Neurobehavioral Responses of Newborn Infants after Maternal Epidural Anesthesia

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Neurobehavioral testing of 41 newborn infants was performed during the first 8 hours of life. All of the infants were normal by the usual clinical criteria. The 28 infants whose mothers had received continuous lumbar epidural blocks with either lidocaine or mepivacaine showed significant differences from the 13 infants in the non-epidural block group. In particular, the epidural-block infants had significantly lower scores on the tests of muscle strength and tone, but not on tests designed to evaluate habituation to repetitive stimulation. (Key words: Anesthesia, obstetrical: neonatal effects; Anesthesia, obstetrical: peridural; Anesthetic techniques, peridural: obstetrical.)

IT IS GENERALLY AGREED and widely taught that well conducted continuous lumbar epidural block during labor and delivery offers major advantages to both the mother and her baby when compared with other approaches in obstetric analgesia and anesthesia. Among the advantages is a lack of drug-induced depression of the newborn as assessed by Apgar scores, despite the ready transplacental passage of local anesthetic drugs[1] and their persistence in the newborn during the early hours of life.[2]

In recent years, increasing numbers of studies have demonstrated subtle behavioral changes in newborns whose mothers had received various sedatives, analgesics, and anesthetics during labor.[3] These changes, in some instances, may be detectable for months after delivery.[4] There has been no attempt to apply similar kinds of testing to infants born after maternal epidural blocks.

We have devised a neurobehavioral examination which has proved to be a simple, rapid, and reproducible technique of assessing some aspects of newborn behavior in the early hours of life. In a comparison of two groups of infants, tested at two-hour intervals in the first 8 hours of life, we have found that those infants born to mothers who had received epidural blocks during parturition responded in a significantly different manner from infants born to mothers who had not received epidural blocks.

Materials and Methods

The Neurobehavioral Examination

The examination is based on standard neurologic testing of newborns as developed by Prechtl[5] and Beintema,[6] as well as some of the behavioral parameters first described by Brazelton.[7] From these experiences, we selected a number of tests which are most easily elicited during the early hours of life and lend themselves to quantitative scoring. The testing procedure and scoring criteria are described in detail in the Appendix.

In brief, the examination involves an assessment of the infant's state of wakefulness, various reflexes, his muscle tone and power, as well as his responses to various stimuli, including pin prick, light, and sound. In addition, the examiner notes and records response decrement behavior, *i.e.*, the ability of the subject to modify his behavior in response to repetitive stimulation.

The examination was performed on 41 newborn infants at two-hour intervals during the first 8 hours of life, for a total of 164 sepa-

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TABLE 1. Study Population*

	Epidural	Non-epidural
Number of infants	28	13
Maternal age (years)	23.5 (16–34)	28.8 (18–37)
Parity	1 (1–3)	2 (1–5)
Duration of labor (hours)	9.4 (3–16)	6.8 (4–15)
Birth weight (pounds, ounces)	6,14 (5,12–8,4)	7,1 (5,14–9,2)
Gestational age (weeks)	40 (38–41)	40 (38–41)
Apgar score (5 minutes)	8 (7–10)	8 (7–10)

* The figures are averages and ranges except that medians are given for parity and Apgar score. None of the differences is statistically significant.

rate examinations. The examiner was unaware of the anesthetic management of the mother and was not involved in the care of the infant. Every infant admitted to the study was the product of a normal pregnancy, labor, and vaginal delivery. All Apgar scores at 1 and 5 minutes were 7 or higher as determined by an independent observer. The routine newborn examinations were performed by a nonparticipating pediatrician and all were normal. All of the infants had entirely normal stays in the hospital and were discharged with their mothers.

EXPERIMENTAL GROUPS

In the epidural-block group (28 infants), continuous lumbar epidural block was administered to the mothers at various times prior to delivery. All mothers received at least two injections of local anesthetic, in nine cases, lidocaine, and in 19 cases, mepivacaine. In addition, 11 of the patients had received either alphaprodine and/or secobarbital six or more hours prior to delivery. The remaining 17 patients received no medication other than the epidural block.

In the non-epidural-block group (13 infants), seven mothers received either low spinal or local anesthesia for delivery. Of these seven patients, four had received alphaprodine and/or secobarbital six or more hours prior to delivery. The remaining six patients received neither analgesia nor anesthesia.

Other pertinent data are presented in table 1. In the epidural-block group, blood samples were taken at birth from the umbilical artery and from an arterialized heel puncture at 8 hours of age. The concentration of local anesthetic was determined by a previously described gas chromatographic method.[8]

In a separate group of five normal infants, the neurobehavioral examination was performed twice on each baby by two different examiners to provide data on inter-observer reliability.

The results of the individual components of the neurobehavioral examination in the two groups of infants were statistically evaluated using a Chi-square test at each time interval.

Results

Tables 2, 3, 4, and 5 present the results in those test parameters where significant differences were observed. Each table presents the number of infants in each scoring category at 2, 4, 6, and 8 hours of age and the results of statistical analyses of the data at that age. In tables 3, 4, and 5, absent or very weak responses were grouped as "low" scores and moderate and brisk responses as "high" scores. The following narrative summary of the results follows the order of testing as given in the Appendix.

In both groups of infants, the average number of state changes during each examination increased with increasing age of the infants,

TABLE 2. Decremental Responses to Pin Prick

	2 Hours		4 Hours		6 Hours		8 Hours	
	Absent	Present	Absent	Present	Absent	Present	Absent	Present
Non-epidural	2	11	0	13	1	12	0	13
Epidural	16	12	14	14	16	12	5	23
P	<0.05		<0.01		<0.01		NS	

TABLE 3. Scores on Tests of Muscle Power and Tone

	2 Hours		4 Hours		6 Hours		8 Hours	
	Low Scores	High Scores	Low Scores	High Scores	Low Scores	High Scores	Low Scores	High Scores
Pull to sitting								
Non-epidural	3	10	5	8	2	11	0	13
Epidural	25	3	18	10	20	8	16	12
	$P < .001$		NS		$P < .01$		$P < .001$	
Arm recoil								
Non-epidural	4	9	3	10	2	11	2	11
Epidural	21	7	23	5	25	3	22	6
	$P < .01$		$P < .001$		$P < .001$		$P < .001$	
Truncal tone								
Non-epidural	3	10	1	12	2	11	2	11
Epidural	16	12	15	13	15	13	11	17
	NS		$P < .05$		$P < .05$		NS	
General tone								
Non-epidural	3	10	3	10	1	12	0	13
Epidural	17	11	15	13	17	11	12	16
	NS		NS		$P < .01$		$P < .05$	

but no significant difference between the two groups was observed.

The magnitude of the response to pin prick was lower in the epidural-block group at 2 hours of age ($P < 0.2$) but not at the subsequent examinations. However, a striking difference was observed in the case of response decrement to pin prick (table 2). At 2, 4, and 6 hours of age, the epidural-block group contained a significantly higher proportion of infants who failed to alter their response to repeated pin-prick stimulation; this difference was no longer apparent at 8 hours of age.

In table 3 are presented the combined results of all the tests aimed at assessing muscle strength and tone. In general, the epidural-block infants scored lower than the non-epidural-block infants at various time periods in all four tests. The differences were most striking in the infants' head control when pulled to a sitting position and in the strength of arm recoil after gentle passive extension of the forearm.

Rooting behavior was less vigorous in the epidural-block group at 4, 6, and 8 hours of age (table 4), but no differences were found in sucking behavior. The epidural-block group showed diminished vigor of the Moro response at 4, 6, and 8 hours of age (table 5), but there was no difference between the responses to repeated Moro stimulation.

No significant difference between the two groups in their responses to light in the eyes, sound, or placing was observed with the exception of a higher incidence of absent decremental response to repeated sound stimulation in the epidural-block group at 2 and 6 hours of age ($P < 0.05$). In the evaluation of overall alertness and in the general assessment of these infants, no significant difference emerged.

An attempt was made to compare, within the epidural group, the responses of those infants whose mothers had received lidocaine with those whose mothers had received mepivacaine. Although there was a trend toward a more rapid recovery in the lidocaine group, the differences were not significant.

Inter-observer Reliability

In the five newborns given two independent examinations by two different experienced observers, 105 different observations were made.

Overall, the observers scored the infants identically in 88 of the 105 tests, for an index of agreement of 84 per cent. Most of the disagreements occurred in the scoring of the infant's state of wakefulness. If these discrepancies in state scoring are excluded, the inter-observer agreement index is 96 per cent. Agreement was always present in the evaluation of the presence or absence of response decrement behavior and in the evaluation of the various tests aimed at assessing muscle strength and tone.

Concentration of Local Anesthetic

The mean concentration of mepivacaine in the umbilical arteries of infants in the epidural-block group at birth was 1.68 μg/ml (range 0.29 to 5.8), and at 8 hours of age, 0.82 μg/ml (range 0.7 to 1.80). In the case of lidocaine, the umbilical-artery concentration averaged 0.48 μg/ml at birth (range 0.35 to 1.23) and 0.13 μg/ml at 8 hours (range 0.03 to 0.42).

Discussion

In previous studies of the potential effects of continuous epidural block for maternal pain relief in obstetrics, the assessment of the infants has been limited to Apgar scoring and occasional evaluation of acid–base status. These data suggest that epidural block, when properly conducted with either lidocaine or mepivacaine, has no significant depressant effect on the newborn despite the presence in the infant at birth of the local anesthetic in a concentration 50 to 70 per cent of that in the mother.[1] Occasional infants have been reported to have low Apgar scores where the concentration of local anesthetic has exceeded 3 μg/ml, although such depression is not always observed.[9,10] In another study from our laboratory,[2] we have shown that both lidocaine and mepivacaine can be found in the blood of the newborn for many hours after birth, with average half-lives of 4 hours for lidocaine and 10 hours for mepivacaine.

Reliance on the Apgar score as the sole criterion of neonatal well-being or as the sole index of potential effects of perinatally administered drugs was never intended,[11] nor does it seem justifiable today in view of the increased sophistication of our knowledge of the complexity of newborn behavior.[12,13]

The present study was therefore undertaken with the aim of applying more complex tests of newborn behavior to a group of selected normal infants whose mothers had received routine, uncomplicated, lumbar epidural blocks and comparing the results with those in a similar group of infants where epidural block had not been used. Although there were differences between the two groups in parity and duration of labor, all of the traditional clinical evaluations of the newborns showed them to be normal. No attempt was made to randomize the mothers into epidural-block or non-epidural-block groups. This was clinically not feasible, but may have introduced an uncontrolled element of bias of indeterminate magnitude. Birth weights, gestational ages, Apgar scores, pH of umbilical-artery blood, routine physical examinations, and hospital courses were identical and normal in both groups.

The neurobehavioral examination itself, based on elements from the work of several investigators, was deliberately designed to be quick and simple. Each examination required roughly five minutes. In our study, the examiner was unaware of the anesthetic management of the mother. Furthermore, we were encouraged by the high degree of agreement between two observers testing the same infants in close succession.

Despite the small size of the study population, we found significant differences between the epidural-block group and the non-epidural-block group. In particular, the epidural-block group was characterized as "floppy but alert." In the majority of tests designed to assess muscle strength and tone, the epidural-block infants scored less well than the non-epidural-block infants.

One can only speculate about the possible mechanisms for these observed differences. Local anesthetics, in higher concentrations than those seen in these infants, are known to affect the physiologic processes of impulse transmission at the neuromuscular junction.[14] The precise mechanism is unsettled, although both prejunctional[15] and postjunctional[16] effects involving largely electrical events at the junction have been observed. Usubiaga and Standaert[15] have described inconstant effects

TABLE 4. Quality of Rooting Behavior

	2 Hours		4 Hours		6 Hours		8 Hours	
	Low Scores	High Scores	Low Scores	High Scores	Low Scores	High Scores	Low Scores	High Scores
Non-epidural	5	8	3	10	2	11	2	11
Epidural	18	10	18	10	15	13	15	13
P	NS		<0.05		<0.05		<0.05	

TABLE 5. Quality of Moro Reflex

	2 Hours		4 Hours		6 Hours		8 Hours	
	Low Scores	High Scores	Low Scores	High Scores	Low Scores	High Scores	Low Scores	High Scores
Non-epidural	2	11	2	11	1	12	0	13
Epidural	11	17	15	13	18	10	14	14
P	NS		<0.05		<0.01		<0.01	

on tetanic tension and, in higher concentrations, on twitch tension.

We are unaware of any study of the effects of local anesthetics on neuromuscular transmission in newborn babies. Studies in the rat, admittedly more mature at birth than the human infant, have documented significant differences between the newborn and the adult in the physiology of neuromuscular transmission.[17]

In addition, local anesthetics have been shown to depress spinal reflex activity, particularly that involving polysynaptic multineuronal reflex pathways.[14] Finally, there is the possibility of modification by local anesthetics of the processes of excitation–contraction coupling in skeletal muscle.[18]

By contrast, little difference between the epidural-block and non-epidural-block groups was observed in tests of "higher" central nervous system function, as exemplified by their response decrement behavior. An extensive body of literature documents the ability of the normal newborn to modify its response to repetitive stimulation of various sorts.[3,4,13,19,20] This has been called by some observers "habituation." It appears that behavioral impairment, including decreased habituation, may result from neonatal asphyxia[20,21] or from the perinatal administration of various drugs to the mother.[3,4,22–25]

With the sole exception of the responses to pin prick, the epidural-block and non-epidural-block infants in our study manifested similar degrees of habituation to repeated stimulation of various sorts. Why the responses to pin prick were different is unexplained, although it is possible that the local anesthetics interfere with the sensory element of this somesthetic response. A similar explanation may be offered for the less striking differences in rooting behavior in response to gentle perioral stimulation.

The results of this study in a small group of infants suggest that neurobehavioral testing may represent a valuable way to assess the effects of maternally-administered drugs on the newborn, effects of a more subtle nature than can be measured by Apgar scoring alone. Since it is not possible in clinical practice randomly to assign parturients to one or another form of anesthetic management, we rigidly selected the subjects for our study as normal by all of the usual clinical criteria. There was a higher proportion of primiparas in the epidural-block group and, consequently, a longer average duration of labor; however, these differences were not statistically significant. In addition, the examiner was unaware of the form of anesthetic management in the infants and he was not in any way involved in their medical care.

In our study, significant differences between neurobehavioral performances in these two groups of normal infants were demonstrated. In particular, those infants born after uncomplicated maternal epidural anesthesia showed significant decreases in muscle strength and tone in the first 8 hours of life, but differed little from the non-epidural-block group in the more complex test parameters. In general, the reverse has been observed by others following the maternal administration of central nervous system depressants.

The significance of our observations in terms of early neonatal adjustments, the development of maternal-infant relationships, and the implications, if any, for future growth and development remain to be elucidated. Follow-up studies of these infants and the study of infants born after complicated labor and delivery are in progress.

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APPENDIX

The Neurobehavioral Examination

Apgar Score

Apgar scoring is done at each examination and recorded as component scores, which are then summed.

State

The infant's state is scored as follows:

Awake States

A–1 The eyes may be opened or closed, the eyelids fluttering, the infant drowsy or semi-dozing. The activity level is variable, with interspersed mild startles from time to time. The infant reacts to sensory stimuli, but delay in response is often seen. State change after stimulation is frequently noted.

A–2 The eyes are open. There is considerable motor activity with thrusting movements of the extremities, and even a few spontaneous startles. The infant reacts to external stimulation with an increase in startles or motor activity, but discrete reactions are difficult to distinguish because of general high activity level. Intermittent fussing does not result in a change of state.

A–3 There is an alert, bright look. The infant seems to focus attention on the source of stimulation, such as an object to be sucked, or visual or auditory stimuli. Impinging stimuli may break through, but with some delay.

A–4 This state is characterized by intense crying, which is difficult or impossible to break through with stimulation.

Sleep States

S–1 There is light sleep with the eyes closed, a low activity level, with random movements, and startles or startle equivalents. The baby responds to internal and external stimuli with startle equivalents, often with a resulting change of state.

S–2 Deep sleep with no spontaneous activity except for startles or startle equivalents, usually at regular intervals. External stimuli produce startles with some delay. Suppression of startles is rapid, and state changes are less likely.

During an examination, state is recorded eight times, immediately prior to each specific test.

Specific Tests

1. *Response to Pin Prick*

With the infant supine, the examiner pricks the sole of the subject's foot lightly with a pin. The response has two components:

a) Local flexion of the involved limb (withdrawal) plus a generalized response characterized by trunk and limb motion, color changes, crying, etc. Only the magnitude of the local withdrawal is scored in the response category as follows:

0 No response
1 Weak or delayed response
2 Fairly brisk response, perhaps delayed, but more vigorous than 1
3 Vigorous, brisk response, easily elicited

b) The response decrement score is recorded as the number of stimuli required before alteration of either the local withdrawal response or the general response, whichever occurs first.

2. *Tone Evaluation*

a) *Pull to Sitting*

The infant is gently pulled by his hands to the sitting position and the movement of his head is observed. Scoring is based on the following criteria for head control against gravity:

0 No evidence of head control
1 Weak head control; unable to maintain head erect
2 More control; head held in erect position for short period
3 Marked control; head consistently held erect

b) *Arm Recoil*

The infant's forearms are gently extended and suddenly released by the examiner. The recoil is scored as follows:

0 Absent
1 Weak recoil, to as much as 45 degrees
2 More marked recoil
3 Very strong, rapid recoil, usually with overshoot

c) *Truncal Tone*

The infant is suspended horizontally by the examiner's hand under its abdomen. The test is scored as follows:

0 Complete floppiness
1 Weak attempt to extend either hips or neck; weak trunk straightening
2 Stronger neck or hip extension; vigorous trunk straightening
3 Rigidity of neck, trunk and hips

d) *General Body Tone*

A composite score is assigned for the subjective evaluation of the infant's muscle tone as follows:

0 Minimal or absent tone
1 Weak tone
2 Average tone
3 Strong tone

3. *Rooting*

The skin of the cheek or the corner of the mouth is gently stroked by the examiner's finger. The infant is observed for head turning and lip movement while supine with his head in the midline. Scoring is as follows:

0 No response
1 Lip movements only, or weak, incomplete head turning

2 Full head turn towards stimulus with much lip movement (even if somewhat delayed)
3 Vigorous turning and sucking lip movements

4. *Sucking*

With the infant in a supine position, the examiner inserts the proximal joint of his index finger into the infant's mouth. Sucking is scored as follows:

0 No response
1 1 to 3 sucks
2 Strong sucks, 3 to 10 per group
3 Long periods of vigorous sucking

5. *Moro Response*

This response is elicited by a rapid, short head drop with the infant in the supine position. The scoring of the infant's optimal Moro response, which is usually observed after the first or second stimulus application, is as follows:

0 No response
1 Slow response with weak arm movements, encirclement incomplete
2 Moderately rapid response, complete encirclement
3 Full, rapid response with encirclement

Stimulus applications are repeated at 5-second intervals and the number counted. The examiner notes the number of stimuli required until the first maximal response and then the number until this stereotyped "best" response is observably altered.

Response decrement is recorded as the number of maneuvers performed from the infant's optimal Moro response until this response becomes different.

6. *Response Decrement to Light in Eyes*

The light from a flashlight is shined briefly into the infant's eyes at approximately 5-second intervals. The examiner records the number of stimuli applied before the infant's initial response, usually a blink, is observably modified.

7. *Response to Sound*

Either a ball or a rattle is sounded a few inches from the infant's ear, out of visual range. The response is observable movement or activity and the infant's maximal response to the stimulus is scored as follows:

0 No response
1 Slight change in activity level in response to sound
2 Some head turning towards sound, searching, alert behavior
3 Definite searching, almost immediate response to sound

The sound stimulus is repeated at approximately 5-second intervals, with the examiner counting the number of applications. Note is made of the number of stimuli required until the optimal response first occurs. The stimulus applications are repeated and counted until the optimal response is observably changed. Response decrement to sound is recorded as the number of stimuli needed from the first optimal response to visible alteration of this "best" response.

8. *Placing*

With the infant in the upright position, the leg is raised until the dorsum of the foot touches a protruding bassinet edge. Scoring is based on flexion of the stimulated leg and placing of the stimulated foot on the edge as follows:

0 No response
1 Minimal flexion and extension of leg; foot not placed
2 Full response, difficult to elicit, foot placed
3 Full response, easily and rapidly elicited

9. *Alertness*

This is a composite, more subjective score, which includes the most alert periods during the entire exam. It takes into account head turning toward a variety of environmental stimuli, widening of eyes, "bright-looking" face, shutting out of interfering activity, etc.

0 Dull or absent response to most stimuli
1 Several short or one moderately long attentive period including at least one A-2 state score during the exam
2 Many fairly long attentive periods including *at least one* A-3 state score during the exam
3 Alerting responses to most all stimuli, either environmental or applied

10. *General Assessment*

This is the examiner's appraisal of the infant's performance on the entire examination. Assessment is scored either Abnormal, Borderline, Normal or Superior. The reasons for putting an infant into this category, such as which scores or tests made up the assessment, are noted.

The dominant state score is entered and the number of state changes is recorded as the lability. The comment space is used to describe any unusual aspect of the examination, any untoward events or interruptions, and such difficult-to-quantitate variables as body color changes and abnormal movements.