Sensitivity to Pain Predicts CNS Sensitivity to Lidocaine

GREGG A. KORBON, M.D.,* JOHN C. ROWLINGSON, M.D.,† COSMO A. DIFAZIO, M.D., PH.D.‡

Local anesthetics apparently provide analgesia when given systemically in substantial doses. In an attempt to better define the relationship between systemic concentrations of local anesthetics and sensitivity to pain, Rowlingson et al. and Friedman et al. infused lidocaine and bupivacaine, respectively, into volunteers and assessed their effects on experimentally induced tourniquet pain. Lidocaine was shown to provide sedation but not analgesia at blood levels of 2–3 μg/ml. Bupivacaine, however, did provide analgesia, but only in subjects who experienced mild central nervous system (CNS) side effects with infusion of the drug. Interestingly, this subgroup of individuals who manifested CNS side effects from bupivacaine also had decreased pain threshold (P < 0.025) and decreased tolerance to tourniquet pain during predrug-infusion (control) tourniquet tests compared with the group that did not exhibit CNS side effects. To assess whether this was a generalized phenomenon associated with systemic infusion of amide local anesthetics, the data of Rowlingson et al. were reexamined to determine whether subjects sensitive to CNS side effects from lidocaine demonstrated an increased sensitivity to pain, as was observed in the bupivacaine subjects.

METHODS

Data previously collected by Rowlingson et al. were reexamined to extract previously unreported information. In this study, 14 healthy male volunteers received, in a double-blind manner, on two separate days, either lidocaine 0.5% or normal saline solution as a 10-ml intravenous bolus, followed by increasingly rapid infusions of the test solution. Subjects underwent the tourniquet ischemia test of Smith to determine their threshold (time to onset of pain) and tolerance (time to unbearable pain) several times prior to each test infusion (at the beginning of each day before any drug was given) and then intermittently during the infusion of the test solutions. The data of Rowlingson then were analyzed with respect to two sets of variables: the presence or absence of CNS symptoms after the first lidocaine 50 mg bolus, and threshold and tolerance to tourniquet pain during the preinfusion control tourniquet tests performed at the beginning of each test day.
The means of times to pain threshold and tolerance for all preinfusion (control) tourniquet tests were compared between groups consisting of those that experienced CNS symptoms with the first lidocaine 50-mg bolus and those who did not. The Wilcoxon rank sum test was used to determine significance.

RESULTS

Nine of the 14 subjects developed symptoms with the first 50-mg lidocaine bolus, consisting of sedation, tinnitus, perioral numbness, and the sensation of increased auditory perception. Those subjects who developed CNS symptoms showed significantly lower times to pain threshold and tolerance (Fig. 1) during the control tourniquet tests when compared with those subjects who were asymptomatic. No significant difference in body weight was found between the two groups of subjects. The decrease in mean times to threshold and tolerance observed in the group exhibiting CNS sensitivity to lidocaine was 18% and 31%, respectively, below the tourniquet times of asymptomatic subjects.

DISCUSSION

The findings of increased sensitivity to pain manifested by the decreased threshold and tolerance to tourniquet ischemia seen in subjects sensitive to CNS side effects from lidocaine agree with the results of Friedman et al., who found a similar effect when using bupivacaine in an identical experimental model. The subjects in the bupivacaine study who experienced CNS symptoms at any time during the drug infusion showed decreased threshold (P < 0.025), as well as a strong trend toward decreased tolerance to pain, when the preinfusion control tourniquet tests were compared. The similar findings in both studies suggest that the association between sensitivity to tourniquet pain and sensitivity to CNS symptoms from systemic blood levels of local anesthetic drug may be a generalized phenomenon associated with amide local anesthetics.

This observation may have clinical implications in the use of intravenous regional anesthesia (IV regional). The experimental method for inducing tourniquet pain used in this study is very similar to the circumstances under which tourniquet pain is seen during IV regional. The only difference is that, in our study, during the first minute of tourniquet ischemia, the subject squeezes a rubber ball with the ischemic hand once per second. This shortens the time to unbearable pain (tolerance) by only a few minutes. In our study, the average time to unbearable pain was about 10 min, analogous to the situation seen at the beginning of IV regional. Most patients complain of significant ischemic pain about 10 min after inflation of the proximal cuff, requiring distal cuff inflation and then proximal cuff deflation after anesthesia is established to reduce tourniquet pain.

Also, the dose of lidocaine used as a bolus in our study (50 mg) is similar to the amount of lidocaine released suddenly into the circulation upon tourniquet deflation at the end of an IV regional anesthetic. Therefore, in performing IV regional, it may be useful to observe "tourniquet-pain-sensitive" individuals particularly closely for CNS local anesthetic effects. Those patients exhibiting the greatest sensitivity to tourniquet pain may be the ones most likely to suffer unwanted CNS local anesthetic effects upon deflation of the tourniquet at the end of the case. This caution must remain speculative, however, until further investigation can substantiate our findings in the clinical setting.

In summary, we have demonstrated here that subjects who develop CNS symptoms with an intravenous bolus of lidocaine 50 mg have decreased pain threshold and tolerance to experimentally induced pain from tourniquet ischemia. These data are in agreement with results observed using the local anesthetic, bupivacaine, in a similar experimental model and suggest that human subjects prone to developing CNS side effects from intravenous infusion of amide local anesthetics have decreased pain tolerance. This finding may have clinical significance in the use of intravenous regional anesthesia, such that those patients who complain most readily of tourniquet pain also may be more susceptible to CNS symptoms from systemic levels of local anesthetic upon tourniquet deflation. Greater caution may be indicated in allowing the local anesthetic to enter the circulation in these pain-sensitive individuals to minimize the possibility of CNS local anesthetic toxicity. This caution is
only speculative. Further investigation is required to substantiate our findings in the clinical setting.

REFERENCES

TENS Reduces Halothane Requirements during Hand Surgery

DENIS L. BOURKE, M.D., BARRY A. C. SMITH, M.B.B.S., JOHN ERICKSON, M.D., BRYAN Gwartz, M.D., LARRY LESSARD, M.D.

The use of electrical stimulation to treat pain began in ancient times but received little serious attention until Melzak and Wall introduced the gate control theory of pain in 1965.¹ Since then a number of electrical stimulation devices have become available and a considerable amount of clinical research has been devoted to the study of electroanalgesia. With varying success, clinicians have attempted to provide surgical anesthesia with electroacupuncture, transcutaneous cranial electrical stimulation (TCES), and transcutaneous electrical nerve stimulation (TENS).²⁻⁶ None of these attempts have proved sufficient or reliable as the sole anesthetic.

In the treatment of both acute and chronic pain, TENS has been the most extensively studied mode of electroanalgesia. Although some report TENS to be a successful pain treatment,⁷⁻⁸ there are also equivocal reports.⁹,¹⁰ Close examination of the methods used reveals that virtually every study of TENS and related modalities of pain treatment has suffered from at least one of the following problems: incomplete elimination of placebo effect, lack of true double blinding, or the difficulties inherent in objective quantification of perceived pain.¹¹,¹² Our study of TENS during general anesthesia is an effort to eliminate the placebo effect, ensure double blindness, and use an objective response variable.

METHODS
With institutional approval we studied 44 informed consenting ASA class I or II patients ranging in age from 18 to 45 yr who were scheduled for elective hand surgery. Patients with any evidence of pulmonary problems were excluded from the study. All subjects fasted for 8 h before receiving anesthesia. Two hours before the anticipated time of anesthesia, subjects received oral premedication or diazepam 0.13 mg/kg (to the nearest 2.5 mg). When the subjects arrived in the operating room holding area, standard monitoring devices were applied: ECG, blood pressure cuff, and precordial stethoscope. An intravenous infusion of 5% dextrose in Ringer's lactate solution was begun, and atropine 0.006 mg/kg iv was given. While the patient still was in the holding area, 2 x 2 cm TENS electrodes were placed on the arm designated for surgery. In an effort to locate the TENS stimulation as close to the bicipital plexus as possible, one electrode was placed high in the axilla over the axillary artery and the second approximately 6 cm distally. Electrodes then were secured and the surgical tourniquet and padding applied.

After administering curare 3 mg iv, anesthesia was induced with thiopental 2 mg/kg, and muscle relaxation