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Systemic Absorption of Mepivacaine in Commonly Used Regional Block Procedures

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Arterial plasma level-versus-time profiles of mepivacaine were determined for 70 surgical patients undergoing epidural, caudal, intercostal-nerve, brachial-plexus, and sciatic/femoral-nerve blocks. A single dose of 500 mg of mepivacaine HCl was used. The conditions studied were route of injection, concentration of drug solution (1 and 2 per cent), and presence or absence of epinephrine, 1:200,000, in the injected solution. Each condition tested resulted in significant changes in maximum plasma levels (Cp_{max}), time to occurrence of Cp_{max} (t_{max}), and areas under plasma level-versus-time curves ($\int Cp.dt$). The highest plasma concentrations (5–10 μg base/ml) were seen after intercostal-nerve blocks using plain solutions, but addition of epinephrine caused these to become comparable to peak levels after the other blocks (2–5 μg base/ml). For those blocks studied at both concentrations, use of the 2 per cent solution was always associated with the higher Cp_{max} and $\int Cp.dt$ values. Mean values of t_{max} using plain solutions ranged from 9 min (intercostal block) to 30 min (sciatic/femoral) and were increased two-to-threefold by the addition of epinephrine. No systemic toxic reactions were encountered, indicating the safety of the dosage used under the conditions of the study. Addition of epinephrine, 1:200,000, to mepivacaine solutions is recommended for the nerve blocks investigated, especially for intercostal-nerve block. (Key words: Regional anesthesia; Mepivacaine; Drug absorption; Pharmacokinetics; Epinephrine; Duration of anesthesia.)

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THE BLOOD LEVEL-VERSUS-TIME profile of a local anesthetic agent provides two pieces of information. It serves as an indicator of systemic toxicity, and it also reflects the amount of drug left near the site of injection for anesthetic action. Measurement of blood drug levels is, therefore, of potential value in determining both the safety and the efficacy of a regional anesthetic procedure.

The purpose of this study was to document and compare blood levels of mepivacaine (Carbocaine) following the regional block techniques most commonly used in surgery (*viz.*, epidural, caudal, intercostal-nerve, brachial-plexus, and sciatic/femoral-nerve blocks), and to evaluate the effect on mepivacaine absorption of adding epinephrine, 1:200,000, to the injected solution.

Similar studies by others have either focused on lidocaine (Xylocaine) and/or prilocaine (Citanest)[1-3] or have considered only one or two of the clinically-used routes of injection.[4-7]

Methods

SELECTION OF PATIENTS AND PREMEDICATION

Subjects of the study were 70 patients for whom regional block would be used routinely in our institution as the anesthetic of choice for the surgical procedure scheduled. Informed consent was obtained from every patient. Patients included were either physical status 1 (35 patients) or physical status 2 (35 patients) as defined by the American Society of Anesthesiologists. Comprehensive patient data, including type of operation, diseases, premedication, and drugs used in the year prior to operation, were recorded, using our computerized anesthetic record system.[8] Batteries of blood tests were not done for all patients.

TABLE 1. Results of Injection of 500 mg of 1.0 or 2.0 Per Cent Solution of Mepivacaine

Type of Block	Concentration (Per Cent)	Epinephrine*	Mean ± SEM				
			Patient Data				Injection Time (Min)
			Male/Female	Age (Years)	Height (Inches)	Weight (Pounds)	
Caudal	2	w/o	1/4	50 ± 8	64 ± 1.0	137 ± 6	1.0 ± 0
	2	w	3/2	46 ± 6	67 ± 2.2	140 ± 10	0.8 ± 0.1
	1	w/o	3/2	49 ± 8	70 ± 1.6	171 ± 21	1.2 ± 0.2
	1	w	3/2	52 ± 2	67 ± 0.8	170 ± 17	1.2 ± 0.2
Epidural	2	w/o	3/2	50 ± 8	66 ± 1.6	141 ± 12	1.0 ± 0.2
	2	w	3/2	49 ± 4	67 ± 1.8	166 ± 12	1.0 ± 0.2
Peripheral nerves Brachial plexus	1	w/o	5/0	38 ± 9	69 ± 1.0	191 ± 13	2.3 ± 0.2
	1	w	2/3	48 ± 5	66 ± 2.6	165 ± 8	2.4 ± 0.2
Intercostal	2	w/o	1/4	62 ± 4	65 ± 0.9	154 ± 10	1.9 ± 0.1
	2	w	4/1	51 ± 3	67 ± 1.1	167 ± 9	1.7 ± 0.2
	1	w/o	2/3	57 ± 9	64 ± 1.9	146 ± 16	2.3 ± 0.2
	1	w	3/2	51 ± 3	66 ± 1.4	162 ± 11	2.4 ± 0.3
Sciatic/femoral	1	w/o	2/3	53 ± 9	67 ± 2.2	154 ± 2	8.2 ± 0.6
	1	w	1/4	41 ± 5	66 ± 1.6	149 ± 16	7.2 ± 0.2

* w = solution contained 1:200,000 epinephrine; w/o = solution contained no epinephrine.

However, where such analyses had been ordered for diagnostic purposes, the results indicated values within normal limits.

When indicated, medication at bedtime on the night before operation usually consisted of pentobarbital (Nembutal), 100 mg, except that patients more than 60 years old received chloral hydrate, 0.5 to 1 g. All patients were premedicated with morphine sulfate (10–15 mg) or meperidine (Demerol) (50–100 mg), together with scopolamine (0.2–0.6 mg) or atropine (0.2–0.4 mg), an hour before operation. Diazepam (Valium) (5–20 mg) was given before arterial puncture and administration of regional anesthesia when paresthesias were not essential for the success of the block procedure and the patient did not wish to "remember" the procedure. Thiopental (Pentothal sodium) and nitrous oxide–oxygen were used during the operation when the patient did not wish to be at all conscious. In patients having epidural blocks or intercostal nerve blocks for intra-abdominal surgery, precautions were taken to prevent regurgitation of stomach content, visceral traction reflexes, sensation from the unanesthetized areas dur-

Hydrochloride with and without Epinephrine in Caudal, Epidural, and Peripheral Nerve Blocks

Mean ± SEM										
Arterial Plasma Concentration (μg Base/ml)										R.S.A.† (Per Cent)
2 Min	5 Min	10 Min	15 Min	20 Min	25 Min	30 Min	45 Min	60 Min	120 Min	
3.08	4.22	4.98	5.43	4.90	4.97	4.65	4.28	3.70	2.92	73
±0.64	±0.60	±0.72	±0.68	±0.67	±0.57	±0.46	±0.60	±0.61	±0.50	
1.46	2.35	3.17	3.70	3.65	4.19	4.31	3.93	3.96	3.09	68
±0.37	±0.51	±0.72	±0.68	±0.66	±0.70	±0.63	±0.53	±0.55	±0.42	
1.94	3.37	4.15	4.33	3.93	3.77	3.66	3.41	2.93	2.25	57
±1.03	±0.92	±0.76	±0.67	±0.53	±0.40	+0.41	±0.41	±0.31	±0.15	
2.92	1.70	1.77	1.81	2.18	2.03	2.14	1.96	1.94	1.98	38
±1.32	±0.27	±0.17	±0.23	±0.26	±0.18	±0.21	±0.20	±0.30	±0.15	
2.07	3.60	4.19	4.65	4.59	4.00	4.21	3.78	3.11	2.39	63
±0.64	±0.63	±0.48	±0.47	±0.24	±0.43	±0.37	±0.49	±0.33	±0.23	
1.13	2.04	2.49	3.00	3.07	2.99	2.92	2.76	2.44	2.21	47
±0.35	±0.30	±0.27	±0.22	±0.24	±0.27	±0.23	±0.40	±0.28	±0.44	
0.43	2.01	3.04	3.36	3.46	3.53	3.43	3.00	2.85	2.22	61
±0.11	±0.25	±0.30	±0.31	+0.39	±0.39	±0.41	±0.43	±0.49	±0.45	
0.34	1.17	1.79	2.23	2.38	2.49	2.47	2.50	2.56	2.20	43
±0.09	±0.15	±0.12	±0.24	±0.20	±0.33	±0.38	±0.45	±0.36	±0.31	
3.12	6.96	7.82	7.49	7.01	6.51	5.94	5.71	5.23	3.60	100
±0.39	±0.59	±0.68	±0.92	±0.51	±0.59	±0.67	±0.90	±0.93	±0.77	
1.70	3.05	3.42	3.37	3.46	3.11	2.99	3.17	2.89	2.17	62
±1.29	±0.50	±0.48	±0.52	±0.40	±0.31	±0.15	±0.19	±0.19	±0.26	
2.05	4.80	5.71	5.60	4.85	4.48	4.33	4.12	3.76	2.60	72
±0.50	±0.49	±0.68	±0.77	±0.60	±0.51	±0.46	±0.44	±0.48	±0.39	
0.98	2.58	3.14	2.93	2.97	3.12	3.28	3.00	3.16	2.36	63
±0.11	±0.20	±0.39	±0.42	±0.23	±0.19	±0.29	±0.16	±0.17	±0.26	
0.60	1.51	2.43	3.03	3.29	3.54	3.25	3.33	2.89	2.23	61
±0.44	±0.21	±0.39	±0.42	±0.44	±0.45	±0.50	±0.40	±0.42	±0.31	
0.43	0.85	1.45	2.00	2.21	2.43	2.40	2.66	2.55	2.51	44
±0.27	±0.30	±0.26	±0.27	±0.30	±0.45	±0.39	±0.42	±0.42	±0.64	

† Relative systemic availability = $\frac{\text{average } \int_0^{120} \text{Cp.dt for drug given by test route}}{\text{average } \int_0^{120} \text{Cp.dt for drug given in 2 per cent plain solution for intercostal block}} \times 100$

ing exploration (pelvis and diaphragm), or all three. These involved: 1) a sleep dose of thiopental (125–250 mg); 2) succinylcholine (Anectine), 60–100 mg; 3) tracheal intubation; 4) nitrous oxide–oxygen with controlled respirations. On the few occasions when this was not adequate, halothane (Fluothane), 0.5 to 1.0 per cent, was added.

Types of Blocks

Lumbar epidural, caudal, intercostal-nerve (bilateral), supraclavicular-brachial-plexus, and sciatic/femoral-nerve blocks were administered as described by Moore.[9] All blocks were done by staff anesthesiologists and residents. The intercostal-nerve blocks were carried out by two anesthesiologists working simultaneously so as to complete the block in less than three minutes.

Dosage of Mepivacaine—Experimental Design

Every patient received 500 mg of mepivacaine hydrochloride. For epidural, caudal, and intercostal-

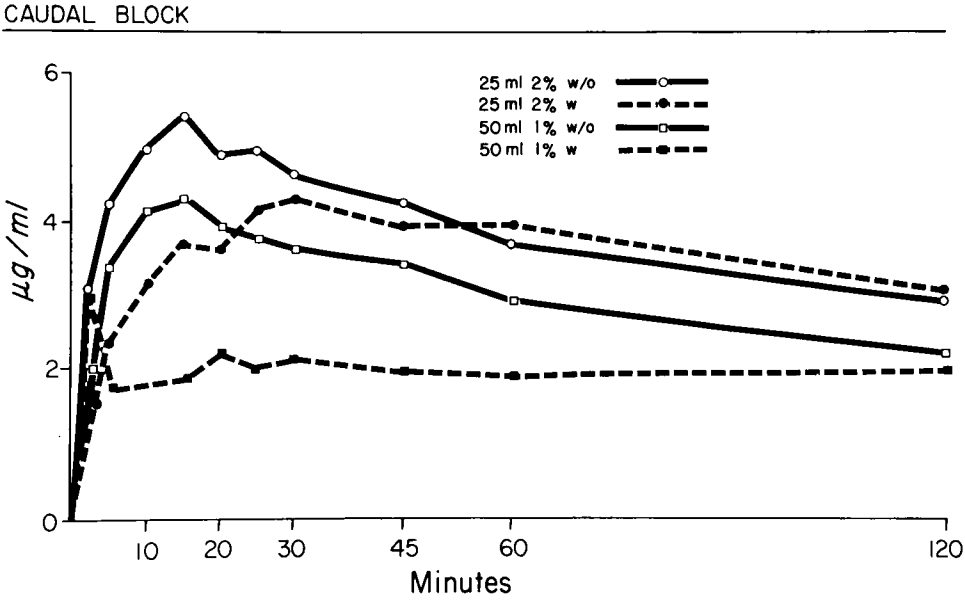

FIG. 1. Mean arterial plasma levels of mepivacaine after caudal block. w/o = plain solution, n = 5; w = plus epinephrine, 1:200,000, n = 5. Two patients in the 1 per cent-plus-epinephrine group showed high levels at 2 minutes, hence the elevated mean level at this time interval. Since blood could not be aspirated into the syringe, direct iv injection of a proportion of the dose did not seem to account for this. These 2-minute levels were not used in estimation of Cp_{max} and t_{max} values.

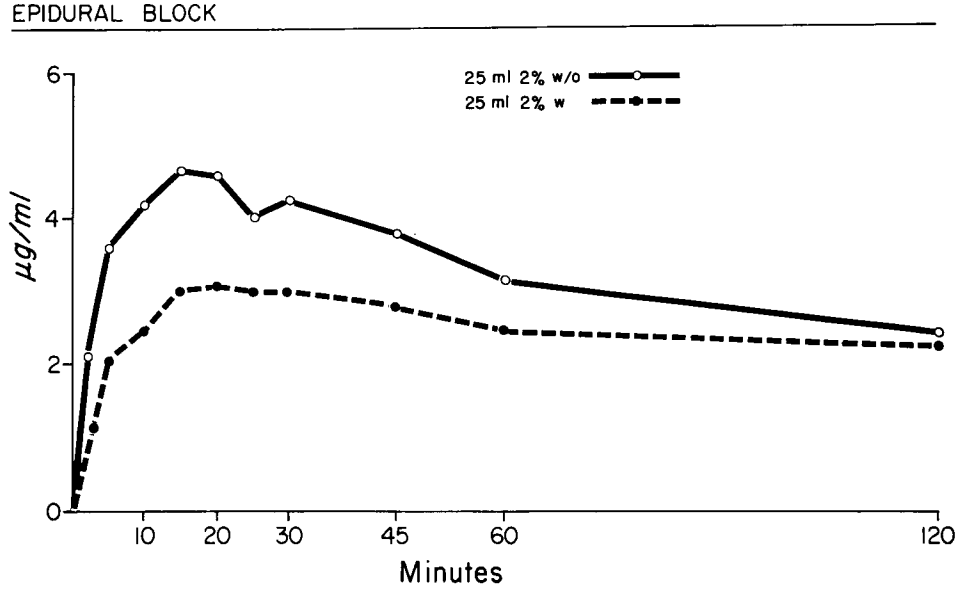

FIG. 2. Mean arterial plasma levels of mepivacaine after epidural block. w/o = plain solution, n = 5; w = plus epinephrine, 1:200,000, n = 5.

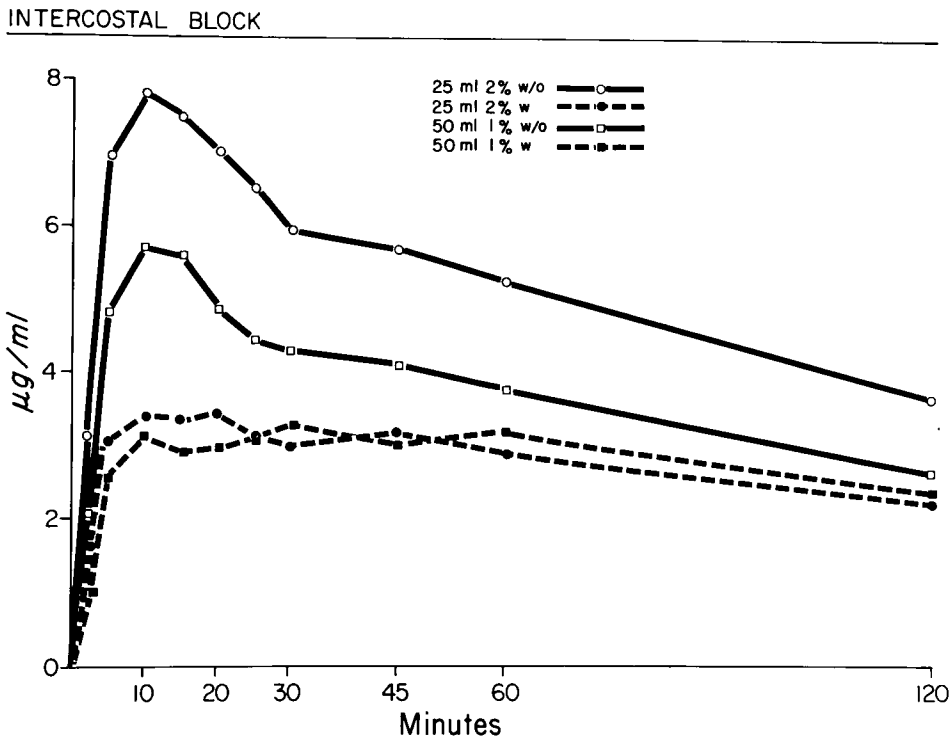

FIG. 3. Mean arterial plasma levels of mepivacaine after intercostal nerve block. w/o = plain solution, n = 5; w = plus epinephrine, 1:200,000.

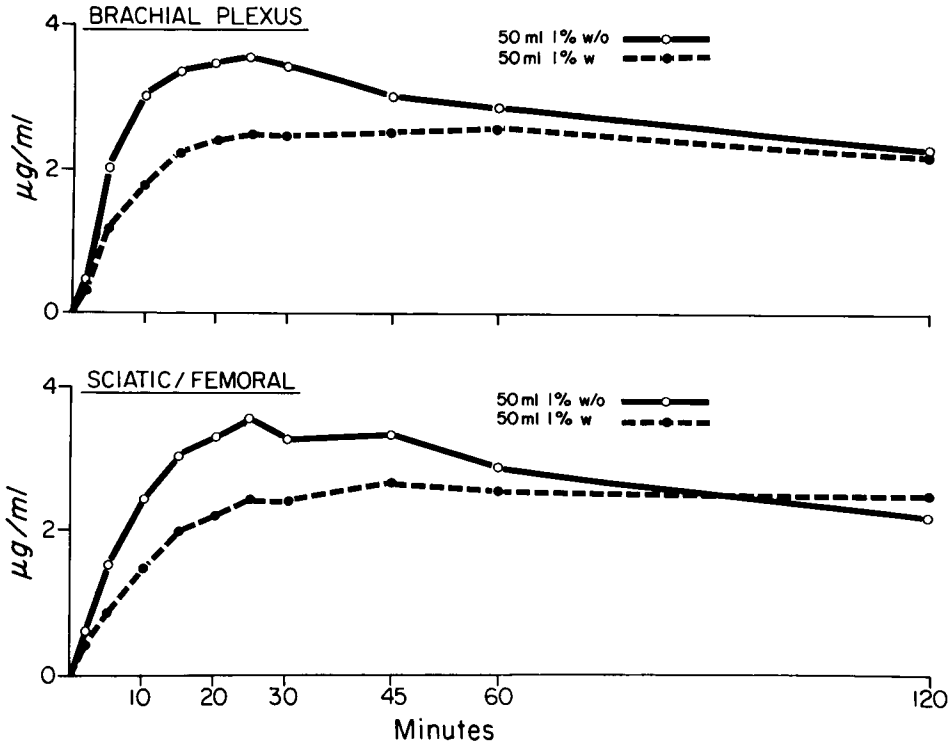

FIG. 4. Mean arterial plasma levels of mepivacaine after brachial plexus and sciatic/femoral nerve blocks.w/o = plain solution, n = 5; w = plus epinephrine, 1:200,000.

nerve, brachial-plexus, and sciatic/femoral-nerve blocks, a 1.0 per cent solution was injected. Each block and each concentration was administered to ten patients—five with and five without epinephrine, 1:200,000.

The dosages (volume and concentration) employed were not necessarily those which we would use routinely for the regional blocks performed, but were used to keep the total milligram dosage of mepivacaine hydrochloride constant, provided this did not result in increased risk to the patient. Epidural block was not done with a 1.0 per cent solution because 50 ml would have been an excessive volume. Neither were supraclavicular-brachial-plexus or sciatic/femoral-nerve blocks done with 2.0 per cent solutions, because 1) 25 ml is an insufficient volume using our standard technique for these blocks, and 2) the incidence of neurologic sequelae increases significantly when concentrations in excess of 1.0 per cent are used for such blocks.

Blood Sampling and Analysis

Arterial blood samples (3–4 ml) were drawn from either a radial or a brachial artery via an indwelling plastic needle prior to injection of mepivacaine and after the start of injection at 2, 5, 10, 15, 20, 25, 30, 45, 60, and 120 minutes. In every case, operation was begun after the 30-minute sample had been obtained.

Plasma was separated from the samples and stored at 4 C until analyzed specifically for mepivacaine by gas chromatography.[10] Arterial levels were measured in preference to peripheral venous levels because: 1) they may more closely reflect changes in drug levels in well-perfused vital organs; 2) they are more sensitive to changes in drug absorption and disposition; 3) estimates of mepivacaine levels associated with toxic effects have been obtained by sampling arterial blood after intravenous infusion of the drug over 20 minutes, *i.e.*, a time period similar to the average time to peak blood levels after clinical administration of the drug for single-dose regional anesthesia.[11]

Plasma levels were measured because plasma stores better and on extraction produces a "cleaner" gas chromatogram than whole blood. Whole-blood levels of mepivacaine would be approximately 80 per cent of plasma levels.[12]

Data Analysis

To simplify comparison and discussion of the plasma-level data, the results were described in terms of three curve characteristics: 1) maximum plasma level recorded for each patient (Cp_{max}); 2) time of maximum plasma level recorded (t_{max}); 3) area under the plasma level-versus-time curve from 0 to 120 minutes ($\int_0^{120}$ Cp.dt), determined by planimetry. Estimation of elimination half-times was not possible since continuing drug absorption was apparent throughout the time period studied.

Statistical analysis of the above characteristics over the 0-minute to 120-minute period was not strictly valid, owing to changes in the blood-sampling interval. The errors involved are negligible in analyses of Cp_{max} and $\int_0^{120}$ Cp.dt values, but they could be considerable for t_{max} values. Therefore, for the latter, values for the 0-minute to 30-minute period only (values designated "t'_{max}") were analyzed.

Statistical analysis of Cp_{max}, t'_{max}, and $\int_0^{120}$ Cp.dt values was carried out as follows:

1) Analysis of variance was done on all intercostal-nerve and caudal block data (2^3 factorial experiment; $n = 40$) to test the null hypotheses that the mean values of the three curve characteristics were not different according to a) route of injection; b) drug concentration (1, 2 per cent); c) presence or absence of epinephrine.

2) Analysis of variance was done on all data (2×5 factorial experiment; $n = 70$) to test the null hypotheses that the mean values of the three curve characteristics were not different according to a) route of injection and b) presence or absence of epinephrine. In this analysis, data for 1 and 2 per cent solutions were combined for those routes which were studied at both concentrations (*viz.*, intercostal-nerve and caudal blocks).

In addition, for each treatment (*i.e.*, combination of route, concentration, and with or without epinephrine), correlation coefficients were calculated for Cp_{max} *vs.* $\int_0^{120}$ Cp.dt and Cp_{max} (and $\int_0^{120}$ Cp.dt) *vs.* patient age, weight, height, and body surface area.

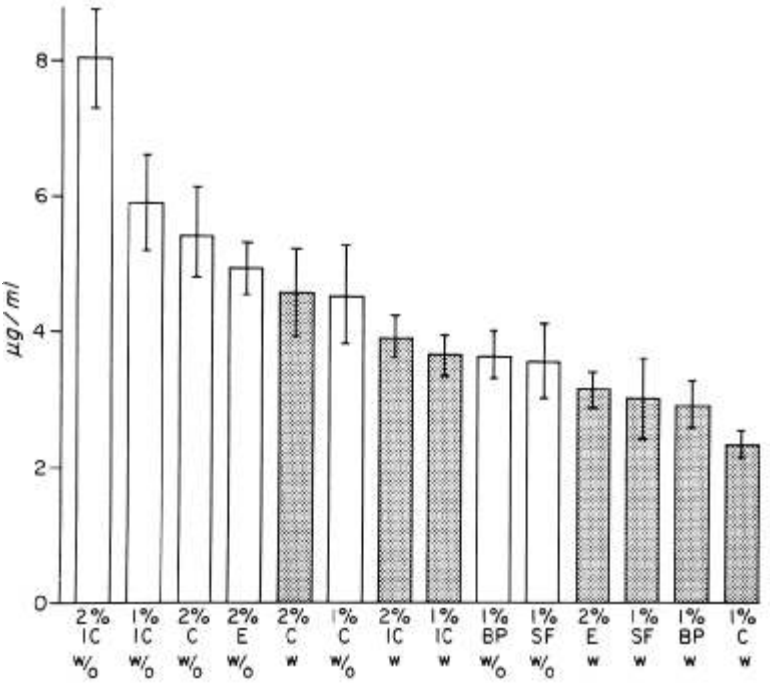

FIG. 5. Relationship between mean maximum plasma level of mepivacaine ($Cp_{max} \pm SEM$) and route of injection. IC = intercostal; C = caudal; E = epidural; BP = brachial plexus; SF = sciatic/femoral; w/o = plain solution; w = plus epinephrine, 1:200,000—stippled blocks.

Results

Plasma mepivacaine levels for each type of block and physical characteristics of the patients are summarized in table 1. Also shown are the mean injection times according to the route of administration. Note that sciatic/femoral-nerve blocks took considerably longer for completion than did the other blocks because after the injection around the sciatic nerve the patient had to be turned supine and landmarks drawn prior to blocking the femoral nerve. All blocks produced satisfactory anesthesia, and no toxic reactions were encountered.

Although intersubject variation in plasma mepivacaine levels for each treatment was quite marked (see table 1), differences in the shapes of mean plasma level-versus-time profiles for the different types of block were apparent (figs. 1–4). The effect of epinephrine in slowing systemic absorption of mepivacaine was also evident (figs. 1–4).

Analysis of variance revealed that differences in Cp_{max} were significant for route ($P < 0.001$), concentration ($P < 0.001$), and epinephrine ($P < 0.0005$); differences in t'_{max} were significant for route ($P < 0.0005$) and epinephrine ($P < 0.0005$); differences in $\int_0^{120} Cp.dt$ were significant for route ($P < 0.025$), concentration ($P < 0.001$), and epinephrine ($P < 0.0005$). Interactions between variables were not significant. (Results of multiple range tests to differentiate between individual treatments are available from the authors.)

The mean Cp_{max} values showed a threefold variation across the treatments investigated. The highest value was found for intercostal-nerve block with 2 per cent plain solution and the lowest for caudal block with 1 per cent solution plus epinephrine (fig. 5). When a block was studied at two concentration levels (1 and 2 per cent), the higher concentration was consistently associated with the higher mean Cp_{max}. For intercostal-nerve block the difference § was 27 per cent for plain solutions and 6 per cent for solutions with epinephrine; for caudal block the difference was 17 per cent for plain solutions and 52 per cent

§ Calculated as:

$$100 - \left[\frac{\text{mean } Cp_{max} \text{ (1 per cent solution)}}{\text{mean } Cp_{max} \text{ (2 per cent solution)}} \times 100\right].$$

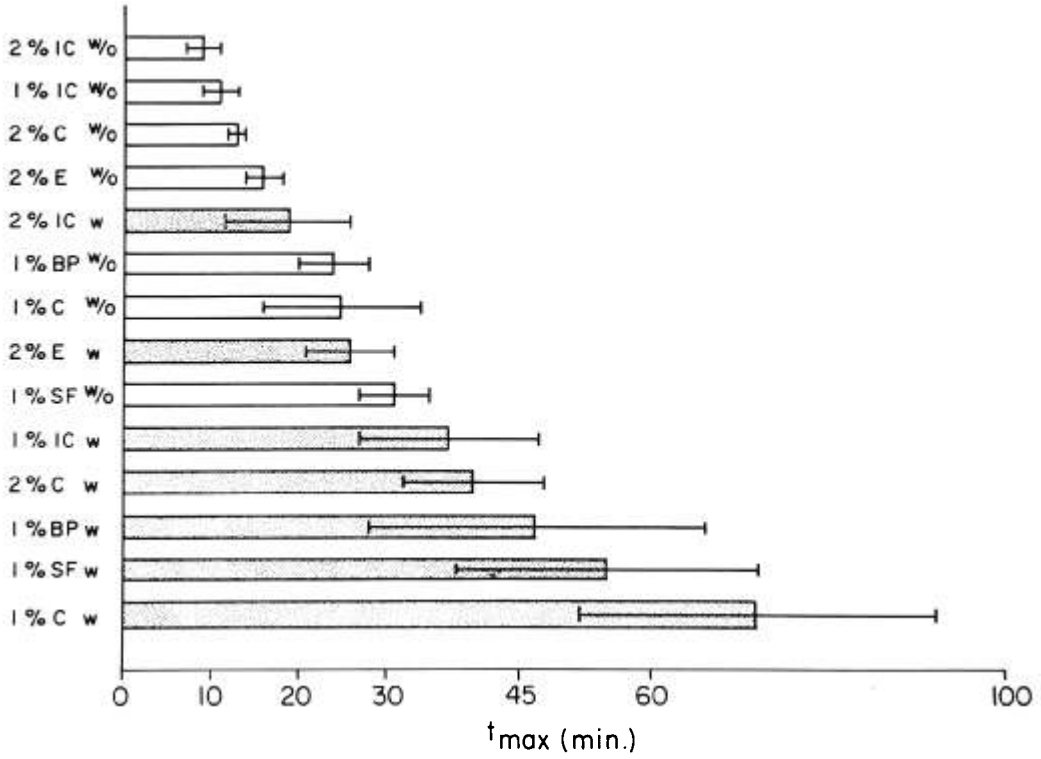

FIG. 6. Relationship between route of injection and mean time to occurrence of maximum plasma level of mepivacaine ($t_{max} \pm$ SEM) (key as in figure 5).

for solutions with epinephrine. Addition of epinephrine to the injected solutions consistently lowered Cp_{max} for each block and mepivacaine concentration. Percentage reductions were 51 per cent for intercostal-nerve block (2 per cent solution); 46 per cent for caudal block (1 per cent solution); 38 per cent for intercostal-nerve block (1 per cent solution); 36 per cent for epidural block (2 per cent solution); 20 per cent for brachial-plexus block (1 per cent solution); 16 per cent for caudal block (2 per cent solution); 15 per cent for sciatic/femoral-nerve block (1 per cent solution).

"Area-under-the-curve" measurements indicated similar differences among the types of blocks, as did Cp_{max} values. Correlation coefficients for Cp_{max} *vs.* $\int_0^{120}$ Cp.dt for the 14 treatments ranged from +0.30 to +0.98 (average = +0.87), and were significant ($P < 0.05$) for all but two of the treatments.

Mean values of t_{max} showed an eightfold variation across the different treatments. The smallest value was found for intercostal-nerve block with 2 per cent plain solution and the largest for caudal block with 1 per cent solution plus epinephrine (fig. 6). A trend for smaller t_{max} values when using the 2 per cent solutions compared with the 1 per cent solutions (intercostal-nerve and caudal blocks) was also seen (fig. 6). Addition of epinephrine to the local anesthetic solution consistently slowed the systemic absorption of mepivacaine following all routes of injection. Mean values of t_{max} were increased two-to-threefold over those observed for corresponding plain solutions (fig. 6). For those treatments with t_{max} values greater than 30 minutes, mean values of t'_{max} occurred earlier than 30 minutes, indicating double peaks in plasma level-*vs.*-time profiles. The presence of this phenomenon

tends to be obscured when mean Cp *vs.* t curves are constructed (figs. 1–4).

Correlation between age and height of the patients and plasma-level data were poor. The average correlation coefficient across all treatments for body weight and Cp_{max} was only −0.40. Although several of the individual treatments showed highly significant correlations (sciatic/femoral-nerve 1 per cent plain, $r = -0.96$; caudal 1 per cent plain $r = -0.94$; intercostal-nerve 1 per cent plain, $r = -0.91$) and all but four had r values in excess of −0.5, good correlation was not consistently found with any particular type of block. Correlation between body surface area and Cp_{max} was only marginally better (average $r = -0.44$). Correlations between weight and surface area and $\int_0^{120}$ Cp.dt were slightly lower than those for Cp_{max}.

Discussion

Intravenous infusion studies in fully conscious volunteers by Jorfeldt *et al.*[11] suggest that arterial plasma levels of mepivacaine sustained between 6 and 10 μg/ml or higher may be associated with toxic effects on the central nervous system. In the present study, only the levels observed after intercostal-nerve block using 2 per cent plain solution consistently fell within this range. Premedication and/or light general anesthesia may have obtunded signs of toxicity in these cases.

The significantly higher systemic mepivacaine levels after intercostal-nerve block with plain solutions, compared with those after epidural block using the same dose, are in agreement with the findings of Braid and Scott,[1] who studied lidocaine and prilocaine.

A trend toward slower net systemic absorption when using more dilute solutions of local anesthetics (same total dosage) has also been found by Braid and Scott[1] following intercostal-nerve block with lidocaine. However, whereas we consistently observed a difference between 1 and 2 per cent solutions of mepivacaine, Braid and Scott detected a difference only on increasing the concentration to 4 per cent lidocaine. These differences presumably reflect the delicate balances between concentration gradients for tissue adsorption at the site of injection, systemic absorption from the site of injection, spread of the anesthetic solution, and vasomotor effects of the agents (see below).

Although addition of epinephrine to the anesthetic solution lowered maximum systemic levels of mepivacaine in all blocks studied, the effect was considerable only after intercostal-nerve block (1 and 2 per cent), caudal block (1 per cent solution only), and epidural block (2 per cent solution) (fig. 5). The quantitative effect of epinephrine is, therefore, dependent upon both the route of injection and the concentration of local anesthetic solution used. However, epinephrine did markedly retard the systemic absorption of mepivacaine following all blocks (fig. 7). Addition of epinephrine, 1:200,000, to mepivacaine solutions for caudal, epidural, and peripheral-nerve blocks is therefore recommended. The value of adding epinephrine to local anesthetic solutions for intercostal nerve block is particularly noteworthy, since this results in systemic drug levels comparable to those observed after the other types of blocks using plain solutions (figs. 1–4). Significant in this regard has been our experience that peripheral-nerve blocks performed with local anesthetic solutions containing epinephrine, 1:200,000, are associated with a lower incidence of toxic reactions compared with epidural and caudal blocks.

Correlations between plasma-drug-level data and the ages and weights of the patients in this study were such that we tend to endorse the opinions of Braid and Scott[2] that little account should be taken of body weight in estimating safe dosage for regional block and that high dosages should be avoided in the elderly.

Precise correlation of the rate of drug absorption from the site of injection with anesthetic activity is not possible from the present data. Nevertheless, a crude comparison can be made using $\int_0^{120}$ Cp.dt values and data from the literature describing the durations of action of mepivacaine following the various block procedures.[13] Assuming that the kinetics of distribution and elimination of mepivacaine are linear and independent of route and rate of systemic absorption,¶ it follows that the

¶ This includes the assumption that the hemodynamic effects of the blocks and of any added epinephrine do not materially affect rates of systemic drug disposition.

greater the $\int_0^{120}$ Cp.dt, the greater the systemic absorption of the drug until 120 minutes after injection and the smaller the amount remaining near the site of injection. Estimation of the systemic absorption rates of drugs following various routes of administration ideally requires comparison of the appropriate blood level-versus-time profile with the profile obtained after intravenous injection.[14] However, in the absence of intravenous data for mepivacaine, it is possible to estimate a "relative systemic availability" (RSA) of the drug after each treatment by relating $\int_0^{120}$ Cp.dt to the highest value observed, *i.e.*, following intercostal-nerve block with 2 per cent plain solution.

Therefore, we define the arbitrary term:

$$\text{RSA} = \frac{\text{average } \int_0^{120} \text{Cp.dt for drug given by test route}}{\text{average } \int_0^{120} \text{Cp.dt for drug given in 2 per cent plain solution for intercostal-nerve block}} \times 100 \text{ per cent}$$

Calculation of RSA's for the various blocks, other than the reference intercostal-nerve block, gives values between 38 and 73 per cent (table 1). It is evident, therefore, that an appreciable proportion of the dose remains to be absorbed 120 minutes after injection by many of the routes of injection, despite the fact that in several cases the plasma-level profiles have peaked relatively soon after drug injection.

Inspection of anesthetic-activity data for mepivacaine following regional block procedures [13] indicates that for a given type of block, the decrease in RSA observed after addition of epinephrine to the injected solution is accompanied by an increase in the duration of anesthesia. This is readily explained by the vasoconstrictor effect of epinephrine, which favors uptake of drug by nerve over systemic dissipation. In contrast, however, the decrease of RSA in going from a 2 per cent solution to a 1 per cent solution is apparently accompanied by a small *decrease* in duration of anesthesia.[13] § At the same time, a greater spread of anesthesia is likely with the more dilute solution.[15] These facts may be reconciled if it is postulated that the 1 per cent concentration allows more *net* "binding" of local anesthetic molecules in the area of injection, owing to more extensive spread of solution. This increased "binding" or distribution overrides any effect of a corresponding increase in the surface area available for systemic absorption of the drug. However, regression to the minimal anesthetic concentration per unit mass of nerve (a function of the number of "bound" molecules per unit mass?) occurs earlier than with the 2 per cent solution. Hence, duration of anesthesia is shorter with the 1 per cent solution despite the greater RSA value.

The RSA values also provide information about the relative efficiency of the doses needed to produce various regional blocks. Despite the fact that the duration of anesthesia is longer following intercostal-nerve block than after caudal or epidural blocks, RSA values for the latter are either similar to or lower than those for the former (table 1). Provided that this trend continues to the point when regression of anesthesia starts, which seems likely, this suggests that the proportion of the dose which has not been absorbed into the systemic circulation is more usefully employed in producing anesthesia after intercostal-nerve block than after caudal or epidural block.

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§ The data referenced do not, however, indicate the volumes of 1 and 2 per cent mepivacaine used. Nevertheless, data for 1 and 2 per cent lidocaine [16] and 2 and 3 per cent prilocaine [17] confirm the impression of longer duration using the same dose of drug in a more concentrated solution.

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Obstetrics

INTRA-AMNIOTIC BICARBONATE AND FETAL ACIDOSIS Forty to 100 mEq of sodium bicarbonate were infused into the amniotic cavities at the time of cesarean section performed with spinal anesthesia in 11 women, the majority of whom had special complications. Eleven other near-term pregnant women served as controls. Five of the patients treated and five in the control group developed post-spinal-block hypotension, all treated by acute hydration. An equilibration period of 15 to 20 minutes was allowed between the time of sodium bicarbonate infusion and delivery. Mean umbilical-artery base excess of infants in the treated group was significantly greater than that of the untreated group (-7.0 vs. -10.9 mEq/l, $P < 0.05$), indicating that a significant bulk transfer of bicarbonate from the amniotic fluid to the fetus occurred, thereby correcting the metabolic component of fetal acidosis. *p*H and base excess concentration gradients between amniotic fluid, gastric aspirate, and fetal blood suggest that the transfer occurs across the gastric mucosa. The bicarbonate-treated group had significantly higher mean Apgar scores at 1 and 5 minutes than the untreated group. (*Hamilton, L. A., Jr., and Behrman, R. E.: Intra-amniotic Infusion of Bicarbonate in the Treatment of Human Fetal Acidosis, Am. J. Obstet. Gynecol. 112: 834–847, 1972.*) ABSTRACTER'S COMMENT: Seeds *et al.* (*Am. J. Obstet. Gynecol. 107: 232, 1970, and Am. J. Obstet. Gynecol. 108: 1245, 1970*) showed that instillation of bicarbonate into the amniotic cavities of rhesus monkeys resulted in a significant increase in fetal bicarbonate. Instillation of THAM caused fetal death. Some increase in fetal bicarbonate can be effected by intravenous infusion of bicarbonate into the mother, but much more transfer will occur from intra-amniotic infusion. The intra-amniotic infusion probably enters the fetus via the gastric mucosa, from fetal swallowing.