The Long-Term Effect of Repeated Intravenous Lidocaine on Central Pain and Possible Correlation in Positron Emission Tomography Measurements

Alex Cahana, MD, DAAPM*, Antonio Carota, MD†, Marie-Louise Montadon, MSc‡, and Jean Marie Annoni, MD§

*Interventional Pain Program, Department of Anesthesiology; †Clinic of Neurological Rehabilitation; ‡Department of Radiology, Division of Nuclear Medicine; and §Clinic of Neurology, Department of Clinical Neuroscience, Geneva University Hospitals, Geneva, Switzerland

Functional neuroimaging suggests that similar brain regions are involved in the processing of pain in healthy subjects and in patients with chronic neuropathic central pain. We present a patient with chronic neuropathic central pain due to a unique lesion to the trigeminal and spinothalamic pathway who had persistent pain relief after repeated IV lidocaine infusions. Positron emission tomography scan results showed a relative hypoactivity of the left posterolateral thalamus before treatment which disappeared after therapy. This case may suggest a stereoselective analgesic effect of lidocaine accompanied by regional cerebral blood flow changes in the thalamus, indicating that sodium channels could, in fact, be highly expressed or modified in the thalamus after thalamic deafferentation.

(Anesth Analg 2004;98:1581–4)

We present a patient with CNCP due to a unique lesion of the spinothalamic pathway who had persistent pain relief after a repeated series of IV lidocaine infusions. On the basis of positron emission tomography (PET) scan results, we discuss the possible mechanisms and action site of lidocaine in CNCP.

Case Report

A 67-yr-old, 54-kg woman, in general good health, was referred to our pain center complaining of a burning pain sensation on the left side of her body, including the lower left face. This symptom had started in 1998, 2 wk after a Listeria rhomboencephalitis, diagnosed by a positive polymerase chain reaction test in the cerebrospinal fluid to Listeria monocytogenes. Magnetic resonance imaging showed a lesion in the left pontine tegmentum (Fig. 1) involving the spinal-trigeminal tract and nucleus, as well as a facial nerve lesion slightly extending to the right side.

The patient complained of “hot” left-sided paraesthesias and burning pain of an intensity of 80 of 100 mm on the visual analog scale (VAS) and maximal (100-mm) pain on the chin and the left palm that was aggravated by fatigue and touch. Pain attacks (lancinating and shooting pains) occurred at a frequency of >30 episodes a day.

Neurological examination revealed left trigeminal hypoesthesia and fascicular facial palsy; left body sensory loss to touch, pain, and temperature, which was most severe at the hand; and mechanical and thermal hyperalgesia and allodynia. Normal somatosensory evoked potential latencies...
confirmed the integrity of the lemniscal pathway, and the
electroneuromyographic study excluded noncentral causes
of pain (such as peripheral neuropathy). A standarized
psychiatric interview and cognitive examination were nor-
mal except for the presence of a moderate depressive state
(global depression scale score of 28).

The pain remained nonresponsive to treatment with nu-
erous drugs, such as amitriptyline, nortriptyline, carbam-
azepine, oxcarbazepine, gabapentin, sodium valproate, lam-
otrigine, baclofen, and clonazepam. At this point, IV
lidocaine was contemplated, and all oral drugs were discon-
tinued 3 wk before the beginning of treatment to allow
washout. The patient’s symptoms did not worsen, and she
gave informed consent for the therapy and the imaging
studies.

Two cycles of daily IV lidocaine (Astra-Zeneca, Zug, Swit-
zerland) infusions (5 mg/kg diluted in 150 mL of 0.9% NaCl
over 30 min without a bolus) for 5 days were arbitrarily
chosen and performed at a 6-mo interval. Hemodynamic
variables (heart rate, oxygen saturation, respiratory rate,
arterial blood pressure, and three-lead electrocardiogram)
were continuously monitored during the infusion while one
of the authors was present to assess and treat any adverse
effects. Mild somnolence and cognitive slowing during the
infusion period and up to the following 6 h were the only
side effects noted. None of the treatments was interrupted
because of lidocaine toxicity.

Spontaneous pain was assessed by using the 100-mm
VAS, and evoked pain was measured by brushing (three
brush strokes) obtained before and 6 h after the completion
of the infusion. Persistent spontaneous pain reduction was
observed immediately after treatment (Day 0); 1, 3, and
7 days after treatment; and 1, 2, and 3 mo after treatment
(Fig. 2) in all body areas but the chin. The frequency of pain
attacks significantly diminished as well (Fig. 3). Although
this was not quantified, hyperalgesia and allodynia evoked
by external stimulation decreased in the same proportion as
spontaneous pain. The depressive state did not change. The
second treatment course 6 mo later produced similar results.

Figure 1. a, Magnetic resonance image showing a left pontine tegmentum lesion involving the spinal-trigeminal tract and nucleus, as well
as a lesion of the facial nerve slightly extending to the right side (the left side of the brainstem is on the left side of the figure). b, Graphic
representation of (a). ALS = anterolateral system, FacNr = facial nerve, SpTTr = spinothalamic tract, SpTNu = spinothalamic nucleus.

Figure 2. Reported spontaneous pain for 3 mo. Note that chin pain gradually returned to pretreatment levels after 60 days.

Figure 3. Reduction of daily pain attacks after the five consecutive
treatments of IV lidocaine.

The procedure, which was similar for both acquisitions,
involved repetitive touch stimuli delivered by one of the
author’s fingers to the left allodynic palm. The patient was
scanned once 24 h before the first lidocaine infusion and was
scanned the second time 24 h after the final infusion. Both
Discussion

The incidence of central pain secondary to CNS disease, specifically encephalitis, remains unknown. It is characterized by the presence of spontaneous burning pain, as well as evoked allodynia and hyperalgesia. Single IV lidocaine infusions offer moderate yet transient analgesic effects (14). We hypothesized that repeated IV lidocaine infusions would provide superior and long-lasting analgesia by reducing the chronic sensitization state present in central pain and that this effect might be stereospecific.

Our patient had refractory CNCP due to a single lesion of the trigeminal and spinothalamic pathways and demonstrated persistent analgesia with repeated cycles of daily IV lidocaine infusions. Because of this prolonged response, oral lidocaine treatment was not sought. Such a protocol has never been tested in humans and may be responsible for the prolonged analgesia observed in the various body regions (4–12 weeks). Continuous systemic infusions of lidocaine have provided analgesia in animal models of neuropathic pain (15). Although cardiac and neurological toxicity was not found in this patient, the potential for major cardiovascular and neurological events (e.g., arrhythmias and convulsions) is present, and the authors stress the importance of performing this protocol under vigilant monitoring.

Another interesting finding is that the PET scan suggested a selective action of the IV lidocaine on the ipsilateral thalamus in a palm stimulation condition; this disappeared after lidocaine infusion. This result is in line with previous case reports that demonstrated asymmetric regional cerebral blood flow (rCBF) in the thalamus in patients with continuing pain due to either peripheral neuropathic pain (16,17) or central pain caused by cortical lesions sparing the thalamus (18). This abnormal thalamic activity was reduced by anesthetic blocks in the case of peripheral neuropathic pain (16) or by motor cortex stimulation in case of central pain (18,19). The role of the thalamus in the persistence of CNCP has also been described in patients after spinal cord injury and deafferentation, where spontaneous neuronal hyperactivity of thalamic cell groups has been registered (20). It has also been hypothesized that allodynic stimuli modify contralateral rCBF in the thalamus of CNCP patients with bulbar lesions (5).

Regional CBF changes in the thalamus, as seen in pain imaging studies, are considered to reflect a general arousal reaction to the presence of pain (21), whereas the frontal, insular, parietal, and cingulate areas are primarily involved in the cognitive, discriminative, perceptual, and emotional aspects of pain processing. If the effect of lidocaine is selective on the thalamus and the arousal component of pain, we should not expect any change in the emotional response to pain. Indeed, in this case, the patient’s depressive state did not improve despite pain reduction. It is possible that lidocaine influenced rCBF by inhibiting platelet aggregation (22); however, its stereospecific effects on the posterolateral thalamus remain unexplained.

The analgesic properties of lidocaine are probably mediated by changes in brain sodium channels (11),

Figure 4. Positron emission tomography transverse sections through the thalamus before (a) and after (b) a 5-day course of IV lidocaine therapy. The left brain structures are on the left side of the figure. *There was relative hypoactivity of the left posterolateral thalamus before the lidocaine infusion (a), whereas the same thalamic area was normally activated after therapy (b).

Figure 5. Thalamic nuclei magnified 40×. *There was relative hypoactivity of the left posterolateral thalamus before the lidocaine infusion (a), whereas the same thalamic area was normally activated after therapy (b).
but very little is known about sodium channel brain expression in CNCP. Our case may suggest a stereo-selective analgesic effect of lidocaine witnessed by rCBF changes in the thalamus, indicating that sodium channels could, in fact, be highly expressed or modified in the thalamus after thalamic deafferentation.

The precise biological nature of sodium channel expression remains unclear. Further studies comparing repeated lidocaine versus single lidocaine versus placebo infusions are needed to assess the long-term efficacy of these treatments. However, this case illustrates that certain brain regions—namely, the posterolateral thalamus—involved in the experience of pain are specifically and repeatedly responsive to IV lidocaine.

References