10]. It is often used as an adjunct to local anaesthetics to increase the anaesthetised area [11]. A randomised controlled trial reported hyaluronidase reduces both post-operative pain and operating time for carpal tunnel release surgery [15]. It also reduces infusion pressures and thus pain during microneedle skin injections [16]. This cohort study of 40 patients aimed to assess the effect of hyaluronidase for reducing pain on local anaesthetic infiltration for carpal tunnel decompression.

The results show that hyaluronidase significantly reduces pain experienced during local anaesthetic infiltration of the proximal and distal palm. This was also found to be the most painful part of the procedure, perhaps due to thicker skin, denser subcutaneous tissue and a higher concentration of nerve endings [18]. There was no observed benefit at reducing pain on initial needle insertion or infiltration of the distal forearm. There was also no change in operating time when using hyaluronidase.

The senior author has tried various methods to reduce injection pain for local anaesthetic administration prior to carpal tunnel decompression. This includes cooling and avoiding puncture of the palmar skin on infiltration, the sole injection site being in the thinner and less sensitive skin of the distal forearm instead [19]. This is also the rationale of avoiding a palmar incision in endoscopic carpal tunnel release techniques which have been reported to cause less scar pain and quicker return to work [20].

However, this in itself does not resolve completely the severe pain from infiltration into the palmar skin and subcutaneous tissue. In our experience this is more intense in the proximal part of the palm. The senior author believes that this is partly due to dense subcutaneous skin with numerous fibrous septae connecting the palmar skin with the underlying palmar aponeurosis. Addition of Hyaluronidase to the local anaesthesia makes the dispersal of the anaesthetic easier, requiring less pressure for the injection. This is why our study finds that use of hyaluronidase was beneficial mainly for the palmar part of the local anaesthesia infiltration, where normally the tissue density appears to be highest and where hyaluronidase is effective at reducing infusion pressures.

Hyaluronidase is relatively inexpensive with a UK price of £13.66 per 1500 U ampoule. There are also few reported side effects related to its use. Adverse reactions in the literature are generally mild including post-injection bruising and swelling. There are, however, reports of allergic reactions causing erythema, pain, itching and oedema [10,14]. In our cohort of patients and in the senior author's experience of over twenty years in a variety of indications, there were no observed complications or adverse reactions from its use.

Despite the positive results supporting the use of hyaluronidase to reduce pain from local anaesthesia infiltration for carpal tunnel release, there are some limitations of the study. There was no randomisation in selecting the groups, patients were allocated merely based on when their operation was scheduled. The first twenty patients received local anaesthetic alone while the next twenty received added hyaluronidase. The outcome of the surgery was also not formally assessed with a scoring system such as QuickDASH score. Post-operative pain measurements were not performed as they were not germane to the study. A further limitation was the small sample size and lack of a power calculation. We therefore recommend a large randomised, controlled trial be performed.

8. Conclusion

The findings of this study suggest that hyaluronidase

is effective at reducing pain from the infiltration of local anaesthesia for carpal tunnel release. We therefore recommend it is routinely administered.

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