LIDOCAINE (LIGNOCAINE) – SUBCUTANEOUS INFUSION FOR NEUROPATHIC PAIN

Dosing, Administration and Monitoring Guidelines

Guideline purpose and related documents

To provide guidance on the dosing, administration and monitoring of lidocaine (lignocaine) when administered as a subcutaneous infusion for neuropathic pain.

Do not confuse with other protocols or guidelines that utilise lidocaine;
- Lidocaine (lignocaine) - intravenous infusion for headache guideline
- ICU protocol - lignocaine infusion (for Ventricular Tachycardia/Ventricular Fibrillation cardiac arrest)

Please also refer to the following SVHM protocols on the intranet;
- Special Analgesia Nursing Observations Policy
- Continuous Subcutaneous Drug Infusion with a Niki T34 Syringe Driver
- Insertion and Management of Subcutaneous Cannulas Policy
- Syringe Driver Drug Compatibilities – Guide to Palliative Care Practice (2016)
- Medication Policy, Section 11 - Medication Administration

Dual-Naming

The Therapeutic Goods Administration has ruled that lignocaine is to be renamed as lidocaine to align with international use. Until 2023 all products will show the dual labelling “lidocaine (lignocaine)”.

Where this guideline mentions “lidocaine” it denotes “lidocaine (lignocaine)”

Prescribing requirements and restrictions

Subcutaneous lidocaine can be initiated by:
- Acute Pain Service or Chronic Pain Service (Barbara Walker Centre for Pain Management at SVHM) for known or suspected neuropathic pain or as an additional analgesic when standard therapies do not provide adequate pain relief.
- Palliative care services for severe cancer related neuropathic pain syndromes not responsive to standard therapies.

Mechanism of Action and Indication

- Lidocaine is a local anaesthetic and antiarrhythmic which decreases the excitability of nerve and myocardial cells by reducing the entry of sodium through cell membranes. Its effects in neuropathic pain are probably mediated within the central nervous system (1). Lidocaine may be administered subcutaneously for the treatment of neuropathic pain.

Pharmacokinetics and Pharmacodynamics

- The rate of absorption is variable depending on the site of administration and absence or presence of a vasoconstrictor. Subcutaneous administration results in the lowest concentration of lidocaine in the bloodstream.
- During continuous subcutaneous infusion (CSCI), steady state is reached after 6 to 8 hours.
- Lidocaine is metabolised mainly in the liver (90%) and excreted by the kidneys (< 10% is excreted unchanged) (5).
Contraindications

- Cardiac disease: Pre-existing hypotension, bradycardia, second or third degree heart block (without PPM), any cardiac conduction defect
- Epilepsy
- Severe liver impairment
- Severe shock
- Myasthenia Gravis
- Known hypersensitivity to amide local anaesthetic agents

Precautions

- Renal disease
- Congestive heart failure
- Severe respiratory failure
- Hypokalaemia, and/or hypomagnesaemia
- Serious CNS disease e.g. meningitis, cranial haemorrhage/tumours or metastatic lesions of the spinal cord may result in toxicity at lower plasma levels
- Elderly

Drug Interactions

- Significant interactions: amiodarone, amprenavir, atazanavir, adrenergic Beta-blockers (e.g. atenolol, metoprolol, propranolol) may increase lidocaine serum concentrations with resultant toxicity - additive cardiac depressant effects, cimetidine, dihydroergotamine, fluvoxamine, fosamprenavir, grapefruit juice, hyaluronidase, itraconazole, lopinavir/ritonavir, phenytoin (additive cardiac depressant effects), propofol, St. John’s Wort (hypericum), suxamethonium, saquinavir, telaprevir.
- Other interactions: cisatracurium, darunavir, etravirine, nitrous oxide, nevirapine (8).

Adverse Effects

COMMON

- Cardiovascular: bradycardia, hypotension (3%), postural light headedness
- Dermatologic: injection site pain
- Gastrointestinal: vomiting; diarrhoea
- Musculoskeletal: back pain (3%)
- Neurologic: dizziness, headache (3%), light headedness, perioral numbness, paraesthesia, shivering (2%), somnolence, tinnitus
- Ophthalmic: blurred vision, diplopia
- Psychiatric: apprehension, confusion, euphoria, nervousness

SERIOUS

- Cardiovascular: cardiac arrest, cardiac dysrhythmia, heart block
- Hematologic: Methaemoglobinaemia
- Neurologic: loss of consciousness, seizure, tremor

Overdose

- Toxicity is dose (and plasma concentration) related and may manifest as central nervous stimulation or cardiac arrhythmias.
- Lidocaine given as a continuous subcutaneous infusion, generally results in stable blood levels (plasma concentration).
- If the dose does not exceed 2 mg/kg/hour, lidocaine plasma concentration is generally less than 3 microg/mL, and toxicity rarely develops. Side effects are dose dependant, predictable, and easily reversed by stopping or slowing the infusion (2). Plasma levels do not need to be measured – monitor for signs of toxicity.
### SIGNS OF TOXICITY

<table>
<thead>
<tr>
<th>Plasma Concentration</th>
<th>Signs/Symptoms of Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 – 6 microg/mL</td>
<td>• Numbness or tingling around the mouth, fingers or toes</td>
</tr>
<tr>
<td></td>
<td>• Light headedness</td>
</tr>
<tr>
<td></td>
<td>• Metallic taste in the mouth</td>
</tr>
<tr>
<td></td>
<td>• Irritability or excitability</td>
</tr>
<tr>
<td></td>
<td>Turn off infusion and call APS or anaesthetist</td>
</tr>
<tr>
<td>At 8 microg/mL</td>
<td>• Dissociation</td>
</tr>
<tr>
<td></td>
<td>• Auditory and visual disturbance</td>
</tr>
<tr>
<td></td>
<td>• Muscle twitching</td>
</tr>
<tr>
<td></td>
<td>• Confusion or sedation</td>
</tr>
<tr>
<td></td>
<td>Turn off infusion, call APS or anaesthetist</td>
</tr>
<tr>
<td></td>
<td>Activate <strong>MET Call</strong> if worried about the patient</td>
</tr>
<tr>
<td>At &gt; 12 microg/mL</td>
<td>• Convulsions</td>
</tr>
<tr>
<td></td>
<td>Turn off infusion, <strong>MET Call</strong> and appropriate anticonvulsant therapy</td>
</tr>
<tr>
<td>At &gt; 20 microg/mL</td>
<td>• Respiratory arrest</td>
</tr>
<tr>
<td></td>
<td>• Cardiovascular collapse</td>
</tr>
<tr>
<td></td>
<td>• Turn off infusion, <strong>Code Blue</strong>, consider giving intralipid as per protocol</td>
</tr>
</tbody>
</table>
For patients admitted to the palliative care inpatient units only and on the recommendation of a palliative care consultant.

Dose and Administration (Palliative Care Protocol)

- The below protocol is a guide only and doses and monitoring may vary according to a patient's age, clinical condition and goals of care.
  - Subcutaneous administration should be slow to avoid inadvertent intravascular injection.
  - Rapid administration will produce dizziness, paraesthesia and drowsiness
  - Dose reduction is required in the elderly, heart failure, shock or liver impairment
  - Commence at 500mg/24hour and assess response after 24 hours. (For 50kg patient rate=0.42mg/kg/hr)
  - If there is an inadequate response, i.e. pain not well controlled, and no evidence of toxicity after 24 hours, increase to 1000mg/24hour.
  - If there is an inadequate response after a further 24 hours and no evidence of toxicity, increase to 1500mg/24hour.
  - If no analgesic response after 24 hours at maximum dose reached cease infusion.
  - If no analgesic response after 24 -72 hours at effective dose.

- Subcutaneous Infusion via NIKI T34 syringe driver:
  - Draw up the lidocaine and make up to 17mls with normal saline, as per the prescription, using 20ml syringe.
  - The Niki T34 pump cannot deliver the full contents of all syringe brands/sizes, therefore the maximum volume has been set at 17ml for the BD 20 ml precise Luer LokTM.
  - Please refer to Subcutaneous Drug Infusion with a Niki T34 Syringe Driver policy on the intranet

Monitoring (Palliative Care Protocol)

Pre -infusion tests and observations
FBC, U&E, LFT, Calcium, Magnesium, Phosphate, heart rate, blood pressure, respiratory rate and 12 lead ECG

During infusion

- BP, heart rate, sedation score:
  - Every four hours for first 24 hours after initiating lidocaine or adjusting dose
  - Once patient has been on stable dose for 24 hours monitoring can be reduced to every 6 hours

- Paraesthesia:
  - Ask patient to report paraesthesia around mouth immediately
  - Ask about paraesthesia around mouth every 4 hours for first 24 hours after initiating lidocaine or adjusting dose
  - Once patient has been on stable dose for 24 hours monitoring can be reduced to every 6 hours

- Pain score:
  - Every 6 hours (omit between 2200 and 0600 if asleep)

- Toxicity/Signs and symptoms of Overdose:
  - Check for signs of toxicity (see Overdose) at least once per shift and specifically record their absence in the nursing notes.
  - If present, cease infusion, give supplementary oxygen and immediately inform the treating unit registrar, or on-call palliative care doctor.

- Daily 12 lead ECG

- Infusion site:
  - Observe for swelling and bruising - refer to hospital policy Insertion and Management of Subcutaneous Cannulas
Dose and Administration (Acute Pain Service Protocol)

- The dosage range is generally 1 - 2 mg/kg/hour.
- Subcutaneous administration should be slow to avoid inadvertent intravascular injection.
- Commence at 1 mg/kg/hour and assess response after 8 – 12 hours.
- If there is an inadequate response, i.e. pain not well controlled, and no evidence of toxicity after 8-12 hours, increase to 1.5mg/kg/hr.
- If there is an inadequate response after 8 - 12 hours and no evidence of toxicity, increase to 2 mg/kg/hour. Do not exceed 2 mg/kg/hour.
- Cease therapy if there is no substantial response within 12 hours at 2 mg/kg/hour (or the dose recommended by the Acute Pain Service.)
- Consider a slower increase of infusion rate (12-24 hourly) in elderly patients and in those with heart failure, liver failure or renal failure.

To administer Infusion via Alaris® pump

Obtain an Alaris pump and choose ‘Lignocaine-Neuropath’ entry available in guardrails
- Pharmacy will make up the Lidocaine during business hours, however if it is outside of business hours, it may require preparation on the ward. If so, the ward nurse can prepare it by using the following procedure;
- Remove 32 mL from a 50 mL bag of 0.9% sodium chloride intravenous infusion (product code: Baxter® AHB 1306A) (Due to overage this should leave ~25mL in the bag. Overage is brand specific so check if not Baxter AHB 1306A)
- Add 2500 mg of Lidocaine (5 x Xylocard® 500 mg/5mL polyamp = 25mL) and label
- The bag will contain 2500 mg/50 mL (= 50 mg/mL) lidocaine
- Connect Alaris® giving set to bag, manually prime line and place in the pump
- Program pump using preprogrammed safety Guardrails
- For starting dose refer to initial rate prescribed on the Analgesia Infusion Treatment Form SV754 (see Table A for guide)
- Insert a scalp vein cannula into subcutaneous tissue (e.g. abdomen, thigh, lateral aspect upper arm)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>1 mg/kg/hour (mL/hour)</th>
<th>1.5 mg/kg/hour (mL/hour)</th>
<th>2 mg/kg/hour (mL/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.8</td>
<td>1.2</td>
<td>1.6</td>
</tr>
<tr>
<td>50</td>
<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
</tr>
<tr>
<td>60</td>
<td>1.2</td>
<td>1.8</td>
<td>2.4</td>
</tr>
<tr>
<td>70</td>
<td>1.4</td>
<td>2.1</td>
<td>2.8</td>
</tr>
<tr>
<td>80</td>
<td>1.6</td>
<td>2.4</td>
<td>3.2</td>
</tr>
<tr>
<td>90</td>
<td>1.8</td>
<td>2.7</td>
<td>3.6</td>
</tr>
<tr>
<td>≥100</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Example of a prescription for initial therapy in a 70 kg patient: To achieve 1 mg/kg/hour: 70 kg x 1 mg/kg/hour = 70 mg/hour
- Concentration is 2500 mg/50 mL = 50 mg/mL i.e. 5% Lidocaine
- Therefore 70 mg/hour divided by 50 mg/mL = 1.4 mL/hour
Monitoring (Acute Pain Service Protocol)

Pre-infusion tests and observations
Heart rate, blood pressure, respiratory rate and 12 lead ECG

During infusion

- BP, heart rate:
  - Every hour for 4 hours, then
  - Every 2 hours for 4 hours, then
  - Every 4 hours

- Sedation score:
  - Every hour for 4 hours, then
  - Every 2 hours for 4 hours, then hourly

- Paraesthesia:
  - Ask patient to report paraesthesia around mouth immediately
  - Ask about paraesthesia around mouth every 4 hours for first 24 hours after initiating lidocaine or adjusting dose
  - Once patient has been on stable dose for 24 hours monitoring can be reduced to every 6 hours

- Pain score:
  - Every hour for 4 hours, then
  - Every 4 hours (omit between 2200 and 0600 if asleep)

- Toxicity/Signs and symptoms of Overdose:
  - Check for signs of toxicity (see Overdose) at least once per shift and specifically record their absence in the nursing notes.
  - If present, cease infusion, give supplementary oxygen, CALL a MET (or CODE BLUE if convulsions occur) and immediately inform the Acute Pain Service Registrar in hours, or Urgent Anaesthetic Registrar after hours.

- Daily 12 lead ECG
- Infusion site:
  - Observe for swelling and bruising - refer to hospital policy Insertion and Management of Subcutaneous Cannulas
Use in pregnancy and lactation

- Lidocaine is considered safe to use in pregnancy. Maternal use does not appear to be associated with an increased risk of adverse pregnancy outcomes (6).
- Small amounts excreted into breast milk following systemic administration, but may be used and unlikely to pose risk to infant (6)

Presentation and Storage

- Lidocaine (Lignocaine) Hydrochloride (Xylocard 500®) 500 mg per 5 mL polyamps
- Store below 25°C at room temperature. Protect from light (5).
- Xylocard solutions contain no antimicrobial agent and should be used in one patient on one occasion only and any residue discarded. Lidocaine Solution is stable for 24 hours when stored below 25°C (7).

References


Authorship and Contributor Details

<table>
<thead>
<tr>
<th>Primary Policy Author(s):</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Andrew Stewart</td>
<td>Consultant Anaesthetist, Anaesthetics Department (2011 &amp; 2015)</td>
</tr>
<tr>
<td>Noni Oborne</td>
<td>Medicines Information Pharmacist, Pharmacy Department (2015)</td>
</tr>
<tr>
<td>Wendy McDonald</td>
<td>Acute Pain Nurse, Anaesthetics Department (2011 &amp; 2015)</td>
</tr>
<tr>
<td>Dr Tamsin Bryan</td>
<td>Palliative Medicine Physician, Palliative Care Department (2011 &amp; 2015)</td>
</tr>
<tr>
<td>Assoc. Prof Mark Boughey</td>
<td>Director, Palliative Care Services (2011 &amp; 2015)</td>
</tr>
</tbody>
</table>

Amendment (August 2016):

Stewart Cockram  Medicines Information Pharmacist, Pharmacy Department (2016)

Others Consulted, including Committees:

| Man Kok Lee               | Senior Manufacturing Pharmacist, Pharmacy Department (2015) |
| Erini Mathiopoulos       | Senior Pharmacist (Education & Training), Pharmacy Department (2015) |
| Gedal Basman             | Medicines Information Pharmacist, Pharmacy Department (2011) |
| Dr Adam Feldman          | Registrar, Anaesthetics Department (2011) |
| Dr Jane Trinca           | Director, Barbara Walker Centre for Pain Management (2011) |

Medication Guideline Review Group 2015

<table>
<thead>
<tr>
<th>Head of Department Responsible for policy:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Assoc. Prof. David Scott</td>
<td>Director, Department of Anaesthesia (2011 &amp; 2015)</td>
</tr>
</tbody>
</table>