David S. Warner, M.D., Editor

Avoiding Subarachnoid or Intravascular Injection of Local Anesthetics

A Single Test Dose

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The Components of an Effective Test Dose Prior to Epidural Block. By Moore DC, Batra MS. ANESTHESIOLOGY 1981; 55:693-6.

Abstract: In 215 surgical patients, the components and monitoring of a single test dose before an epidural block were established. Test doses (3 ml) of bupivacaine, chloroprocaine, lidocaine, or mepivacaine in concentrations sufficient to cause spinal block, with or without 0.0015 mg epinephrine, were given separately *via* intravenous and epidural injection. No evidence of spinal block was observed with epidural injection of any anesthetic. With intravenous injection, no cardiovascular responses were observed in the absence of epinephrine. In the presence of epinephrine, heart rate rapidly increased from 79 ± 14 to 111 ± 15 beats/min. Within 2 min of its injection, the local anesthetic test dose containing epinephrine was sufficient to provide definitive clinical evidence that a needle's bevel rested intravascularly or in the cerebrospinal fluid for all four anesthetics.

THIS study established the components and monitoring of a single test dose of a local anesthetic solution before single dose epidural block for surgical procedures, which within 2 min of its injection produced definitive clinical evidence that the needle's bevel lies intravascularly or in the cerebrospinal fluid.[1] Based on these results, this test has been used likewise to detect incorrect needle or catheter placement for obstetric delivery, perioperative epidural analgesia/anesthesia, and peripheral nerve blocks in close proximity to the vertebral column, *e.g.*, interscalene brachial plexus block or stellate ganglion block (fig. 1). It is the single most important step to avoid cerebral and cardiovascular toxicity.[2–4] Despite the test dose investigation occurring before the clinical use of ropivacaine or levobupivacaine, it, in all probability, is applicable to those local anesthetics as well. Although an epinephrine-containing test dose was previously thought to lack 100% sensitivity and/or 100% specificity for an intravascular and subarachnoid injection, this has been refuted.[5–11]

Various methods to avoid unintended intravascular or intrathecal injection of large doses of local anesthetics had been proposed and were used in performing epidural anesthesia, but systematic examination of their efficacy and efficiency in a busy anesthetic practice had not been evaluated. Our practice was to routinely add epinephrine to local anesthetics for epidural anesthesia and use the same anesthetic for the test dose that was intended for surgical anesthesia. We decided to examine the specificity and sensitivity of these components of an epidural test dose to detect intravenous or intrathecal injection.

With Institutional Review Board Approval and written informed consent, the study was conducted first on volunteers and then patients. Volunteers consisted of two staff anesthesiologists (Gale E. Thompson, M.D., first volunteer, and Robert I. Balfour, M.D., second volunteer), three anesthesia residents, four CRNAs, and one visiting anesthesiologist from Chile. They received no premedication. The study was conducted in a single day. None of them, despite witnessing the results of a previous volunteer's experience,

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D. C. Moore (94) has spent 71 years as an anesthesiologist. This article is his 51st in ANESTHESIOLOGY and marks the occasion of having published under each of its 11 Editors-in-Chief.‡

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believed an intravenous injection of 0.015 mg epinephrine would result in symptoms or signs of epinephrine reactions in them personally. Each volunteer was administered 3 ml saline with 1:200,000 epinephrine (0.015 mg) intravenously in the cubital fossa at the rate of 1 ml/s; these were administered by D. C. Moore. Every 15 s for 3 min after the injection, heart rate was monitored by palpation of the radial artery and arterial blood pressure measured by sphygmomanometry. The volunteers were observed for at least another 10 min.

All volunteers had a typical epinephrine response, *i.e.*, circumoral pallor, palpitation, and nervousness. The maximum mean increase in heart rate and systolic blood pressure was 32 ± 7 beats/min ($P < 0.0001$) and 22 ± 14 torr ($P < 0.0001$), respectively. These signs and symptoms occurred within 20–40 s and lasted about 3 min, except for nervousness, which lasted at least 10 min.

Surgical patients were then studied; 215 patients received 3 ml of one of the following solutions intravenously at the rate of 1 ml/s before an epidural block for surgery: 0.75% bupivacaine (22.5 mg), 1.5% mepivacaine (45 mg), 1.5% lidocaine (45 mg), and 3.0% chloroprocaine (90 mg). These dosages when injected into the cerebrospinal fluid produce evidence of spinal anesthesia in 2 min. Forty of these patients were not medicated, and they received local anesthetic solutions with no epinephrine (n = 10 for each drug). The remaining 175 patients received epinephrine 1:200,000 (0.015 mg) along with the local anesthetic solution. Fifteen minutes before the injection, these patients were medicated with 0.1 mg intravenous fentanyl and 10–15 mg intravenous diazepam. They were divided into groups of 25. Each group was given a different preparation of the local anesthetic drug so as to simulate as closely as possible the solutions usually employed for epidural block (table 1).

The 3 ml of local anesthetic solution injected intravenously was that which was to be used for the therapeutic dose, or the dose needed to establish the required anesthesia. The injection was made, unknown to the patient, into the port in the unclamped intravenous tubing closest to the plastic catheter needle. The 40 patients who received no epinephrine were monitored the same as the volunteers. The 175 patients who received epinephrine were monitored by an electrocardioscope with a heart rate indicator, and questioned when their heart rates increased. An electrocardiogram was obtained before the intravenous injection. Upon completion of the injection, the electrocardiograph was immediately started, and was continued until the increased heart rate slowed and approximated the control rate.

No epinephrine response (heart rate changes) occurred in those patients who received 3 ml of local anesthetic drug with no epinephrine intravenously. When questioned, some reported changes such as feeling relaxed, drowsiness, or buzzing in their ears. The others had no symptoms from the injection.

The heart rates of the patients who received the local anesthetic drug plus epinephrine increased from a mean of 79 ± 14 to 111 ± 15 beats/min starting within 23 ± 6 s after injection. The rate returned to approximately the control rate in 32 ± 33 s. When these patients were aroused and questioned during the increased heart rate, only 56 (32%)

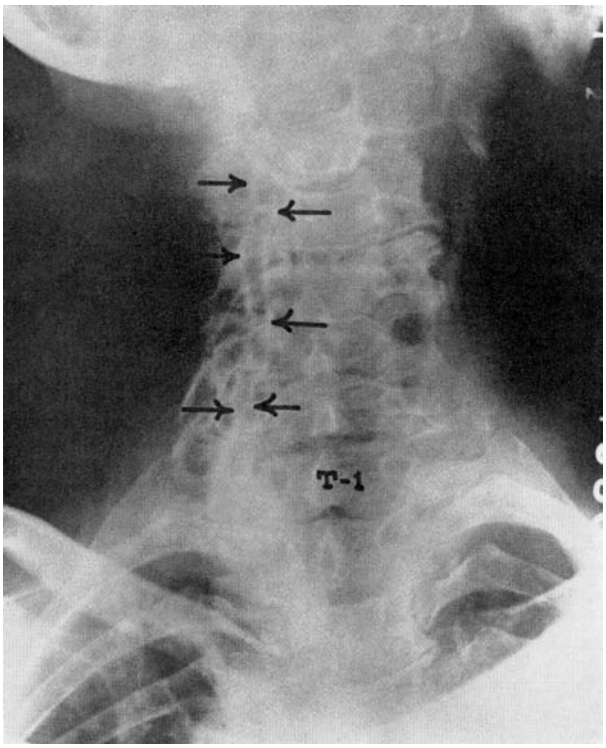

Fig. 1. Arteriogram from a test dose of 2 ml of a Diodrast-local anesthetic solution inadvertently deposited in the vertebral artery. This complication occurred during the execution of a stellate ganglion block, although attempts to aspirate blood were unsuccessful. It is our custom in this block procedure to inject a 2 ml test dose and wait 15–30 s before discharging another 8–10 ml of the solution into the area of the stellate ganglion. The 2 ml deposited in the artery made the patient complain immediately of dizziness, the feeling of "blacking out," and nausea. Had the total dosage been injected, a severe systemic toxic reaction would probably have ensued.

reported a response, namely, palpitation. The others simply said they were sleepy.[1]

We concluded that for a single test dose of a local anesthetic solution to be of value in signaling in all patients the possibility of an intravascular or subarachnoid injection while performing epidural block, it must contain 0.015 mg epinephrine and a dose of the local anesthetic drug, which would rapidly result in evidence of spinal anesthesia. Furthermore, it must be monitored meticulously with vital signs monitors and tested precisely for evidence of spinal anesthesia. In our hands, the test dose has been "foolproof."[8] Since its inception, no systemic toxicity or high or total spinal anesthesia have resulted in more than 10,000 surgical cases and 7,000 obstetrical single or intermittent injection epidural blocks.

During the study, three of the heavily medicated patients had been taking propranolol, a long-acting nonselective synthetic β-adrenergic receptor blocking agent. Although it had been discontinued 2 days before surgery,[1] 0.015 mg epinephrine given intravenously evoked no electrocardiographic changes. Therefore, after 15 min had elapsed, they were challenged with another 0.015 mg and their blood pressures were also monitored. Again, no electrocardiographic changes occurred, but their systolic and diastolic pressures rose from 50 to 70, and from 20 to 25 torr from baseline, respectively, 50–60 s following the injection. No subjective evidence of the injection resulted. Patients with chronic β blockade, using newer agents, also show heart rate and blood pressure changes with the standard test dose containing 0.015 mg of epinephrine.

An intermittent-injection technique was never developed for 0.75% bupivacaine. When bupivacaine became available for clinical use (March 1973), the package insert and the Physicians' Desk Reference clearly provided this information.[12] They stated in their table 2: "For single-dose use, not for intermittent (catheter) epidural technique." Nevertheless, this warning was ignored, resulting in a significant number of encephalopathies or deaths, particularly in mothers and/or their newborns for which cardiotoxicity of bupivacaine – not its improper use – was blamed. In an intermittent-injection technique, there is no reason to use 0.75% bupivacaine. If inadequate muscle relaxation or sensory anesthesia results from the initial therapeutic dose of 0.5% or a lesser concentration of bupivacaine, a reinforcing dose, using the same or a lesser volume and concentration, will reestablish either within a few minutes.

If using a small top-up dose, a test dose is not needed, but it is still monitored as if it were a test dose because cumulation with the amino amides, *e.g.*, bupivacaine, may result.[13] On the other hand, if a contemplate vaginal delivery is converted to a cesarean section requiring a greater volume and/or concentration of bupivacaine, a test dose is administered. A catheter in the epidural space for a period of time could migrate into a blood vessel.

When injecting through a standard epidural catheter, the injected dosage rate of 0.2 ml/s should not be exceeded.[8] Nonetheless, we have found that injecting 3 ml of a local anesthetic containing 1:200,000 epinephrine (0.015 mg) at this rate will identify an intravascular injection into an epidural blood vessel. During its injection and for 45 s after it, the laboring patient must not be stimulated by a uterine contraction, nor should anyone talk to, move, or examine her.[8] Otherwise, a false positive may result; that is, a heart rate increase which, on cessation of stimulation, immediately returns to the control level.

Since the introduction of the recommended test dose and its monitoring, local anesthetic systemic toxicity and total spinal block has been greatly reduced. In addition, anesthesiologists have adopted the practice of incremental injections and using lower concentrations of local anesthetics to achieve the desired block. The value of a properly administered test dose during epidural analgesia/anesthesia and the noted peripheral nerve blocks with careful monitoring of heart rate/rhythm and blood pressure remains the cornerstone of prudent and safe practice.

Table 1. Heart Rate Increases from 3 ml of Local Anesthetic Drugs with Epinephrine 1:200,000 (0.015 mg) Injected Intravenously

Drugs (Each, No. = 25)	Heart Rate (Beats/Min)		Time from Injection to Start of Increase in Heart Rate (s)*	Duration of Maximum Increase in Heart Rate (s)*	Time Elapsed from Slowing of Maximum Heart Rate Until Control Rate Approximated (s)*
	Control (Prior to Injection of Epinephrine)*	After Epinephrine*			
Bupivacaine (Marcaine®), 0.75%					
Commercially prepared†	76 ± 13	109 ± 13‖	24 ± 7	25 ± 8	31 ± 22
Mixed by anesthesiologist‡	81 ± 18	111 ± 17‖	24 ± 7	37 ± 19	36 ± 45
Chloroprocaine (Nesacaine-CE®), 3.0%					
Mixed by anesthesiologist‡	82 ± 14	121 ± 17‖	22 ± 5	43 ± 19	43 ± 45
Lidocaine (Xylocaine®), 1.5%					
Commercially prepared†	78 ± 13	109 ± 14‖	23 ± 4	38 ± 20	31 ± 20
Commercially prepared§	80 ± 14	108 ± 16‖	22 ± 6	20 ± 10	23 ± 12
Mixed by anesthesiologist‡	81 ± 11	111 ± 11‖	24 ± 5	27 ± 7	19 ± 9
Mepivacaine (Carbocaine®), 1.5%					
Mixed by anesthesiologist‡	77 ± 14	109 ± 19‖	22 ± 6	25 ± 15	43 ± 45
All drugs (175 patients)	79 ± 14	111 ± 15‖	23 ± 6	31 ± 17	32 ± 33

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* Means ± SD. † Not autoclaved prior to use. ‡ Both drugs autoclaved prior to mixing by anesthesiologist. Autoclaving: 114°C, under 13.5 kg pressure for 28 min (complete cycle including vacuum). § Autoclaved prior to use. ‖ $P < 0.0001$.

Conscient responsible anesthesia demands a test dose with precise continuous monitoring of heart rate and rhythm, blood pressure, and arterial oxygen saturation, in every patient. And, in addition, in the parturient, fetal heart rate monitoring.

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