Lidocaine Infusion - Full Clinical Guideline

Reference no.: CG – PAIN/2015/001

Aim and scope:

This guideline is for the use of an intravenous lidocaine infusion to manage perioperative pain in adults only, with the aim to reduce post-operative opiate requirements, and to improve return to normal bowel function in patients undergoing the following operations:

- Laparoscopic or open bowel resection (elective only - Not to be used in septic patients)
- Cystoprostatectomy
- Major Gynae surgery with bowel involvement
- Complex spinal surgery
- Laparoscopic Upper GI surgery

Absolute Contraindications

- Known or suspected allergy to amide type local anaesthetics

Relative Contraindications

- Hypovolaemia
- Cardiac disease (unstable coronary artery disease; Recent MI; Heart failure; Cardiac arrhythmia disorder)
- Electrolyte disorders (for example hypokalaemia will antagonise the effects of lidocaine)
- Seizure disorders
- Renal or hepatic impairment (eGFR <30ml/min/1.3m2 and significantly deranged liver function)
- Pregnancy/breastfeeding
- Neurological disorders (Myasthenia Gravis)
- Hypoxia
- Acid-base disturbance
- Acute Porphyria
- Other administration of local anaesthetic (see below)

High risk patients = elderly, obese, hepatic and renal dysfuntion (risk of respiratory depression).

Instructions for anaesthetist:

Please note:

- **Ideal Body weight is used for dose calculations if BMI > 30kg/m2, see Appendix 1 for dosing table if patient's BMI is >30kg/m2**
- **Should not be used in patients weighing <40kg**
- **No more than 120mg/hr should be infused**
- **Not to be used at the same time, or within the period of action of other local anaesthetic administration.**
    - Single-shot spinal blockade is acceptable to use in conjunction with IV lidocaine
- **Reduce bolus and rate if potential for drug interactions, see Appendix 3**
- Infuse with Arcomed syringe driver loaded with 50ml syringe containing lidocaine 1%**.** Select lidocaine programme, confirm concentration, and programme patient's weight.
- Pharmacology of Lidocaine is described in Appendix 4.

Loading dose at induction: no more than 1.5mg/kg

• Select loading dose 1-1.5mg/kg to be delivered over 10 minutes

Peri-op maintenance dose: 1-1.5mg/kg/hr
• Select maintenance dose in ml/kg/hr
• A good starting rate **1.5mg/kg/hr** (ie for 80kg man - 120mg/hr = 12ml/hr)
• Run at the same rate for the duration of surgery or until the patient leaves recovery.

Post op:
1-1.5mg/kg/hr (maximum of 120mg/hr) and should not generally exceed 24hrs

To run a Lidocaine infusion post-operatively in Recovery
Ensure the lidocaine infusion is stopped and discarded on leaving recovery.
Run through a 'PCA' line with anti-reflux and anti-syphon valve.
A minimum of 10ml/hr of 0.9% Sodium Chloride should flush in the lidocaine
Ensure there is also an adequate separate iv access point.
The infusion and program must be handed over to the recovery staff by the anaesthetist, and the patient reviewed in recovery by the anaesthetist before being discharged.
The anaesthetist should remain immediately available until the patient has been in recovery for 1 hr, and the minimum stay in recovery should be 1 hr.
If going to the ward the infusion should be stopped 15mins before discharge from recovery
The infusion line should be clearly labelled with grey lidocaine stickers along the length of the line.

If the infusion is thought to be required after discharge from recovery then the patient should ideally go to a level 2 environment (HDU). If required for over 24hrs, the rate should be reduced by 50% after 24hrs and this decision should be made by a consultant anaesthetist, consultant intensivist or acute pain consultant.

Instructions for recovery:
If extending post operatively, please follow the following instructions:
• The lidocaine infusion should run at the same rate through an Arcomed pump until the patient leaves recovery
• Do not change the syringe – if the pump runs out, discontinue and discard, unless provided with a new syringe and changed by the anaesthetist.
• Ensure that the infusion line is clearly labelled.
• Do not change the rate, unless adverse symptoms or signs occur.
• If any signs of toxicity occur, stop the infusion and contact the anaesthetist.
• See Appendix 2 for signs of toxicity.
• If unsure for any reason, and unable to get help or advice from an anaesthetist, stop the infusion.

Monitoring should be recorded on a separate chart. Vital signs as per standard recovery protocols is sufficient.
The recovery nurse must verify the medication (type, concentration and dose), and the pump settings with the anaesthetist on arrival of the patient into recovery
Instruct the patient to notify the recovery nurse if experiencing any of the following:
• Twitching/ tremors
• tinnitus
• perioral numbness
• metallic taste
• dizziness
• blurred or double vision
• visual hallucinations

Documentation Controls

Development of Guideline:	Dr Imogen Sisley, Consultant Anaesthetist Reviewed by Dr Sarno 14/3/23
Consultation with:	
Approved By:	Acute Pain & Anaesthetics BU – 14/3/23 Surgery Division - March 2023
Review Date:	March 2026
Key Contact:	Dr Imogen Sisley or Dr Sarno, Consultant Anaesthetist

Appendix 1: Dosage regimens:

If the patient's BMI is >30, use Ideal Body Weight (IBW) to dose lidocaine, which can be calculated as follows:
Height (cm) – 100 cm = IBW for women, kg.
Height (cm) – 105 cm = IBW for men, kg.

Lidocaine 1% (via an infusion pump, only for intraoperative use)
Concentration 10mg/ml, doses expressed as ml.
Give specified volume as loading dose then run at specified ml//hr for maintenance.
NB: Suggested starting rate of 1.5mg/kg/hr). This can be altered if there are drug interactions or signs of toxicity.

Female Dosing Table for BMI >30kg/m2:

Height (feet, inches)		5'1''	5'3''	5'5''	5'7''	5'9''	5'11''	6'1''
Height (cm)		155	160	165	170	175	180	185
Minimum Actual Body Weight (kg) for BMI to be >30kg/m2		72	77	82	87	92	97	103
IBW (kg)		50.0	55.0	60.0	65.0	70.0	75.0	80.0
Bolus dose based on IBW	1.0mg/kg	5.0	5.5	6.0	6.5	7.0	7.5	8.0
(mls of 1% Lidocaine)	1.5mg/kg	7.5	8.2	9.0	9.7	10.5	11.2	12.0
Infusion rate based on IBW	0.5mg/kg	2.5	2.7	3.0	3.2	3.5	3.7	4.0
(mls/hr of 1% Lidocaine)	1.0mg/kg	5.0	5.5	6.0	6.5	7.0	7.5	8.0
	1.5mg/kg	7.5	8.2	9.0	9.7	10.5	11.2	12.0

Male Dosing Table for BMI >30kg/m2:

Height (feet, inches)		5'1''	5'3''	5'5''	5'7''	5'9''	5'11''	6'1''
Height (cm)		155	160	165	170	175	180	185
Minimum Actual Body Weight (kg) for BMI to be >30kg/m2		72	77	82	87	92	97	103
IBW (kg)		55.0	60.0	65.0	70.0	75.0	80.0	85.0
Bolus dose based on IBW	1.0mg/kg	5.5	6.0	6.5	7.0	7.5	8.0	8.5
(mls of 1% Lidocaine)	1.5mg/kg	8.2	9.0	9.7	10.5	11.2	12.0	12.0
Infusion rate based on IBW	0.5mg/kg	2.7	3.0	3.2	3.5	3.7	4.0	4.2
(mls/hr of 1% Lidocaine)	1.0mg/kg	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	1.5mg/kg	8.3	9.0	9.7	10.5	11.2	12.0	12.0

Appendix 2: Signs of toxicity and Management

Symptom severity increases with plasma concentration, mild to moderate symptoms are usually self-limiting following immediate cessation of the infusion for 1-2hrs and resumption of infusion at a lower rate (e.g. 50% or initial rate). Any severe symptoms would require immediate cessation of infusion and call for help. Half-life is short and plasma levels will drop quickly, so it is likely that the patient will improve with only supportive measures. However, if seizures, loss of consciousness or cardiac arrest were to occur, then immediate life support and infusion of intralipid would be indicated. See AAGBI safety guideline on the 'Management of Severe Local Anaesthetic Toxicity' below.

Mild Symptoms: numbness of tongue, peri-oral tingling, metallic taste, light-headedness, tinnitus

Moderate symptoms: visual disturbances, tremors

Severe symptoms:

CNS symptoms

- altered mental status, drowsiness, muscle twitching, severe agitation, unconsciousness and seizures.
- if undetected or untreated these will proceed to coma and the possibility of respiratory arrest or cardiovascular collapse

CVS effects

- negative inotropy
- bradycardia
- conduction blocks – widened PR and QRS, leading to sinus arrest or partial/complete atrio-ventricular block
- myocardial infarction
- hypertension then hypotension
- ventricular tachyarrhythmias
- cardiorespiratory arrest

AAGBI Safety Guideline

Management of Severe Local Anaesthetic Toxicity

1 Recognition

Signs of severe toxicity:

- Sudden alteration in mental status, severe agitation or loss of consciousness, with or without tonic-clonic convulsions
- Cardiovascular collapse: sinus bradycardia, conduction blocks, asystole and ventricular tachyarrhythmias may all occur
- Local anaesthetic (LA) toxicity may occur some time after an initial injection

2 Immediate management

- Stop injecting the LA
- Call for help
- Maintain the airway and, if necessary, secure it with a tracheal tube
- Give 100% oxygen and ensure adequate lung ventilation (hyperventilation may help by increasing plasma pH in the presence of metabolic acidosis)
- Confirm or establish intravenous access
- Control seizures: give a benzodiazepine, thiopental or propofol in small incremental doses
- Assess cardiovascular status throughout
- Consider drawing blood for analysis, but do not delay definitive treatment to do this

3 Treatment

IN CIRCULATORY ARREST

- Start cardiopulmonary resuscitation (CPR) using standard protocols
- Manage arrhythmias using the same protocols, recognising that arrhythmias may be very refractory to treatment
- Consider the use of cardiopulmonary bypass if available

GIVE INTRAVENOUS LIPID EMULSION
(following the regimen overleaf)

- Continue CPR throughout treatment with lipid emulsion
- Recovery from LA-induced cardiac arrest may take >1 h
- Propofol is not a suitable substitute for lipid emulsion
- Lidocaine should not be used as an anti-arrhythmic therapy

WITHOUT CIRCULATORY ARREST

Use conventional therapies to treat:

- hypotension,
- bradycardia,
- tachyarrhythmia

CONSIDER INTRAVENOUS LIPID EMULSION
(following the regimen overleaf)

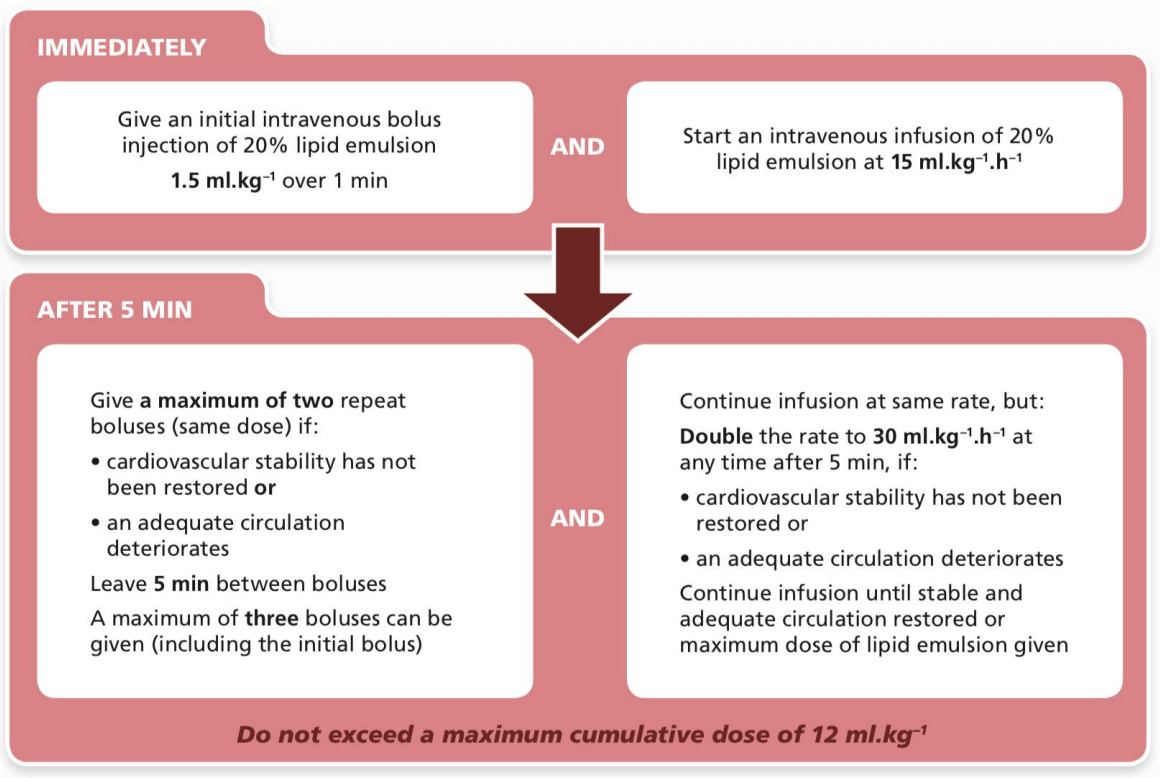
- Propofol is not a suitable substitute for lipid emulsion
- Lidocaine should not be used as an anti-arrhythmic therapy

4 Follow-up

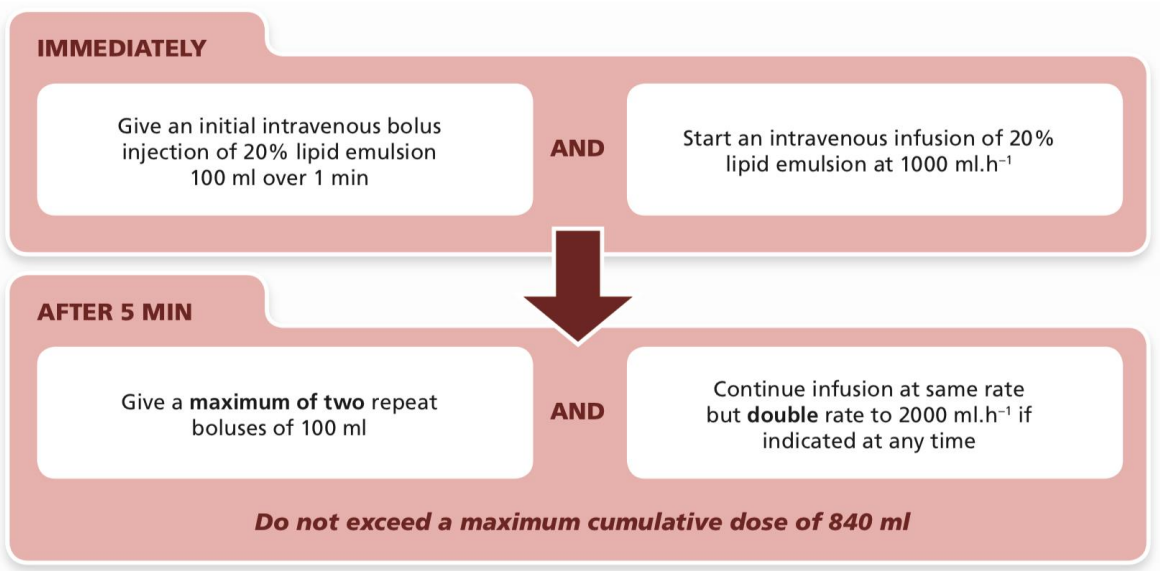
- Arrange safe transfer to a clinical area with appropriate equipment and suitable staff until sustained recovery is achieved
- Exclude pancreatitis by regular clinical review, including daily amylase or lipase assays for two days
- Report cases as follows:
  - in the United Kingdom to the National Patient Safety Agency (via **www.npsa.nhs.uk**)
  - in the Republic of Ireland to the Irish Medicines Board (via **www.imb.ie**)

If Lipid has been given, please also report its use to the international registry at **www.lipidregistry.org**. Details may also be posted at **www.lipidrescue.org**

Your nearest bag of Lipid Emulsion is kept .....



An approximate dose regimen for a 70-kg patient would be as follows:



This AAGBI Safety Guideline was produced by a Working Party that comprised:
Grant Cave, Will Harrop-Griffiths (Chair), Martyn Harvey, Tim Meek, John Picard, Tim Short and Guy Weinberg.

This Safety Guideline is endorsed by the Australian and New Zealand College of Anaesthetists (ANZCA).

https://anaesthetists.org/Portals/0/PDFs/Guidelines%20PDFs/Guideline_management_severe_local_anaesthetic_toxicity_v2_2010_final.pdf?ver=2018-07-11-163755-240&ver=2018-07-11-163755-240

Appendix 3: Drug interactions:
The following may increase the effect of lidocaine or the interacting drug.

- **Suxamethonium** – neuromuscular blockade enhanced and prolonged
- **Pregabalin** is a Ca-channel blocker. Consider reducing the dose of pregabalin for patients on Acute Pain Service to avoid potential hypotension. This is, however, an unlikely interaction. Similarly, exercise caution with patients on **Calcium-Channel Blockers** for the same reason, such as diltiazem, nifedipine, verapamil.
- **Diuretics and acetazolamide** – causing hypokalaemia

Lidocaine is metabolized in the liver by the cytochrome P450 enzyme system (CYP450). However, the clearance of lidocaine is more dependent on liver blood flow than actual liver enzyme activity. Drugs affecting hepatic blood flow will have an impact on lidocaine plasma concentration.

The following may increase lidocaine serum levels and toxic side effects by decreasing metabolism of lidocaine:

- **Anti-arrhythmics** - Amiodarone Class I anti-arrhythmics (including procainamide, quinidine, mexiletine, phenytoin) exert their therapeutic effect by blocking sodium channels. Additive toxicity with lidocaine may be seen causing myocardial depression.
- **Antibiotics** - ciprofloxacin, norfloxacin, erythromycin, clarithromycin
- **Antifungals** - fluconazole, itraconazole, ketoconazole (inhibit CYP3A4)
- **Antidepressants -** fluoxetine, fluvoxamine, sertraline, citalopram, paroxetine (inhibit CYP2D6)
- **Beta-blockers** - They reduce hepatic blood flow and can cause an increase in lidocaine plasma levels by 20 to 30%. Patients on beta-blockers may require lower doses of lidocaine when given as a continuous infusion and lidocaine levels should be followed closely.
- **Other CYP2D6 inhibitors** - By inhibiting CYP2D6, the following drugs may lead to increased serum lidocaine concentrations: SSRIs (above), bupropion, terbinafine, and quinidine.
- **Other CYP3A4 inhibitors** -By inhibiting CYP3A4, the following drugs may lead to increased serum lidocaine concentrations: protease inhibitors (ritonavir, indinavir, nelfinavir), macrolide antibiotics (erythromycin, clarithromycin), azole antifungals (above), nefazodone, verapamil, and cimetidine

The following may decrease lidocaine serum levels by inducing metabolism of lidocaine:

- **Herbal Remedies** - The best known herbal product affecting CYPP450 is St-John's Wort although there is no data to document an interaction. St-John's Wort induces CYP3A4 and could theoretically reduce lidocaine levels.

Appendix 4: Pharmacology of Lidocaine

Lidocaine is an amide local anaesthetic which blocks sodium channels intracellularly, causing prevention of action potential propagation via membrane stabilization. Target plasma concentration is 2.5-3.5mcg/ml. Without an initial bolus it will take up to 4-8hrs to maintain a stable plasma concentration. Due to its short plasma half-life an infusion needs to be started immediately following a bolus to maintain the correct plasma concentration. Toxicity is seen with plasma levels above 5mcg/ml; it therefore has a narrow therapeutic index. Initially symptoms of toxicity will be neurological; when plasma levels exceed 10mcg/ml cardiovascular symptoms will be present. Very rarely will patients have hypersensitivity reactions, reduced tolerance or idiosyncrasy with lidocaine. As seen below, plasma concentration can be significantly affected by dose, speed of injection, acid/base balance, hypercapnia, hypoxia, low plasma protein levels and renal/hepatic/cardiac failure.

Drug availability

pKa 7.9 and at pH7.4, 25% of the drug is unionized. A weak base, therefore an acidic environment reduces the unionized portion (active portion of the drug)

Distribution

70% protein bound, largely alpha1-acid glycoprotein.
Volume of distribution is 0.7-1.5L/kg
Plasma half-life is 6mins after initial bolus

Metabolism

High hepatic extraction, therefore blood flow main determinant
Metabolised in the liver to mainly: Monoethylglycine-xylidide and Glycinexylidide; the former may potentiate seizures and has antiarrhythmic properties, it is converted to glycinexylidide by the liver that is metabolised and excreted by the kidneys. Glycinexylidide has significantly reduced activity when compared to lidocaine.

Elimination

<10% is excreted unchanged
Clearance is 7-11ml/min/kg – reduced in hepatic and cardiac failure
Elimination half-life is 100mins after a single bolus or infusion under 12hrs

Appendix 5: Prescription and Monitoring chart

It is common for mild sedation and/or euphoria, which may be beneficial. It is also common for mild dizziness and nausea, these do not indicate imminent toxicity, but should be relieved by anti-emetics.

Monitoring parameter	First 2 hours	Thereafter
Infusion pump rates	15 min	Hourly
Blood pressure	15 min	Hourly
Heart rate	15 min	Hourly
Enquire about toxic effects	15 min	Hourly
Enquire about side effects	15 min	Hourly
Check for change to ECG	15 min	Hourly
Pain numerical rating scale	Hourly	At the end