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Newborn Blood Levels of Lidocaine and Mepivacaine in the First Postnatal Day Following Maternal Epidural Anesthesia

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Distribution and elimination of lidocaine and mepivacaine were studied in 114 subjects after obstetric epidural anesthesia. Epinephrine significantly lowered the concentrations of lidocaine in the mothers' circulations by about 33 per cent, and the concentrations of mepivacaine by about 22 per cent. It also significantly altered their concentrations in the newborns' circulations at delivery and in the first 4 hours after birth. More mepivacaine than lidocaine crossed the placenta. The mepivacaine concentration in the cord blood was 36 to 47 per cent higher, and the mean fetal to maternal ratio for mepivacaine without epinephrine was 0.64, in contrast to 0.52 for the equivalent lidocaine group. Of importance was the long persistence of either drug in the newborns' circulation. Detectable levels of lidocaine and mepivacaine were present until 8 and 24 hours after birth, respectively. Pharmacokinetic models revealed that the long-term rate of disappearance of lidocaine was approximately three times as fast as that of mepivacaine. Computed half-times averaged 3 hours for lidocaine and 9 hours for mepivacaine. (Key words: Anesthesia, obstetric; Anesthetic techniques, peridural; Anesthetics, local, lidocaine; Anesthetics, local mepivacaine; Pharmacokinetics, local anesthetics.)

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LUMBAR EPIDURAL BLOCK is a widely accepted method of pain relief during labor and delivery, with the major advantage of providing prolonged effective analgesia without the necessity for narcotics, sedatives or general anesthetics. All local anesthetic drugs administered epidurally to women in labor appear within a few minutes in the maternal and fetal bloodstreams. The present study of lidocaine and mepivacaine is a comparison of their distributions in and disappearances from newborns' blood following maternal epidural analgesia. Significant differences between the two drugs were observed.

Materials and Methods

One hundred and fourteen mothers and their infants were studied after informed consent had been obtained. All pregnancies were full-term and uncomplicated. The mothers had been selected to have epidural anesthesia, and the choice of local anesthetic drug was determined randomly. Ninety-four of these subjects were divided into four groups according to which local anesthetic was used and whether epinephrine had been added to the local anesthetic solution. Forty-one women received lidocaine (1.5 or 2.0 per cent), 30 with 1/200,000 epinephrine and 11 without epinephrine, while 53 were

TABLE 1. Characteristics of Study Population

	Epidural Drug			
	Lidocaine		Mepivacaine	
	Plain (n = 11)	With Epinephrine (n = 30)	Plain (n = 42)	With Epinephrine (n = 11)
Maternal age (years)	26 ± 1.3*	24 ± 0.8	24 ± 0.6	22 ± 1.1
Maternal height (inches)	64 ± 0.8	64 ± 0.4	64 ± 0.5	64 ± 0.5
Maternal weight (pounds)	152 ± 5.7	145 ± 3.1	144 ± 2.5	150 ± 5.0
Primiparas (number studied)	6	16	25	7
Pitocin stimulation (number)	9	24	25	9
Length of labor (min)	485 ± 48	555 ± 62	477 ± 30	604 ± 58
Outlet forceps (number)	11	26	36	10
Total dose of local anesthetic (mg)	423 ± 40	414 ± 36	374 ± 21	349 ± 34
Doses of local anesthetic (number)	4	4	3	3
Time from initial dose of local anesthetic to delivery (min)	183 ± 10	190 ± 20	136 ± 10	261 ± 25
Time from last dose of local anesthetic to delivery (min)	22 ± 5	32 ± 3	27 ± 2	33 ± 6
Birth weights of babies (g)	3,462 ± 146	3,169 ± 77	3,177 ± 69	3,240 ± 111
Apgar scores				
1 min	8 (7–9)†	8 (2–9)	8 (5–9)	8 (7–9)
5 min	9 (8–9)	9 (7–10)	9 (8–10)	9 (9–10)
pH				
Umbilical venous blood	7.41 ± 0.01	7.38 ± 0.01	7.37 ± 0.01	7.38 ± 0.03
Umbilical arterial blood	7.30 ± 0.02	7.30 ± 0.01	7.29 ± 0.01	7.30 ± 0.03

* Mean ± standard error.
† Median (range).

given like concentrations of mepivacaine, 11 with 1/200,000 epinephrine and 42 without epinephrine. Some of the characteristics of this study population are presented in table 1. The remaining 20 subjects were divided into two groups. In one group, ten mothers received 1.5 or 2.0 per cent lidocaine, and in the other group, ten were given 1.5 or 2.0 per cent mepivacaine. Epinephrine was not added to the local anesthetic drug.

The lumbar epidural catheter was inserted at L2–3, L3–4, or L4–5 through a Weiss needle. Following introduction of the catheter, it was advanced for about 2 cm in a caudad direction and a test dose of 2 ml of local anesthetic was injected. Satisfactory anesthesia was established and maintained by intermittent injection of local anesthetic through the indwelling catheter. Prior to the epidural anesthesia, 61 of the 94 subjects received one or two doses of alphaprodine, 20–30 mg, and promazine, 25 mg; hydroxyzine, 50 mg; diazepam, 5–10 mg; or secobarbital, 100 mg. The numbers of mothers receiving the medications were about equally divided among the four groups. This was also the case in the separate series of 20 subjects. Following delivery, Apgar scores were obtained for the newborns at 1 and 5 minutes of life (table 1).

A blood sample was taken from an upper-extremity vein of the mother at delivery. Samples of umbilical venous and arterial blood were obtained from a doubly clamped

TABLE 2. Lidocaine and Mepivacaine in Blood of Mother and Baby

Sample Site	Mean Concentration (μg/ml) ± SE			
	Lidocaine		Mepivacaine	
	Plain (n)	With Epinephrine (n)	Plain (n)	With Epinephrine (n)
Maternal vein (delivery)	2.30 ± 0.29 (11)	1.53 ± 0.12 (30)	2.89 ± 0.16 (42)	2.26 ± 0.22 (11)
Baby (delivery)				
Umbilical vein	1.17 ± 0.14 (11)	0.89 ± 0.07 (30)	1.84 ± 0.12 (42)	1.54 ± 0.15 (11)
Umbilical artery	0.94 ± 0.10 (11)	0.73 ± 0.07 (30)	1.56 ± 0.10 (42)	1.37 ± 0.15 (11)
Fetal/maternal ratio UV/MV*	0.52 ± 0.02 (11)	0.59 ± 0.03 (30)	0.64 ± 0.02 (42)	0.69 ± 0.04 (11)
Heel puncture				
2 hours	0.52 ± 0.05 (11)	0.40 ± 0.04 (30)	1.07 ± 0.06 (42)	0.99 ± 0.11 (11)
4 hours	0.38 ± 0.04 (10)	0.28 ± 0.03 (30)	0.89 ± 0.05 (42)	0.79 ± 0.09 (11)
8 hours	0.17 ± 0.03 (11)	0.15 ± 0.02 (28)	0.64 ± 0.04 (40)	0.63 ± 0.07 (11)
24 hours	0.02 ± 0.01 (11)	0.03 ± 0.01 (30)	0.23 ± 0.02 (39)	0.21 ± 0.04 (10)

* UV/MV = umbilical vein concentration/maternal vein concentration.

segment of cord at birth, usually before the placenta had separated. Then, 2, 4, 8, and 24 hours after birth, approximately 0.3 ml of the baby's blood was collected from a heel puncture using antiseptic technique. The heel puncture was made with a #11 blade, and the blood was collected into a heparinized Pasteur pipette.

The blood samples were refrigerated and processed within 72 hours of collection. The concentration of local anesthetic was determined by a gas chromatographic technique, a modification of that of Pratt, Warrington, and Grego.[1,2] The technique analyzed only the unchanged form of the drugs. The internal standard was mepivacaine for lidocaine assays and lidocaine for mepivacaine assays. The method employed a means of dry sample application to the chromatograph, permitting assay of the whole sample and eliminating the problem of solvent fronts.[3] This method greatly increased not only the sensitivity but also the accuracy and reproducibility of the analyses. In this study, the technique was sensitive to 0.05 μg/ml lidocaine and 0.07 μg/ml mepivacaine in a sample volume of 0.2 ml. The reproducibility of the method was evaluated during the study and the coefficient of error was found to be 5.2 per cent for lidocaine and 7.4 per cent for mepivacaine. These values were better than those previously reported by our laboratory.[2]

In addition to the local anesthetic levels, *p*H of umbilical venous and arterial blood was determined at delivery (table 1).

The time courses of disappearances of lidocaine and mepivacaine from the newborns' circulations were analyzed, first by using the 2-, 4-, 8-, and 24-hour concentration data with the concentration at zero-time determined by extrapolation; second, by using the 2-, 4-, 8-, and 24-hour concentration data with the umbilical arterial blood value as the zero-time or birth level. In the first

TABLE 3. Multiple Comparisons of Concentration Data and Fetal-to-maternal Distribution Ratios for the Four Drug Groups, and Sequence of Testing Using the Newman-Keuls Method

Sample Sites	Groups*						Means in Ascending Order
	LP vs. LE	LP vs. MP	LP vs. ME	LE vs. ME	LE vs. MP	MP vs. ME	
Maternal vein	<0.01	<0.01	NS†	<0.01	<0.01	<0.01	LE ME LP MP
Umbilical vein	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	LE LP ME MP
Umbilical artery	<0.01	<0.01	<0.01	<0.01	<0.01	<0.05	LE LP ME MP
Fetal/maternal ratio	<0.01	<0.01	<0.01	<0.01	<0.05	<0.05	LP LE MP ME
Heel puncture							
2 hours	<0.05	<0.01	<0.01	<0.01	<0.01	NS	LE LP ME MP
4 hours	<0.05	<0.01	<0.01	<0.01	<0.01	<0.05	LE LP ME MP
8 hours	NS	<0.01	<0.01	<0.01	<0.01	NS	LE LP ME MP
24 hours	NS	<0.01	<0.01	<0.01	<0.01	NS	LP LE ME MP

* LP = lidocaine plain; LE = lidocaine with epinephrine; MP = mepivacaine plain; ME = mepivacaine with epinephrine.
† N.S. = not significant.

instance, the process of drug elimination was grossly described by the first-order pharmacokinetic model:

$$L = A \cdot \exp(-B \cdot t) \quad (1)$$

where L represents the concentration of drug in the blood in μg/ml; A is the extrapolated zero-time concentration; B is the rate constant for drug disappearance, and t is the time in hours.[4] This model expresses the long-term rate of disappearance. In the second instance, we assumed that the concentration in the umbilical arterial blood was the zero-time level, to explore the possibility of a more rapid disappearance of the drug in the early minutes of life. In using the umbilical arterial blood concentration, therefore, the process of drug disappearance had to be refined into a two-compartment model, represented by the following equation:

$$L = A_1 \cdot \exp(-B_1 \cdot t) + A_2 \cdot \exp(-B_2 \cdot t) \quad (2)$$

where L again denotes the concentration of drug in the blood in μg/ml; A_1 and A_2 reflect the umbilical arterial blood concentrations; B_1 and B_2 are the rate constants for the disappearance of drug; and t is the time in hours.[4] Model 2 implies that there is an initial phase in which the drug is distributed and eliminated simultaneously, followed by a second phase, the long-term elimination of the drug. The second phase of Model 2 is identical in rate to Model 1. Constants A and B in Model 1 were calculated for the four drug groups using the method of least squares. Constants A_1, B_1, A_2, and B_2 in Model 2 were calculated using the method of exponential peeling.[5,6] The half-time ($T_{\frac{1}{2}}$)—the time required for the drug level to decrease by half—was obtained from the rate constant B by the formula[4]:

$$T_{\frac{1}{2}} = \frac{0.693}{B}$$

In the separate group of 20 subjects, the concentrations of lidocaine and mepivacaine in the newborns' umbilical arterial bloods at delivery were compared with the concentrations in their heel bloods collected 2 to 15 minutes after delivery. This was an attempt to determine the relationship between the concentration of local anesthetic in the umbilical arterial blood at delivery and that in heel blood in the early minutes of life. The average total doses of local anesthetic drugs administered to these mothers were 382 mg for lidocaine and 344 mg for mepivacaine.

Several methods were used in the statistical evaluation of the results. In studying the characteristics of the four groups shown in table 1, chi-square values were computed for the numbers of primiparas, pitocin-augmented labors, and forceps deliveries.[7] Analy-

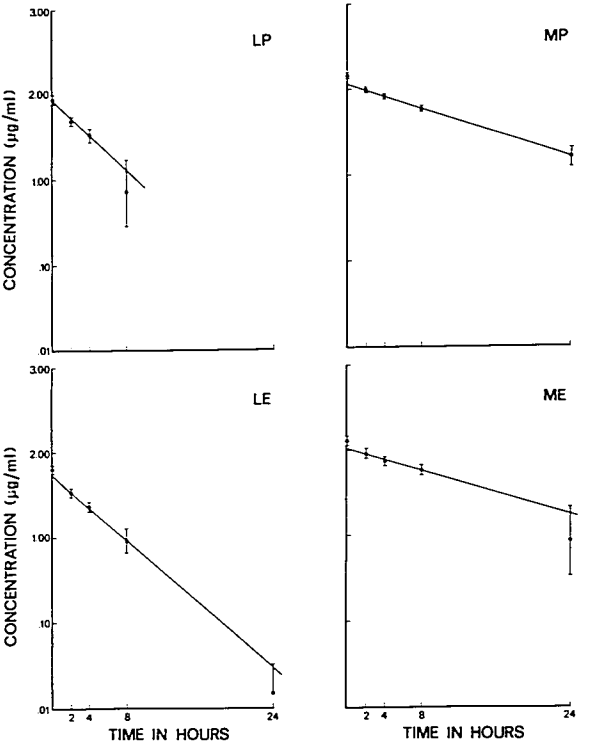

FIG. 1. Time courses of lidocaine and mepivacaine in the newborns' blood as calculated for each of the groups using Model 1. The estimated constants for Model 1 are listed in table 4. Each point represents the geometric mean ± SE for the concentration data. The geometric mean at 24 hours is not shown for the lidocaine-plain group since the value was below the precision of the assay technique. LP, lidocaine plain; LE, lidocaine with epinephrine; MP, mepivacaine plain; ME, mepivacaine with epinephrine.

sis of variance was examined for each of the other characteristics.[8] The Newman-Keuls method was used for comparison of the means for the time from initial dose of local anesthetic to delivery.[8] The t test for paired data was applied to the difference between the drug levels in the mother and baby.[9] Analysis of variance was also used to compare the maternal level, neonatal level, and fetal-to-maternal ratios among the four drug groups. Multiple comparisons were then determined for the drug concentrations at delivery and 2, 4, 8, and 24 hours later using the Newman-Keuls method. Multiple correlation coefficients were calculated from the data of the 94 subjects.[10] In the separate group of 20 infants, the t test for paired data was used to test the differences between concentrations of local anesthetic in umbilical arterial blood and heel blood.

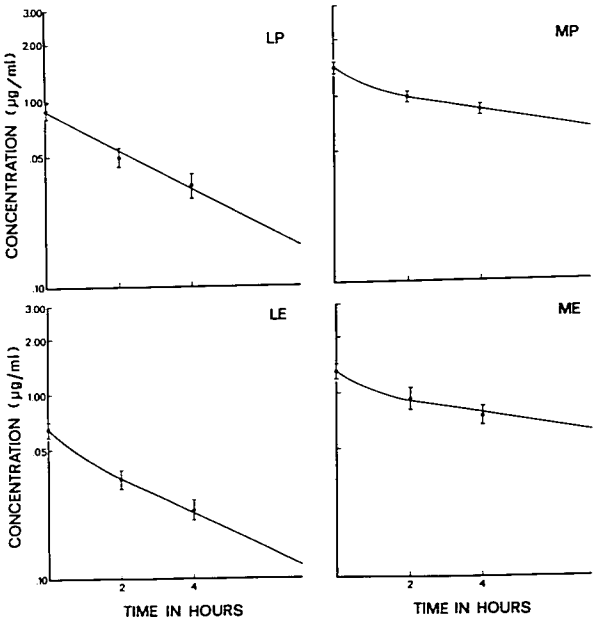

FIG. 2. Time courses of lidocaine and mepivacaine in the newborns' blood as calculated for each of the groups using Model 2. The estimated constants for Model 2 are listed in table 4. Each point represents the geometric mean ± SE for the concentration data. LP, lidocaine plain; LE, lidocaine with epinephrine; MP, mepivacaine plain; ME, mepivacaine with epinephrine.

Results

Comparisons of the characteristics of the four groups in table 1 revealed no significant difference except for the time from initial dose of local anesthetic to delivery. This period was significantly shorter for mepivacaine without epinephrine compared with each of the other groups ($P < 0.01$).

Table 2 shows the concentrations of lidocaine and mepivacaine in mothers' and babies' bloods at delivery for the four groups. The multiple comparisons of the concentration data and fetal-to-maternal distribution ratios are shown in table 3. The mean concentration of lidocaine in maternal blood in the lidocaine-without-epinephrine group was significantly higher than that in the epinephrine group ($P < 0.01$). The mean mepivacaine levels also differed significantly between the groups with and without epinephrine. Analysis across the lidocaine and mepivacaine series in the mother disclosed significant differences in the average concentrations, ($P < 0.01$), except for the comparison between the lidocaine-with-epinephrine group and the mepivacaine alone group.

The concentrations of local anesthetic drugs in the umbilical venous bloods of the newborns were significantly lower than those in the maternal circulations in all four drug groups ($P < 0.001$). The fetal-to-maternal concentration ratios averaged 0.52 and 0.59 for the lidocaine-alone and lidocaine-with-epinephrine subjects, respectively, and 0.64

TABLE 4. Estimated Constants for the Pharmacokinetic Models Describing Disappearances of Lidocaine and Mepivacaine from Newborn's Circulation and Related Half-times

Groups*	Model 1	Long-term Half-time (Hours)	Model 2	Initial-phase Half-time (Min)
LP	$L = 0.859 \cdot \exp(-0.237t)$	2.9	$L = 0.859 \cdot \exp(-0.237t)$	None
LE	$L = 0.543 \cdot \exp(-0.219t)$	3.2	$L = 0.107 \cdot \exp(-2.214t) + 0.543 \cdot \exp(-0.219t)$	19
MP	$L = 1.153 \cdot \exp(-0.082t)$	8.5	$L = 0.277 \cdot \exp(-1.761t) + 1.153 \cdot \exp(-0.082t)$	24
ME	$L = 1.042 \cdot \exp(-0.074t)$	9.4	$L = 0.275 \cdot \exp(-1.869t) + 1.042 \cdot \exp(-0.074t)$	22

* LP = lidocaine plain; LE = lidocaine with epinephrine; MP = mepivacaine plain; ME = mepivacaine with epinephrine.

and 0.69 for the mepivacaine-alone and mepivacaine-with-epinephrine subjects. The presence of epinephrine significantly affected the fetal-to-maternal ratios for both lidocaine ($P < 0.01$) and mepivacaine ($P < 0.05$). The use of epinephrine also significantly lowered the concentrations of lidocaine and mepivacaine in the baby's umbilical venous and arterial blood at delivery. In comparing the fetal-to-maternal ratios of the lidocaine groups with those of the mepivacaine groups, significant differences were found. The mean concentrations of lidocaine and mepivacaine in the umbilical bloods at delivery differed as well.

The concentrations of local anesthetic in the newborns' heel bloods at 2, 4, 8 and 24 hours of age are also shown in table 2, and the multiple comparisons in table 3. It is evident from the standard errors that there was considerable variation from baby to baby. The concentration of mepivacaine was significantly higher than that of lidocaine at each sampling period both with and without epinephrine ($P < 0.01$). Mean concentrations of the local anesthetics in the groups without epinephrine differed significantly from those in the epinephrine groups at 2 and 4 hours in the case of lidocaine and at 4 hours in the case of mepivacaine.

The data and the exponential models for the process of disappearance of lidocaine and mepivacaine from the newborns' circulations are shown in graphic form in figures 1 and 2. The fitting of models to data was quite good, as is evident from the figures. The estimated constants for the pharmacokinetic models and the related half-times are listed in table 4. The half-time values for long-term disappearance, as estimated for Model 1, were about 2.9 hours for the lidocaine alone group, 3.2 hours for the lidocaine-with-epinephrine group, 8.5 hours for the mepivacaine-alone group, and 9.4 hours for the mepivacaine-with-epinephrine group. The initial phase half-times as estimated from Model 2 were about 19 minutes for the lidocaine-with-epinephrine group, 24 minutes for the mepivacaine-alone group, and 22 minutes for the mepivacaine-with-epinephrine series. The initial phase half-time for the lidocaine-alone group was not observable since the extrapolated initial concentration was nearly the same as the umbilical arterial blood level at zero time. The second-phase half-times with Model 2 were the same as those determined from Model 1.

In terms of the correlation coefficients, we found no correlation between the Apgar scores of the newborns and the concentrations of local anesthetic at delivery. The total epidural dose of local anesthetic was positively correlated with the maternal and newborn levels of these drugs through 8 hours of age for the four drug groups ($r = 0.55$ to 0.80). In the lidocaine-alone group the total epidural dose correlated well with the babies' weights ($r = 0.82$). The *p*H of cord blood did not correlate well with any of the drug levels in the blood or with total epidural dose, length of labor, or duration of anesthesia.

In the separate group of 20 infants, the concentrations of lidocaine and mepivacaine in the heel bloods 2 to 15 minutes after delivery were significantly lower than those found in the umbilical arterial blood at delivery, as shown in table 5 ($P < 0.01$ and $P < 0.05$, respectively).

Of the 94 infants, only five had Apgar

scores of less than 7 at 1 minute of age, and by 5 minutes of age all except one had Apgar scores of 8 or more. Two of the five infants were in the lidocaine-with-epinephrine group. In one baby, after a difficult forceps delivery, the 1-minute Apgar score was 3, increasing to 8 at 5 minutes. The *p*H of umbilical venous blood was 7.24 and the concentration of lidocaine 0.64 μg/ml. In the second baby, the Apgar score was 2 at 1 minute and 7 at 5 minutes; the infant required assisted ventilation for 7 minutes. The *p*H of umbilical venous blood was 7.42 at birth, and the concentration of lidocaine in umbilical venous blood was 1.11 μg/ml. The remaining three babies who scored less than 7 at 1 minute were in the mepivacaine-alone group. In two of these babies, the 1-minute Apgar scores were 6. One infant had 2.99 μg/ml mepivacaine in the umbilical venous blood at delivery, and the *p*H was 7.35. The other baby had an umbilical venous blood concentration of 1.47 μg/ml mepivacaine, and the *p*H of the blood was 7.34. Neither of these newborns required resuscitation. The third infant had a 1-minute score of 5 and required oxygen and stimulation. The concentration of mepivacaine in the venous blood was 2.12 μg/ml and the *p*H was 7.23.

Five other neonates besides the two mentioned above had umbilical venous blood pH's of 7.26 or less. These five babies had high Apgar scores. In the infant with an umbilical venous blood *p*H of 7.23 at delivery, the fetal–maternal ratio of mepivacaine was the highest recorded in our series, 0.97. The total dose of mepivacaine received by the mother of this baby was 300 mg over 2½ hours, with a 20-minute interval between the last dose and delivery of the baby.

Six mothers had transient decreases in systolic blood pressures to below 90 torr during labor. None of the mothers manifested symptoms suggestive of toxic reaction to the local anesthetic drug.

Discussion

Many studies have amply demonstrated the rapid transplacental passages of both lidocaine and mepivacaine following maternal epidural analgesia in labor. There is general agreement that, at delivery, the concentrations of these local anesthetics in umbilical venous blood are approximately 50 to 70 per cent of those found in maternal blood,[11] and this was confirmed by our data as well. We found that epinephrine significantly affected these fetal-to-maternal concentration ratios. We also found that the ratios in the patients receiving mepivacaine were significantly higher than those in the equivalent lidocaine groups, and that the level of lidocaine in the cord blood was significantly lower than that of mepivacaine, suggesting a difference between the capacities of the two drugs to cross the placenta.

TABLE 5. Lidocaine and Mepivacaine in Umbilical-artery Blood at Delivery and in Heel Blood 2–15 Minutes Later

	Mean Concentration (μg/ml) ± SE	
	Lidocaine (n = 10)	Mepivacaine (n = 10)
Umbilical arterial blood	0.91 ± 0.16	1.30 ± 0.26
Heel blood	0.76 ± 0.15	1.20 ± 0.25
*P**	<0.01	<0.05

* The difference between concentrations in umbilical arterial and heel bloods.

The present study was aimed primarily at measuring the time courses of the disappearances of these two drugs from the bloodstream of the newborn. The most important finding was the remarkably long persistences of both lidocaine and mepivacaine in the blood of the neonate. In the case of lidocaine, measurable levels were still present at 8 hours of age in 34 of the 39 babies of the two subgroups sampled, but at 24 hours of age only seven of the 41 babies sampled had detectable concentrations of lidocaine. By contrast, at 8 hours of age the infants of the mepivacaine groups had mean concentrations of local anesthetic that were still higher than those observed in the lidocaine series at 2 hours of age. The mean concentrations of mepivacaine were 0.21 and 0.23 μg/ml for the groups with and without epinephrine 24 hours after birth. These values were approximately the same as the average concentrations found for the lidocaine groups at 8 hours of age. Of the infants exposed to mepivacaine, 46 of the 49 sampled still had detectable levels of the anesthetic in their bloodstreams 24 hours after birth.

In an attempt to compare the disappearance rates of lidocaine and mepivacaine in a more quantitative fashion, the two pharmacokinetic models were used and the half-times calculated as described above. Model 1 seemed a valid approach since heel-puncture blood was not obtained at birth, and since the concentration data after 2, 4, 8, and 24 hours displayed linearity in the log (level)–time plot. In considering Model 2 we felt that the use of the umbilical venous blood value as the initial concentration would markedly overstate the systemic concentration of the drug in the newborn since it resembled more nearly the concentration in the maternal blood. On the other hand, we were unsure of the relationship between the concentration of local anesthetic in the umbilical arterial blood at delivery and that in heel blood in the early minutes of life. In order to answer this question, in 20 additional newborns the concentrations of lidocaine and mepivacaine in umbilical arterial blood at delivery were compared with those in heel blood samples taken 2 to 15 minutes after birth. The drug levels were significantly lower in the heel blood than in umbilical arterial blood. The concentrations of lidocaine in heel blood averaged 82 per cent of those in the umbilical arterial blood while corresponding concentrations of mepivacaine averaged 92 per cent. Since it was not possible to obtain a sample of heel blood immediately at delivery, the difference between concentrations observed may have reflected, at least in part, the ongoing process of drug distribution and elimination. If this were the case, then the level of lidocaine seemed to decrease the most in the first minutes of life ($P < 0.01$ for lidocaine, but $0.05 > P > 0.01$ for mepivacaine). Although the relationship between concentrations in blood samples from these two sites remains somewhat unclear, we believe that the umbilical arterial blood concentration represents the initial concentration reasonably well. Nevertheless, it is apparent that there is no real advantage of using Model 2, since the process of drug elimination is primarily slow, lasting hours and not minutes.

Our exponential models and half-time results show that lidocaine disappears more rapidly than mepivacaine from the baby's blood. The long-term half-times were around 3 hours in the two lidocaine groups and 9 hours for mepivacaine. This difference between the disappearance rates of lidocaine and mepivacaine in the newborns remains to be explained. Several hypotheses come to mind. The total dose of mepivacaine received by the neonate was probably about 40 per cent higher than that of lidocaine, on the basis of the average umbilical venous blood concentrations. Jusko[4] has pointed out that dose-dependent pharmacokinetics are more likely to occur in infants than in adults in view of the immaturity of many drug transport and reaction mechanisms in the former.

Meffin and associates[12] have shown that the neonate has very little, if any, capacity to metabolize mepivacaine and is dependent on renal excretion to clear the drug in the unchanged form. Preliminary data from our laboratory suggest that the newborn is able to metabolize lidocaine. Renal excretion in the newborn is restricted, but wide variations in urine-flow rates, osmolality, and clearances have been observed.[13] It is therefore tempting to speculate that the major reasons for the prolonged persistence of mepivacaine compared with lidocaine are both the higher dose of mepivacaine received by the newborn and his lesser capacity to metabolize it. The wide individual variations may denote both differing abilities to metabolize these drugs from newborn to newborn and individual variations in renal function.

Other factors may have contributed to the difference between the disappearance rates of lidocaine and mepivacaine from the baby's blood. Lidocaine is apparently more lipid soluble than mepivacaine,[14] and the protein-binding capacity of mepivacaine is greater than that of lidocaine.[11] Both these physicochemical properties would favor faster disappearance of lidocaine from the circulation.

Several interesting points emerge from a consideration of the measurements made in the mothers of these babies. The use of epinephrine with lidocaine and mepivacaine was associated with significantly lower levels of these local anesthetics in maternal blood, as has been reported.[15] In comparing lidocaine and mepivacaine both with and without epinephrine, it was obvious that the

levels of mepivacaine exceeded those of lidocaine. This finding may also point to differences in their physicochemical properties, metabolism, or excretion in the mothers.

Finally, we have recently demonstrated that infants born after maternal epidural block with either lidocaine or mepivacaine scored significantly lower in certain neurobehavioral tests, particularly those involving muscle tone and power, compared with infants whose mothers had not received epidural analgesia.[16] If these neonatal effects are related to concentration of local anesthetic, one would expect, on the basis of the present data, that the effects would be more profound and long-lasting after mepivacaine than after lidocaine. This was indeed our impression, although the numbers were small and the examinations were carried out only until 8 hours of age, and no definite conclusion could be reached.

In conclusion, our study indicates that the use of epinephrine with the local anesthetic drug for maternal epidural block significantly lowers the level of lidocaine or mepivacaine in the mother's circulation and alters the concentration of lidocaine or mepivacaine in the newborn's circulation at delivery and in the first 4 hours after birth. In addition, mepivacaine may cross the placenta in greater amounts compared with lidocaine. Of importance are the remarkably long persistences of both lidocaine and mepivacaine in the bloodstream of the neonate, detectable levels of lidocaine being observed through 8 hours of age and mepivacaine through 24 hours of age. Pharmacokinetic analysis of the newborn data indicates that lidocaine disappears from the baby's circulation at a rate which is approximately three times that found for mepivacaine, and that the half-time of lidocaine in the infant's blood is about 3 hours, compared with 9 hours for mepivacaine.

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