Study Title: Does a Different Local Anesthetic Improve Pain After Carpal Tunnel Release?

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Does addition of longer-acting local anesthetic improve the post-operative pain after carpal tunnel release? A randomized controlled study

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Background and rationale

Carpal tunnel syndrome, the most common compressive neuropathy of the upper extremity, has been shown to cause significant functional and occupational disability. This condition is caused by compression of the median nerve at the wrist, leading to pain, numbness, tingling, and finger weakness. While non-operative management can improve symptoms, definitive management of refractory cases involves carpal tunnel release (CTR)—the surgical division of the transverse carpal ligament overlying the median nerve. Historically, this procedure was performed in the operating room under general anesthetic or conscious sedation. However, in recent years many surgeons in Canada have transitioned to performing CTR in the clinic under wide-awake local anesthesia with no tourniquet (WALANT)(1). This technique has been shown to provide a near painless experience during CTR. Additionally multiple studies have demonstrated improved patient satisfaction and significant benefits in cost-savings compared to other methods (2-4).

In our clinic, CTR is performed under WALANT. This involves superficial infiltration of the incision site with 10mL of 1% lidocaine with 1:100,000 epinephrine and 1mL of 8.4% sodium bicarbonate. A previous study by the senior author (Billard et al., manuscript in preparation, REB Bio 1439), maximal pain was experienced 8 hours after CTR (Visual Analogue Scale (VAS) pain score 1.91 at 2 hours, 4.65 at 8 hours, 3.81 at 24 hours).

Lidocaine is the most common local anesthetic (LA) used for CTR due to its rapid onset of action (2-5 minutes) and efficacy in pain blockade. However, it has a relatively short half-life and duration of pain relief is only 50-120 minutes (60-180 minutes when combined with epinephrine)(5). Some surgeons (including the senior author) will add sodium bicarbonate to the anesthetic, as it has been shown to increase the duration of LA, as well as decrease pain during initial administration(6, 7).

Longer-acting agents alone (e.g. bupivacaine) are less often used in the outpatient setting for local anesthetic due to a slightly longer onset of action (5-10 minutes). However, duration of pain relief can last up to 8 hours(5). As such, a reasonable compromise might be to use a solution that combines a short- and longer-acting agent. A previous randomized controlled trial by Pressman et al. showed that subcutaneous infiltration of 2% lidocaine with epinephrine + 0.5% bupivacaine or 0.5% ropivacaine resulted in lower pain scores at 4 and 6 hours after CTR compared with lidocaine with epinephrine alone(8). No other RCTs have been performed studying the effects of different local anesthetics on post-op pain for CTR. Furthermore, no studies have compared the effects of these anesthetics with the addition of bicarbonate. Therefore, the aim of our study is to determine whether a combination of lidocaine + bupivacaine with epinephrine and bicarbonate provides increased pain relief compared with lidocaine with epinephrine and bicarbonate (current regimen) over the first 24 hours after CTR.

Research question: Does the addition of bupivacaine to the current LA regimen of lidocaine with epinephrine and bicarbonate provide increased pain relief compared for carpal tunnel release? Secondarily, does this new anesthetic regimen affect eventual outcome at 3 months?

Methods

Study design: Prospective randomized control trial

A research nurse will meet with each patient presenting for outpatient CTR surgery at the Saskatoon City Hospital procedure room. The following exclusion criteria will be applied: age <18 years, repeat CTR on the same side, simultaneous procedures for other hand/wrist pathology, and patients with rheumatoid arthritis or a history of trauma or surgery to the local area.

The research nurse will obtain informed consent for interested participants. The patient will be assigned a subject number and be randomized to standard vs. bupivacaine treatment based on a computer algorithm. Participants will complete the Boston Carpal Tunnel Questionnaire as a baseline for comparison as well as a brief questionnaire on demographics. For those patients that are having both sides released during the study period, the first side will be randomized based on the study protocol and the second side will be anesthetized with the other treatment. They will be blinded to both procedures such that we can directly compare their operative experience.

The surgeon (Dr. Sauder or Dr. Sims) will draw up and mix the pre-determined anesthetic for each patient based on the randomization protocol. The research nurse (who will be performing all assessments) and the patient will remain blinded to the type of anesthetic.

The two types of anesthetic will be:

1) 10mL 1% lidocaine with 1:100,000 epinephrine and 1mL 8.4% sodium bicarbonate (standard treatment)
2) 5mL 1% lidocaine with 1:100,000 epinephrine + 5mL 0.5% bupivacaine with 1:100,000 epinephrine and 1mL 8.4% sodium bicarbonate (bupivacaine treatment)

The participants will be anesthetized in the standard fashion, with all 11mL of LA infiltrated subcutaneously into the area of the incision. After a delay of 20-40 minutes, the CTR will be carried out using the standard mini-open approach. Patients will be provided with the standard post-operative instructions regarding activity and wound care.

After the procedure, participants will complete a short questionnaire (VAS) about any pain experienced during the administration of the local anesthetic and during the procedure. Patients will be sent home with instructions to complete a pain and numbness assessment at 2, 4, 6, 8, 10, 24, 48, and 72 hours after surgery. They will be provided with a form containing the VAS and numbness scale and the times at which they are to self-administer these questionnaires. Additionally, they will be provided with 20 Tylenol tablets (325mg each) and 20 ibuprofen tablets (200mg each), with instructions to take 1-2 tablets of one or both analgesics every 6 hours as needed during the first 72 hours. They will be asked to document the times at which they took the medications, as well as the dosages taken. They will be asked to refrain from using other types of pain medications, if possible. They will also be asked to document use of any other analgesics including Cannabis. Any questions will be answered by the research nurse before leaving clinic.

The day after surgery, at the 24 hour mark, the research nurse will call each patient and inquire about their pain scores and numbness at 2, 4, 6, 8, and 10 hours, as well as the present time (24 hours). He or she will also ask about the number of Tylenol and/or ibuprofen pills taken during the first 24 hours, as

well as the timing of consumption. The research nurse will call the patient again at the 72 hour mark to ask about pain and analgesic consumption between 24-72 hours post-surgery. This information recorded on a password-protected datasheet which contains only the subject number (no identifiers).

The patient will return for their standard follow-ups. At 3 months, the research nurse will repeat the Boston Carpal Tunnel Questionnaire to assess outcome. At this time, if the patient wishes, they may be unblinded.

For patients wishing for bilateral CTR, the first will be performed according to the randomization protocol as described above. The contralateral CTR will be performed 2-8 weeks later (as standard in our practice), with the alternate anesthetic (e.g. first CTR with standard treatment, second CTR with bupivacaine treatment). The same post-operative assessment will be performed for the second CTR. Patients will remain blinded to their type of anesthetic in each wrist until 3 months after the second surgery is performed. At that time, they will be asked by the research nurse whether the first or second surgery provided a better pain experience. Only after this will they be unblinded, if desired.

Statistical analyses:
Based on power analysis, the minimum number of participants needed is 128. Assuming a 10% attrition rate, we aim to recruit 140 participants (70 in each group).

Descriptive statistics will be used to show the patient characteristics of each treatment group. We will compare VAS scores at injection, and 2, 4, 6, 8, 10, 24, 48, and 72 hours after surgery. Additionally, we will compare the amount of post-op oral analgesia (number of Tylenol and/or ibuprofen tablets) required in each group, and the time to first consumption. Finally, we will compare the pre- and post-surgery Boston Carpal Tunnel scores between the two groups. Continuous variables will be analyzed with an independent samples t-test or ANOVA, and categorical variables with a chi-square test.

Results overview
Our study cohort included 139 patients: 67 in the control group and 72 in the intervention group. Post-operative pain scores were significantly lower in the intervention group at 6 hours (2.29 vs. 3.19, p=0.01) and 8 hours (2.92 vs. 3.87, p=0.02). Additionally, patients in the intervention group reported longer time to first analgesic use than those in the control group (5.2 hours vs. 3.7 hours, p=0.02). A greater proportion of patients in the intervention group reported post-operative numbness at nearly all time points, compared to the control group.

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