Intravenous Lidocaine Infusions and Intralipid Rescue

Acute Pain Service-LHSC VH and UH sites

History

- Lidocaine and procaine used by IV infusion in the 1950s and 1960s for "general analgesia"
- Often continued postop
- Lidocaine infusions in the 1970s and 1980s following MI were standard therapy in attempt to reduce arrhythmias
- First "modern" anesthesia related publication 1985 in chronic pain

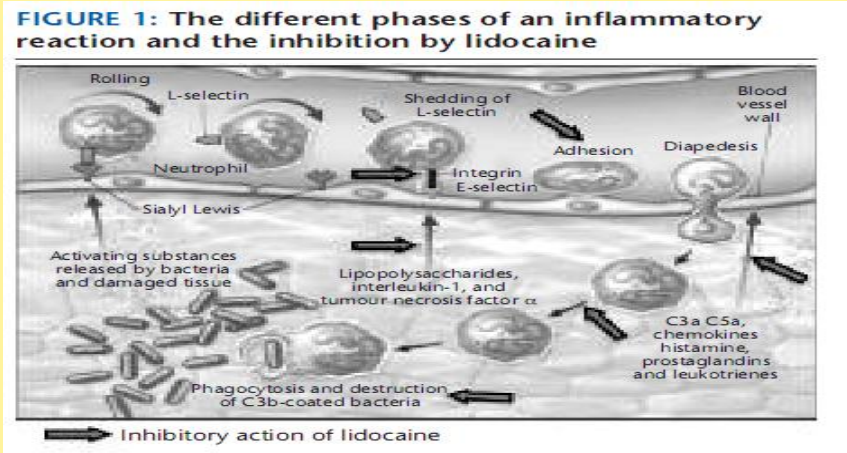
Why Lidocaine Infusions?

- Reduces pain score at rest and with movement
- Decreases post-operative narcotic requirements by up to 30%
- Reduces post-operative ileus (by 8 hours to first flatus and 14 hours to first BM)
- Reduces hospital length of stay (by up to one day in some studies)
- Reduces nausea and vomiting

Mechanisms of action of systemic lidocaine

- Not due to classic local anesthetic effects on Na channels
- Not fully understood
- Animal studies for obvious reasons
- Not conventional pain pathways
- Peripheral nervous system
- Spinal and supraspinal mechanisms
- Anti inflammatory

Anti inflammatory actions



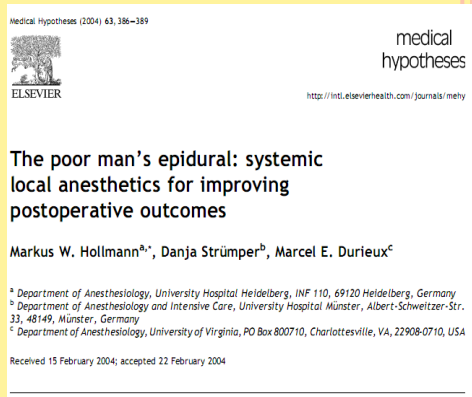
Anesthesiology Rounds 2008 ; 7 : 1-6

Which Patients Could Benefit?

- Patients with pre-existing chronic pain
- Patients with pre-existing opioid use
  - Chronic pain
  - Drug abuse or methadone maintenance
- Patients who have contraindications to or refuse a regional technique
- Patients in whom a laparoscopic procedure unexpectedly converts to an open procedure

POOR MAN'S EPIDURAL

- Will not mimic all beneficial effects of epidural infusion of LA.
- Nevertheless, may be of benefit in patients who cannot or will not have an epidural



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The poor man's epidural: systemic local anesthetics for improving postoperative outcomes

Markus W. Hollmann[a,*], Danja Strümper[b], Marcel E. Durieux[c]

[a] Department of Anesthesiology, University Hospital Heidelberg, INF 110, 69120 Heidelberg, Germany
[b] Department of Anesthesiology and Intensive Care, University Hospital Münster, Albert-Schweitzer-Str. 33, 48149, Münster, Germany
[c] Department of Anesthesiology, University of Virginia, PO Box 800710, Charlottesville, VA, 22908-0710, USA

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WHERE WILL YOU SEE THEM?

- Initially in monitored settings
  - PACU
  - ICU
  - CCU
  - Surgical step-down units
    - Vascular
    - Thoracics
- Eventually with telemetry on the surgical floors
- Palliative care
- Can be run centrally or peripherally, does not need a dedicated line but check compatabilities

How Are They Run?

- May be run through peripheral or central access
- Initial bolus of 1.5 mg/kg up to 100 mg IV push over 2-4 minutes by MD
  - Use 1% or 2% preservative free vials
- Continuous infusion of 1-3 mg/kg/hour
  - No evidence for most effective dose/duration of infusion
  - Use premade bag of 2g/500ml D5W (4mg/ml lidocaine)

Monitoring

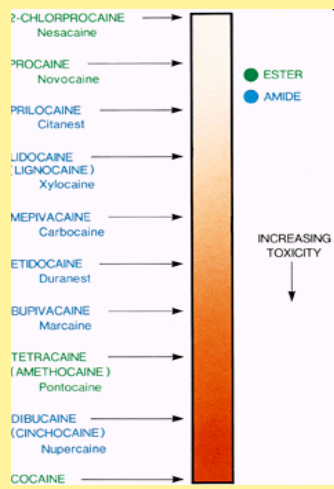
- Continuous ECG or telemetry
- Vital signs and VAS score q15 minutes x 3, then q1h x 12, then q2h x 12, then q4h and prn for reminder of therapy
- O2 sat, respiratory rate, and sedation score q1h for duration of therapy

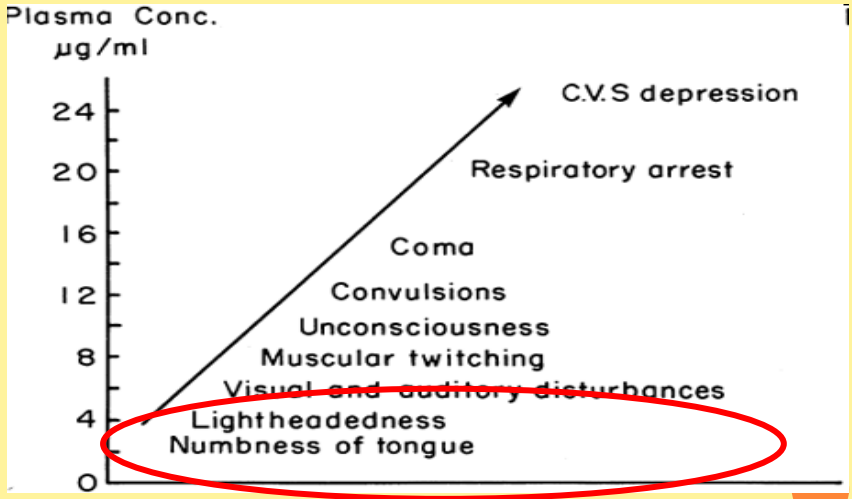
Adverse Effects-Common

- Nausea
- Sedation
- Light-headedness
- Minor degrees of toxic blood levels were observed in some studies but no adverse events were reported

Lidocaine

– intrinsically one of the least toxic LA drugs





PLASMA LEVELS SUMMARY

	Surgery	Regime	Levels µg/ml
Groudine SB Anesth Analg 1998 ; 86 : 235-9.	Open Prostatectomy	1.5mg/kg bolus 3mg/min	1.3-3.7
Koppert W Anesth Analg 2004 ; 98 ; 1050-5	Major Abdominal	1.5mg/kg bolus 1.5mg/kg/hr	1.9+/-0.7
Kaba A Anesthesiology 2007 ; 106 : 11-18	Laparoscopic colectomy	1.5mg/kg bolus 2mg/kg/hr	1.3-4.6
Herroeder S Ann Surg 2007 ; 246 : 192-200	Colorectal surgery	1.5mg/kg bolus 2mg/min	1.1-4.2
Martin F Anesthesiology 2008 ; 109 ; 118-123	Hip Arthroplasty	1.5mg/kg bolus 1.5mg/kg/hr	2.1+/-0.4
Bryson GL Can J Anes 2010 ; 57 : 759-66	Total Abdominal Hysterectomy	1.5mg/kg bolus 3mg/kg/hr	2.63 SD 0.6

	Epidural	IV Lidocaine	
	n = 20	n = 22	*P*
Patients with 1 or more adverse events	20 (100)	22 (100)	—
Adverse events with moderate severity	12 (57)	16 (67)	0.53
Anemia	1 (5)	1 (5)	1.00
Anxiety	0 (0)	1 (5)	1.00
Supraventricular tachycardia	1 (5)	3 (14)	0.61
Back pain	1 (5)	0 (0)	0.48
Bradycardia	1 (5)	0 (0)	0.48
Confusion	0 (0)	2 (9)	0.49
Decreased oxygen saturation level	0 (0)	1 (5)	0.48
Dizziness/lightheadedness	1 (5)	1 (5)	1.00
Fever	1 (5)	1 (5)	1.00
Hyperglycemia	0 (0)	3 (14)	0.23
Hypertension	0 (0)	3 (14)	0.23
Itching	3 (15)	3 (14)	1.00
Lower-extremity numbness	6 (24)	1 (5)	0.10
Nausea	4 (20)	4 (18)	1.00
Intravascular device infection	1 (5)	0 (0)	0.48
Syncope	1 (5)	0 (0)	0.48
Vomiting	0 (0)	1 (5)	1.00
Wound infection	1 (5)	0 (0)	0.48
Adverse events with severe severity	1 (5)	3 (14)	0.61
Arrhythmia	1 (5)	1 (5)	1.00
Confusion	0 (0)	1 (5)	0.48
Facial numbness	0 (0)	1 (5)	0.48
Shortness of breath	0 (0)	1 (5)	0.48

CAUTION WITH COMORBIDITIES

Table 17-10. EFFECTS OF CARDIAC, HEPATIC, AND RENAL DISEASE ON LIDOCAINE PHARMACOKINETICS

	VD_{SS} ($l \cdot kg^{-1}$)	CL ($ml \cdot kg^{-1} \cdot min^{-1}$)	$T_{½}$ (hr)
Normal	1.32	10.0	1.8
Cardiac failure	0.88	6.3	1.9
Hepatic disease	2.31	6.0	4.9
Renal disease	1.2	13.7	1.3

VD_{SS} = volume of distribution at steady state; CL = total body clearance; $T_{½}$ = terminal elimination half-life.

Data from Thomson PD: Ann Intern Med 78:499, 1973.

- Caution if on drugs inhibiting Cyt P450 system eg

Ca Blockers	SSRIs
Cimetidine	Proteasr inhibitors
Ciprofloxacin	Clarithromycin
Antifungals	

Management of major Neurological Toxicity

- Stop infusion immediately
- Notify anesthesia on call
- Activate CCOT
- If agitation, twitching or seizures, administer midazolam 1-2 mg IV prn by order of physician, titrating to effect
- Lidocaine serum levels take a week to be processed, they can be sent to confirm diagnosis but cannot be used to guide management

Management of Cardiac Toxicity

- Stop infusion immediately
- Notify anesthesia on call and activate CCOT
- If cardiopulmonary arrest occurs, standard Advanced Cardiac Life Support is recommended with the following modifications:
  - Vasopressin is not recommended.
  - Avoid calcium channel blockers and ß-adrenergic receptor blockers.
  - If ventricular arrhythmias develop, amiodarone is preferred; treatment with local anesthetics (lidocaine or procainamide) is not recommended.
- If arrest is unresponsive to conventional therapy, consider lipid rescue

Lipid Rescue for Cardiac Toxicity

- Initial bolus - 1.5 mL/kg over 1 minute
- Follow immediately with an infusion at a rate of 0.25 mL/kg/min.
  - **Note:** infusion rate of 0.25 mL/kg/minute cannot be achieved for patients greater than 65 kg due to maximum pump infusion rate of 999 mL/h.
  - Additional Intralipid® to supplement infusion rate must be given IV push (see next slide).
- Continue chest compressions to ensure circulation of lipid.
- Bolus of 1.5 mL/kg may be repeated after 3-5 minutes if circulation has not been restored.
- Continue infusion until hemodynamic stability is restored.
- A maximum total dose of 10 mL/kg is recommended

Supplemental Bolus dose

Patient Weight	Bolus volume (1.5 mL/kg)	Infusion volume required over 30 minutes (0.25 mL/kg/min)	Supplemental IV push volume required to equal 0.25 mL/kg/min over 30 min.	Maximum total volume recommended (10 mL/kg)
45 kg (99 lbs)	68 mL	338 mL	n/a	450 mL
50 kg (110 lbs)	75 mL	375 mL	n/a	500 mL
55 kg (121 lbs)	83 mL	413 mL	n/a	550 mL
60 kg (132 lbs)	90 mL	450 mL	n/a	600 mL
65 kg (143 lbs)	98 mL	488 mL	n/a	650 mL
70 kg (154 lbs)	105 mL	525 mL	25 mL	700 mL
75 kg (165 lbs)	113 mL	563 mL	63 mL	750 mL
80 kg (176 lbs)	120 mL	600 mL	100 mL	800 mL
85 kg (187 lbs)	128 mL	638 mL	138 mL	850 mL
90 kg (198 lbs)	135 mL	675 mL	175 mL	900 mL
95 kg (209 lbs)	143 mL	713 mL	213 mL	950 mL
100 kg (220 lbs)	150 mL	750 mL	250 mL	1000 mL
105 kg (231 lbs)	158 mL	788 mL	288 mL	1050 mL
110 kg (242 lbs)	165 mL	825 mL	325 mL	1100 mL
115 kg (253 lbs)	173 mL	863 mL	363 mL	1150 mL
120 kg (264 lbs)	180 mL	900 mL	400 mL	1200 mL
125 kg (275 lbs)	188 mL	938 mL	438 mL	1250 mL
130 kg (286 lbs)	195 mL	975 mL	475 mL	1300 mL

Adverse Effects of Intralipid

- CVS: Cyanosis, flushing, chest pain
- Hepatic: Hyperlipemia, hepatomegaly
- Respiratory: Dyspnea
- Miscellaneous: Local thrombophlebitis, sepsis

Contraindications To Intralipid

- Severely disordered fat metabolism such as severe liver damage, acute myocardial infarction and shock.
- Hypersensitivity to fat emulsion and severe egg or legume (soybean) allergies.

Other Notes

- Intralipid® use has been reported in the treatment of life-threatening toxicity without cardiac arrest.
- Although some propofol preparations are provided in Intralipid®, these are not a suitable alternative, due to the significant cardiovascular depression caused by the propofol and the low lipid concentration of these solutions. This does not preclude the use of small, incremental doses of propofol to control seizures.

Some Useful References

- Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. Sun et.al. Dis Colon Rectum 2012 Nov;55(11):1183-94.
- Perioperative intravenous lidocaine infusion for postoperative pain control: a meta-analysis of randomized controlled trials. Louise Vigneault et.al. Can J Anesth 2011 (58):22–37
- Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. McCarthy et.al. Drugs 2010 Jun 18;70(9):1149-63.
- ASRA Practice Advisory on Local Anesthetic Systemic Toxicity. Neal et.al. Reg Anesth Pain Med 2010;35: 152-161