



Dear Doctors,

Re: Ambulatory Infusions of Lidocaine and Ketamine for Management of Chronic Pain: A Prospective Observational Study

Primary Investigator: Dr. Ramin Safakish, MD, FRCPC

Anesthesiologist, chronic pain intervention

We are pleased to announce that the Allevio Pain Management Team is conducting a Prospective Observational Study for the assessment of an intervention to help patients with **chronic neuropathic pain**. Study participants will be receiving 5 intravenous infusions of lidocaine + ketamine within 2-month intervals between infusions. The intervention will be done at Allevio Pain Management, located at #101 - 240 Duncan Mills Road, Toronto, Ontario. All the infusions will be done under the direct supervision of Anaesthesiologist and Anesthesia Assistant.

The purpose of the study is to evaluate the effectiveness of lidocaine and ketamine, administered through IV. These two pain medications have been used to control neuropathic pain with respectively different mechanisms. Neuropathic pain is a challenging condition to manage due to its severity, chronicity, and resistance to currently available analgesics.

As you know, Lidocaine is a sodium channel blocker that exerts its effects by attenuating peripheral nociceptors sensitization and central hyperexcitability. Ketamine is *N*-Methyl-D-aspartate (NMDA) receptor antagonist. It has been shown that activation of NMDA receptors would cause central sensitization and potentially could be the cause of neuropathic pain after a severe and prolonged acute pain. The combination of these two medications may produce a synergistic effect and allow us to use a lower dose of each drug.

In last 10 years, intravenous lidocaine and ketamine infusion have been used to control neuropathic pain; however, there is no extensive and well-controlled study showing which subgroup of neuropathic pain patients respond to this intervention., nor is there evidence telling us if quality of life can be increased by using this intervention.



While the major cause of neuropathic pain is diabetes, every neuropathic pain patient is welcome to apply for this study. Also, we would like to invite people who developed neuropathic pain due to the treatment of cancer, drug-related neuropathic pain, **platinum-based** antineoplastic and **taxans** group drugs, and radiation-related neuropathic pain in people who have had radiation therapy.

Inclusion/exclusion criteria for this study are following this letter. If you would like to introduce a patient for this study, please send us:

- a short description of the current illness;
- past medical history;
- a list of all known medications and allergies; and
- completed Allevio clinic referral form. In the Reason for Referral section please check Other and write: Lidocaine and Ketamine study. **Please fax the referral with supporting documentation to the following number: 647-957-2255 or mail it to us.**

You may send the package either by mail or fax. Patients who are considered for the study will be streamlined for the study and seen within a 2 week timeframe.

We appreciate your support,

Allevio Pain Management

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The **inclusion/exclusion** criteria for Ambulatory Infusions of Lidocaine and Ketamine for Management of Chronic Pain: A Prospective Observational Study:

Inclusion criteria:

1. Age 18-90;
2. **Neuropathic Pain** duration > 3 months;
3. Multifocal and/or non-dermatomal neuropathic pain per Pain Diagram;
4. Failed medical management with at least 2 neuromodulation agents (e.g., gabapentinoids, antidepressants, cannabinoids);
5. Neuropathic component (12 or more points on S-LANSS);

Exclusion criteria:

1. Non-English speakers;
2. Refusal to sign informed consent;
3. Allergy to ketamine and/or lidocaine;
4. Known relative contraindications to ketamine use which include poorly controlled systemic illnesses: hypertension, hyperthyroidism, ischemic heart disease, heart failure, psychiatric comorbidity (e.g., psychosis, schizophrenia, dissociative state);
5. Known contraindication to lidocaine use which includes current symptomatic or clinically significant brady- or tachyarrhythmia, systolic blood pressure <90 or >180 mmHg;
6. Scheduled interventions targeting neuropathic pain: epidural injections, peripheral nerve blocks, Bier block, radiofrequency of dorsal root ganglia and peripheral nerves, additional lidocaine or ketamine infusions;
7. Newly added analgesic or neuromodulating medications within 30 days;
8. Recently performed neuromodulating interventions within 90 days;
9. Previous lidocaine-ketamine, lidocaine or ketamine infusion within 6 months;
10. Acute intoxication or active illegal substance abuse;