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Bupivacaine and Etidocaine for Lumbar Epidural Anesthesia for Intra-abdominal Pelvic Surgery, A Double-blind Study

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Subsequent to the introduction of etidocaine by Adams in 1972,[1] a number of well-controlled clinical studies were reported.[2–4] Clinical comparisons were then made between etidocaine and other local anesthetic agents currently in use.[5–7] Most recently, studies in animals[8] and man[9,10] have investigated the toxicity and physiologic side effects of these drugs. Some of those preliminary studies raised questions regarding the relative potencies of two concentrations of etidocaine, 1.0 and 1.5 per cent,[5] and also the relative efficacies of bupivacaine, 0.75 per cent, and etidocaine, 1.0 per cent, in providing satisfactory "visceral" anesthesia for lumbar epidural anesthesia.[7]

This study represents a controlled, prospective double-blind study of etidocaine, 1.0 and 1.5 per cent, and bupivacaine, 0.75 per cent, comparing the clinical variables of sensory, motor, and "visceral" anesthesia for lumbar epidural anesthesia for pelvic surgery.

METHODS

Sixty female patients were randomly assigned to three drug groups according to a predetermined code. All patients were classified ASA 1 or 2 and were scheduled for elective abdominal hysterectomy. They ranged in age from 20 to 68 years. They were informed of the nature of the study and oral consent was obtained. A standardized premedication regimen included chloral hydrate, 500 mg, for sleep the night before operation and meperidine, 50–100 mg, plus atropine, 0.4 mg, im, 60 minutes prior to administration of the anesthetic.

A standard lumbar epidural puncture was performed at the L2 interspace and 20 ml of local anesthetic drug were administered. (A nurse in the Anesthesia Department who had no other contact with the study prepared a coded syringe filled with appropriate local anesthetic and delivered it to the anesthesiologist.) All three local anesthetic solutions (etidocaine, 1.0 and 1.5 per cent, and bupivacaine, 0.75 per cent) contained epinephrine, 1:200,000. Patients were awake and responsible during all measurements. When the quality of the epidural anesthesia was insufficient to accommodate intraoperative stimulation, supplemental anesthesia with methohexital drip or N_2O–O_2 (3 l:1.5 l) was administered.

Following administration of the unknown local anesthetic agent, measurements of times to onset and to complete sensory and motor blockade were made. Initial onset was defined as the time between the start of the injection and the first detectable loss of sensation in

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VISCERAL PAIN DATA SHEET

Date:_____ Case #_____

Anesthesiologist:_____

Observer:_____

Point Evaluated	Time	Grade of Response*
1. Skin Incision		
2. Abdominal Relaxation		Supplemented, (or) adequate (circle one)
3. Upper Abdominal Relaxation		
4. Uterine Traction		
5. Appendix Traction		
6. Closure of Peritoneum		
7. Closure of Skin		

Comments:

Technique:_____ Drug and Dose:_____

*Grades of Response: 1 = No detectable response in the awake patient
2. = Mild and transient response in the awake patient
3 = Moderate and/or sustained response requiring frequent or constant sedation
4. = Severe or sustained response requiring inhalation anesthesia supplementation

FIG. 1. Data sheet used for evaluation of visceral pain.

response to skin pinch with an Allis forceps. The time to complete sensory anesthesia was the time to achievement of maximal dermatomal spread. Measurements for onset of motor blockade were made every 2 minutes and continued every 5 minutes until no further change could be identified. The classification system of Bromage[11] was used for these measurements (table 1). Patients who had not achieved +3 motor blockade 45 minutes after the injection were not recorded as having achieved complete motor blockade. Postoperatively, similar testing of sensory and motor blockade was done every 30 minutes until regression (two sensory dermatomes), and finally cessation of any detectable anesthetic effect (duration) occurred.

Intraoperatively, a specific set of criteria was used to evaluate each patient's response to surgical stimulation, both somatic and visceral (manipulation of intra-abdominal contents) (fig. 1). Patient response was graded 1 through 4, ranging from no response in the awake patient (1) to severe or sustained response necessitating supplementation with

TABLE 1. Grades of Motor Anesthesia*

0	Free movement of legs and feet
1	Just able to flex knees; legs move freely
2	Unable to flex knees; feet move freely
3	Unable to flex knees; unable to move feet

* After Bromage.[11]

TABLE 2. Sensory Analgesia*

	1.0 Per Cent Etidocaine Group A (n = 20)	1.5 Per Cent Etidocaine Group B (n = 20)	0.75 Per Cent Bupivacaine Group C (n = 20)
Initial onset	3.5 ± 1.6	3.2 ± 1.4	4.4 ± 2.2
Complete onset	15.1 ± 5.1†	16.9 ± 5.1‡	21.0 ± 8.4
Regression of two segments	241 ± 44	232 ± 52	272 ± 84
Total duration	530 ± 76	540 ± 82	563 ± 97
Time to first narcotic	326 ± 130	303 ± 129	396 ± 125

* All values expressed as mean ± standard deviation in minutes.
† A vs. C, $P < .05$.
‡ B vs. C, $P < .05$.

TABLE 3. Motor Blockade*

	1.0 Per Cent Etidocaine Group A (n = 20)	1.5 Per Cent Etidocaine Group B (n = 20)	0.75 Per Cent Bupivacaine Group C (n = 20)
Initial onset	10.0 ± 4.6†	8.6 ± 2.7‡	15.8 ± 7.2
Complete onset			
Latency to 2+ blockade	16.3 ± 3.3†	14.4 ± 5.2‡	27.2 ± 8.4
Frequency of 2+ blockade	95 per cent	100 per cent	80 per cent
Latency to 3+ blockade	31.2 ± 10.2	32.3 ± 8.3	37.5 ± 8.8
Frequency of 3+ blockade	65 per cent†	85 per cent‡	30 per cent
Total duration	332 ± 125	379 ± 98	338 ± 88

* All values expressed as mean ± standard deviation in minutes.
† A vs. C, $P < .05$.
‡ B vs. C, $P < .05$.

inhalational anesthesia (4). In addition, the adequacy of abdominal relaxation was judged satisfactory when supplemental neuromuscular relaxation was not necessary.

All observations of sensory, motor, and visceral responses were made by a single assistant who had no other involvement with the study. Administration and management of the anesthesia were done by one of several anesthesiology residents, under the direct supervision of the principal investigator.

RESULTS

One-way analysis of variance (ANOVA) was carried out on each of the anesthetic-evaluation modalities involving time. Statistically significant differences among group means were determined by t tests after an ANOVA indicated statistical significance among the three groups for a given variable. Chi-square tests were utilized to determine statistical significances of differences among the groups for variables involving frequency data.

Sensory Analgesia (Table 2)

There was no significant difference among the three drug groups in times to initial onset of sensory analgesia. Complete onset occurred significantly faster with the two concentrations of etidocaine (15.1 and 16.9 minutes for 1.0 and 1.5 per cent, respectively) than with bupivacaine (21 minutes). Times to regression and total durations of sensory analgesia were approximately the same with all three drug solutions.

Each drug showed two-segment regression in approximately four hours and had a total duration of approximately nine hours.

A parallel set of measurements of sensory analgesia made specifically of the S1 segment revealed no significant difference in times to initial or complete onset or in total durations. Time to regression from total sensory analgesia at the S1 segment was significantly shorter with 1.0 per cent etidocaine (212 minutes) than with either 1.5 per cent etidocaine (312 minutes) or 0.75 per cent bupivacaine (308 minutes).

Motor Blockade (Table 3)

Both concentrations of etidocaine had significantly faster onsets than bupivacaine (10.0 and 8.6 minutes *vs.* 15.8 minutes). The two concentrations of etidocaine did not differ significantly from each other, however. Complete onset of motor blockade revealed a similar pattern. Since not all patients achieved 3+ motor blockade, the times to achievement of 2+ motor blockade and 3+ motor blockade were analyzed separately. A 2+ motor blockade occurred in mean times of 16.3 minutes for 1.0 per cent etidocaine, 14.4 minutes for 1.5 per cent etidocaine, and 27.2 minutes for 0.75 per cent bupivacaine. This latency to 2+ motor blockade was significantly longer for bupivacaine than for either concentration of etidocaine. The difference between the two concentrations of etidocaine was not significant. A 3+ motor blockade occurred in 85 per cent of the patients who received 1.5 per cent etidocaine, in 65 per cent of patients receiving 1.0 per cent etidocaine, and in 30 per cent of those receiving bupivacaine. Statistically, the differences between each etidocaine group and the bupivacaine group are significant. For those patients in whom 3+ motor blockade was achieved, the mean times were not statistically different; however, the small number of patients (5 of 20) in the bupivacaine group makes meaningful comparison difficult. Total durations of motor block did not differ significantly among the three groups, averaging 5.5 to 6 hours. Also, total duration of motor blockade did not exceed the total duration of sensory analgesia in any group.

Visceral Analgesia (Table 4)

The efficacy of each drug in providing adequate relief of surgical pain, both somatic and visceral, was subjected to a frequency distribution analysis of each grade of response. Chi-square analysis of each variable evaluated revealed no significant difference among drug groups for any of these variables.

Discussion

The results of this study are in agreement with those of the majority of previous studies[12,13] in terms of the similarities and differences between etidocaine and bupivacaine. These two long-acting local anesthetic agents produce approximately equal durations of sensory analgesia and motor blockade. They differ, however, in times to onset of action and intensities of motor blockade produced. Etidocaine had a significantly faster complete onset and provided more intense motor blockade.

This study, which culminated 24 to 36 months of clinical investigation of etidocaine, illustrates the need to repeat work that provides equivocal or highly subjective data. An early study of various concentrations of etidocaine[1] included data from five patients who had received 1.5 per cent for lumbar epidural anesthesia. For no apparent reason, other than spatial, the total duration of sensory anesthesia was shorter than that

TABLE 4. Frequency Distribution of Graded Patient Responses to Painful Stimuli during Operation

	Upper Abdominal Exploration	Uterine Traction	Appendiceal Traction
Etidocaine, 1.0 per cent			
1	1	12	4
2	11	4	0
3	7	3	0
4	0	0	0
N	1	1	16
Etidocaine, 1.5 per cent			
1	3	10	3
2	3	1	2
3	12	6	1
4	1	0	0
N	0	3	14
Bupivacaine, 0.75 per cent			
1	6	15	5
2	7	1	1
3	5	1	0
4	0	0	0
N	2	3	14

1 = no detectable response in awake patient.
2 = mild and transient response in the awake patient.
3 = moderate and/or sustained response necessitating frequent or constant sedation.
4 = severe or sustained response necessitating inhalation anesthesia supplementation.
N = no data recorded.

reported for the 1.0 per cent concentration. This study corrects that misinterpretation and indicates a slightly but insignificantly (548 vs. 530 minutes) longer mean duration with 1.5 per cent compared with 1.0 per cent.

The early observation that patients who had satisfactory somatic and motor anesthesia responded to surgical manipulation of intra-abdominal viscera stimulated interest in the evaluation of "visceral" pain. Earlier studies merely reported the presence or absence of response to intra-abdominal manipulations. In later studies attempts were made to define and quantitate the locations and magnitudes of the patients' responses. The result of such a subjective evaluation is that the response is *not* related to the local anesthetic agent the patients receive. It also reflects the clinical need to provide supplemental central sedation if *all* patients are to remain pain-free throughout the entire surgical anesthetic experience.

In most of our clinical studies we recorded the time in the postoperative period when patients first needed a narcotic *without definition of reason*. Crude as this observation may be, over several studies (this one included), it does point out the discrepancy in relating "total duration of sensory anesthesia" data to postoperative analgesia. Whereas the mean total duration of these long-acting local anesthetic agents is approximately nine hours, the average time until patients needed narcotic analgesia for any reason was five to six hours. At least these studies would indicate that anesthesiologists should not encourage their patients to believe they will be pain-free for eight to ten hours.

Finally, the significance of the data in this study as they relate to clinical practice should be examined. Both drugs provided rapid and effective somatic sensory anesthesia. Only one patient in the entire series needed supplemental neuromuscular relaxation, and both drugs provided significantly longer uncomplicated postoperative analgesia than is available with other popular analgesic therapy. The need for some degree of intraoperative supplementation should be anticipated with many epidural anesthetics.

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