Subcutaneous Lidocaine Infusion for Chronic Pain: The LIDO-CHRON Study

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Introduction

Lidocaine is a local anesthetic that blocks peripheral and central sodium channels including those in the spinal dorsal horn. Lidocaine is considered a therapeutic option for neuropathic pain unresponsive to usual therapies; IV lidocaine has been shown to be superior to placebo for treating predominantly neuropathic pain.

The Vancouver Island Health Authority Regional Pain Program has a number of patients with difficult to treat chronic pain who receive intermittent subcutaneous infusions of lidocaine. No studies have been published on the use of intermittent subcutaneous lidocaine for the treatment of chronic pain.

We set out to estimate the extent and duration of pain relief in patients receiving subcutaneous lidocaine in our Nanaimo pain clinic.

Objectives

Primary Objective:

- Estimate the extent and duration of benefit for pain intensity that chronic pain patients experience from intermittent subcutaneous infusions of lidocaine using a numerical rating scale (NRS) from 0 - 10

Secondary Objectives:

- Estimate the extent and duration of benefit that chronic pain patients experience from intermittent subcutaneous infusions of lidocaine using:
  - Patient's impression of change in pain
  - Breakthrough medication (PRN) use as a marker of increasing pain
  - Self-reports of global change in function
- Describe the occurrence and rate of adverse effects from subcutaneous lidocaine infusion

Methods

Design

- Single center
- Observational
- Chart review and prospective survey
  - At baseline and daily for the dosing interval of 14 or 21 days
  - Either online or paper-based

Inclusion Criteria

- All patients ≥18 years of age receiving intermittent subcutaneous infusions of lidocaine for chronic pain
  - Dose of 5 – 15 mg/kg; lidocaine 2% solution
  - Administered at 2 or 5 mL/hour using elastomeric infusion pump (Baxter Infusor)
  - Infused into the subcutaneous tissue of the abdomen or upper arm
  - Infusion started by nursing staff at an ambulatory pain clinic
  - Infusion removed at home by patient once complete (approximately 6 to 18 hours)
- Received lidocaine between Jan 7 2011 and Feb 11 2011 at the Vancouver Island Health Authority Regional Pain Program at the Nanaimo Regional General Hospital

Exclusion Criteria

- Receiving subcutaneous lidocaine infusions for an indication other than chronic pain
- Not able to read/write in English
- Does not have computer access/computer skills necessary to complete an online survey and does not wish to complete a paper survey
- Unwilling/unable to provide written informed consent

Results

Figure 1: Study Flow Diagram

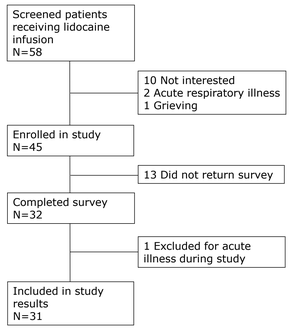
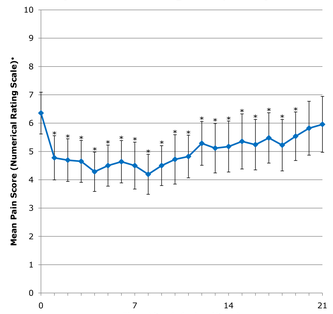


Figure 2: Primary Outcome: Pain Intensity• (Numerical Rating Scale; 0-10)



• Point estimates indicate the mean, error bars indicate the 95% confidence interval of the mean
* Statistically significant difference from day 0; p< 0.05 by a two-tailed paired t-test

Table 1: Baseline Characteristics

Demographics	
Male – no.(%)	11 (35.5)
Age – years; median (range)	52 (38-79)
Weight – kg; median (range)	82 (49-119)
BMI – kg/m² (n= 19); median (range)	25.8 (17.2-34.1)
Lidocaine	
Dose – mg/kg; median (range)	15 (5-17.1)
Interval – no.(%)	
14 days	2 (6.5)
21 days	29 (93.5)
Indication – no.(%)	
Headache	1 (3.2)
Neuropathic facial pain	4 (12.9)
Neuropathic neck/back pain	10 (32.2)
Neuropathic limb pain	8 (25.8)
Complex regional pain syndrome	4 (12.9)
Fibromyalgia	2 (6.5)
Pancreatitis	1 (3.2)
Unknown/unclear	4 (12.9)
Duration of chronic pain – yrs; median (range)	10.5 (0.5-48)
Duration of lidocaine therapy – yrs; median (range)	1 (0-3.7)
Regular pain medications – no.(%)	
Acetaminophen	1 (3.2)
NSAID	3 (9.7)
Tramadol	3 (9.7)
Opioid	13 (41.9)
Antidepressant (TCA, SNRI)	9 (29)
Gabapentin / pregabalin	9 (29)
Benzodiazepine	3 (9.7)
Anticonvulsant	4 (12.9)
Cannabis/cannabinoid	5 (16.1)
Ketamine infusion	1 (3.2)
Breakthrough pain medications – no.(%)	
Acetaminophen	5 (16.1)
NSAID	13 (41.9)
Tramadol	3 (9.7)
Opioid	8 (25.8)
Benzodiazepine	7 (22.6)
Cannabis	3 (9.7)
Mean regular pain medications¶	2.0±1.5
Mean breakthrough pain medications¶	1.3±1.6
Mean non-pain medications¶	2.6±2.2

Does not including lidocaine
¶ Plus-minus values are mean standard deviation

Figure 3: Patient's Impression of Change in Pain (Compared to Day Before Lidocaine)

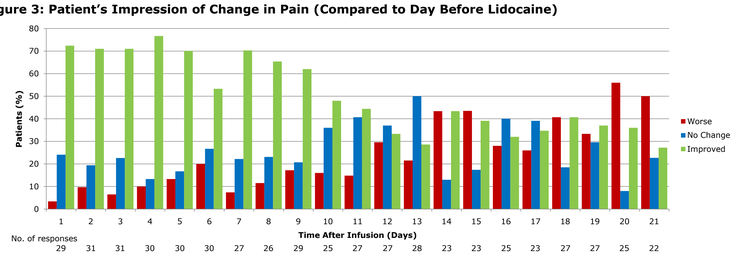


Figure 4: Breakthrough Pain Medication Use in Past 24H

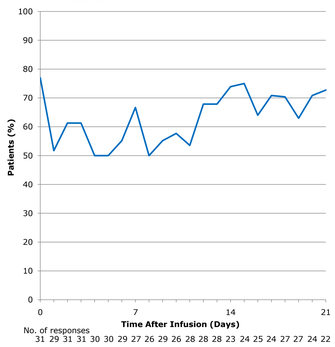
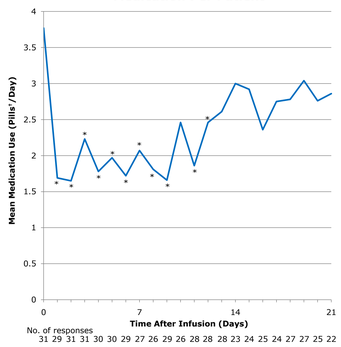


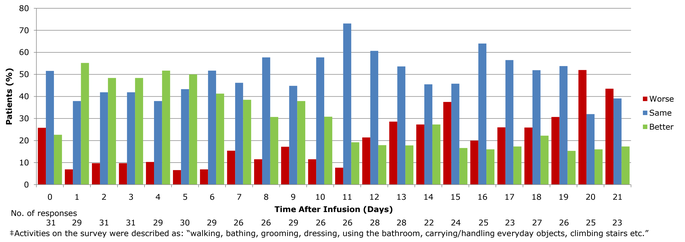
Figure 5: Number of Pills† of Breakthrough Pain Medication Per Patient



† Patients provided their medication use by indicating number of pills. Some patients reported smoking cannabis for breakthrough relief of their pain; this has been included with each use counted as one "pill"
• Statistically significant difference from day 0; p< 0.05 by a two-tailed paired t-test

Results

Figure 6: Ability to Perform Activities‡ (Compared to their "Normal Day")



‡Activities on the survey were described as: "walking, bathing, grooming, dressing, using the bathroom, carrying/handling everyday objects, climbing stairs etc."

Table 2: Adverse Effects

Adverse Effect	*Patients reporting on day 1 (n=29) – no. (%)*	*Time to resolve in ≥ 90% of patients (days)*
Tired, drowsy, fatigue (more than usual)	13 (44.8)	2
Taste changes (metallic)	6 (20.7)	5
Numbness (around mouth, eyes, nose or other)	3 (10.3)	8
Dizziness	3 (10.3)	4
Ringing in the ears	2 (6.9)	4
Headache	2 (6.9)	2
Arm pain	2 (6.9)	2
Nausea	1 (3.4)	4
Itch	1 (3.4)	4
Any Adverse Effect	19 (65.5)	

Discussion

Mean Pain Intensity (Numerical Rating Scale 0–10)

- Prior to lidocaine: 6.4 (standard deviation 2.1)
- On day 1: reduced by 1.6 (95% confidence interval 0.8-2.2)
- Greatest reduction on day 8 (2.2; 95% confidence interval 1.2-2.9)

Clinically Meaningful Pain Reduction

- May require a change of 30% or approximately 2 points
- Day 1: 72% of patients reported an improvement in pain
  - Between days 7 and 13 this was reduced from 70% to 29% of patients

Use of Breakthrough Medication for Pain

- Number of patients using breakthrough medication increases after day 8
- Reduction in the number of pills used per patient was no longer statistically significant after day 12

Activity

- The percentage of patients reporting "better than normal" ability to perform activities increased from 23% to 55% after receiving lidocaine
  - By day 11 levels were similar to baseline

Adverse Effects

- Common; reported by 66% of patients 24 hours after receiving lidocaine
- Most were resolved by day 4

Study Limitations:

- Small sample size
- Open label
- No control group
- Responses on paper-based survey may be completed on the wrong date
- Responses may be influenced by history of concern for withdrawal of funding for lidocaine therapy

Conclusions

Subcutaneous infusions of lidocaine appear to provide a mean reduction of pain intensity of up to 2.2 points (NRS from 0-10) in patients with chronic pain (predominantly neuropathic in origin).

Initial improvements in pain intensity, use of breakthrough pain medications and the ability to perform activities start to diminish for many patients between days 8 and 14.

Subcutaneous lidocaine for chronic pain merits further investigation. Future studies should attempt to control for placebo effects, compare lidocaine doses and intervals and determine which pain conditions are most likely to benefit from lidocaine therapy.

References available on request – Kyle.Grieve@viha.ca