PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #180
PARENTERAL LIDOCAINE FOR NEUROPATHIC PAIN

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Background In recent years reports have described the use of parenteral lidocaine for neuropathic pain. This *Fast Fact* reviews the use of parenteral lidocaine for neuropathic pain.

Mechanism Lidocaine is a local anesthetic that is a nonselective sodium channel blocker. Animal and human studies demonstrate that injured nerves develop abnormal, spontaneously active sodium channels at sites of nerve injury, along damaged nerves, and at the dorsal root ganglia of damaged nerves. Lidocaine can suppress this ectopic, spontaneous firing of aberrant sodium channels at concentrations that do not affect normal nerve or cardiac conduction and thereby modulate neuropathic pain (1).

Clinical Trial Data
- Small controlled studies have shown effective relief of neuropathic pain associated with spinal cord injury, diabetic neuropathy, central pain syndrome, chronic regional pain syndrome, and post-herpetic neuralgia with the use of parenteral lidocaine in adults (2-6).
- A meta-analysis concluded that systemic lidocaine is superior to placebo for neuropathic pain, is as effective as other adjuvant analgesics, and is well tolerated in adults (7).
- Two small controlled trials in cancer pain found no benefit of systemic lidocaine (8,9). However, other case reports and one retrospective study support its use (10).
- One trial indicated that an analgesic response to lidocaine is a predictor of a response to mexiletene, an oral congener of lidocaine (11). In practice, the validity of this finding has been questioned and a high rate of side effects (predominantly gastrointestinal) from mexiletene have limited its use.

Dosing Multiple regimens have been described.
- Typically a bolus dose between 1-5 mg/kg is administered intravenously over 15 to 60 minutes depending on the dose.
- A retrospective analysis suggested that a flat-rate trial dose of 500 mg IV over 30 minutes was effective in managing neuropathic pain in adults; however it was associated with a high prevalence of iatrogenic lightheadedness (12).
- Time to analgesia from the bolus dose has been reported to be between 1-45 minutes (13).
- If patients respond to initial bolus, ongoing IV or subcutaneous infusions can be provided over days to months depending on response.
- Serum lidocaine levels should be followed at steady state (t½ ~100 minutes, so 3-5 half-lives for steady state ~5-8 hrs) and intermittently afterwards as clinically indicated. A target level of 2-5 mg/liter is based on dose-response studies and avoidance of side effects as below (13).

Adverse Reactions Lidocaine has dose-related side effects that become progressively more severe at levels higher than 5 mg/liter, including myoclonus (~8 mg/l), seizures (>10 mg/l), and cardiovascular collapse (>25 mg/l) (14). Lightheadedness is the most frequently reported side effect and can occur even at levels less than 5 mg/liter (12). Although lidocaine after a myocardial infarction has been associated with a trend towards increased risk of arrhythmias, cardiac monitoring during studies of normal volunteers and patients has noted no cardiac risks at clinically appropriate levels. Lidocaine is rapidly and extensively metabolized by the liver. Metabolites are excreted by the kidney, thus adjustments may be needed in the case of liver and renal insufficiency, guided by monitoring steady state blood levels.

Pediatric Patients The dosing and efficacy of intravenous lidocaine for pain has not been well established in pediatrics. Case reports and a retrospective analysis have described the safe and effective use of parenteral lidocaine to treat cancer related neuropathic pain, sickle cell pain, and chronic pain in children, adolescents, and young adults at a typical dose of 25-80 mcg/kg/minute (15-17).

Summary There is weak evidence that systemic lidocaine can relieve neuropathic pain in selected patients. Definitive evidence to support its use in cancer pain (both neuropathic and opioid-refractory)

awaits further prospective trials. Most practitioners, however, would not use it as a first line treatment and a pain or palliative care consult should precede its use.

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