Anesthesiology
54:29–32, 1981

Assessment of Neuromuscular Function in Infants

Robert S. Crumrine, M.D.,* and Edmund H. Yodlowski, Ph.D.†

This study was conducted to measure neuromuscular transmission in newborn infants. Age-dependent differences in neuromuscular transmission and the effect of nitrous oxide anesthesia upon neuromuscular function were assessed in pediatric surgical patients following induction of anesthesia with methohexital by the use of the frequency sweep electromyogram (FS-EMG). Children older than 12 weeks' chronologic age usually had FS-EMG responses similar to those of adults, whereas infants less than 12 weeks old had significantly less pronounced FS-EMG responses at high stimulation frequencies (>50 Hz). Administration of 70 per cent nitrous oxide induced 11–38 per cent reductions in the amplitudes of the FS-EMG responses at all frequencies of stimulation in the younger group. A positive correlation was found between inability to sustain a tetanic contracture (FS-EMG fade) in the 50–100-Hz region of stimulation and percentage depression of the FS-EMG response induced by nitrous oxide. (Key words: Anesthesia, pediatric. Anesthetics, gases: nitrous oxide. Monitoring: electromyogram. Neuromuscular transmission.)

THERE ARE CONFLICTING REPORTS of infant sensitivity to muscle relaxants. Stead,[1] Sabawala,[2] and Bennett *et al.*[3] found that the newborn is more sensitive to *d*-tubocurarine (*d*Tc) than are older children. Other investigators, however, have not found any age-dependent hypersensitivity to *d*Tc.[4,5] The observed differences in sensitivity may have been due to morphological differences in the neuromuscular junctions,[6] types of anesthetics administered,[7,8] or different criteria used to determine dosages and/or levels of relaxation.[9,10]

In the rat[11,12] and human[13] embryos, innervation and morphogenesis of the neuromuscular junction are not completed at birth. Comparing the full-term infant and the premature infant, Koenigsberger *et al.*[14] showed that premature infants are more susceptible to posttetanic exhaustion than are their full-term counterparts. These data suggest that the infant neuromuscular junction may not be fully developed at birth, and that maturation of the neuromuscular junction continues during neonatal development.

The purpose of this study was to measure myoneural function in the newborn and to relate maturation of the neuromuscular junction to neuromuscular transmission during anesthesia. Myoneural function was assessed using the frequency sweep electromyogram (FS-EMG) technique.[15,16]

Methods

Twenty-five surgical patients (ASA class 1) undergoing elective surgical procedures were included in this study. This study was approved by the university human investigations committee, and parental informed consent was obtained. The patients were 1 day to 5 years of age. All had been products of full-term pregnancies and were without known neuromuscular disease. Serum electrolytes were within normal limits. All subjects except one were within normal limits for growth and development. The exception, a 20-month-old female infant, was in the fifth percentile for weight and height and had been diagnosed as having "failure to thrive."

Premedication consisted of atropine, 0.014 mg/kg, im. Anesthesia was initiated by intramuscular injection of 5 per cent methohexital, 10 mg/kg. Blood pressure, ECG, and temperature were monitored.

Neuromuscular function was monitored using the FS-EMG recorded from the tibialis anterior muscle. The FS-EMG response is produced by recording the compound muscle action potential (CMAP) induced by intramuscular electrical stimulation. The stimulus consisted of regulated current pulses with a duration of 0.1 msec. Stimulus amplitude was adjusted (12 mA maximum) to produce supramaximal stimulation of intramuscular motor neurons without direct excitation of muscle fibers.[16] Rather than testing at fixed frequencies, the stimulus rate was made to increase exponentially from an initial rate of 1 pulse/sec to a final frequency of 100 Hz over a stimulation period of 10 sec. The exponential increase in frequency allows assessment of neuromuscular transmission at tetanic rates but without inducing fatigue.

Thin coiled-wire electrodes[16] were used for stimulation and recording of the induced electrical activity. Stimulation was achieved by passing the stimulus pulse between an intramuscular electrode inserted into the body of the tibialis anterior muscle and a second, larger, surface electrode, located on the skin over the muscle. The CMAP was recorded from a second intramuscular electrode. This bifilar recording electrode was positioned within the same muscle but slightly distal to the stimulating electrode. The integral

---

* Associate Professor, Department of Anesthesiology.

† Instructor, Department of Anesthesiology and Department of Physiology and Biophysics.

Received from the Department of Anesthesiology, University of Tennessee Center for The Health Sciences: LeBonheur Children's Medical Center, Memphis, Tennessee 38103. Accepted for publication July 18, 1980. Supported in part by an ASA starter grant from the Parker B. Francis Foundation.

Address reprint requests to Dr. Yodlowski: Pediatric Anesthesiology, LeBonheur Children's Hospital, One Children's Plaza, Memphis, Tennessee 38103.

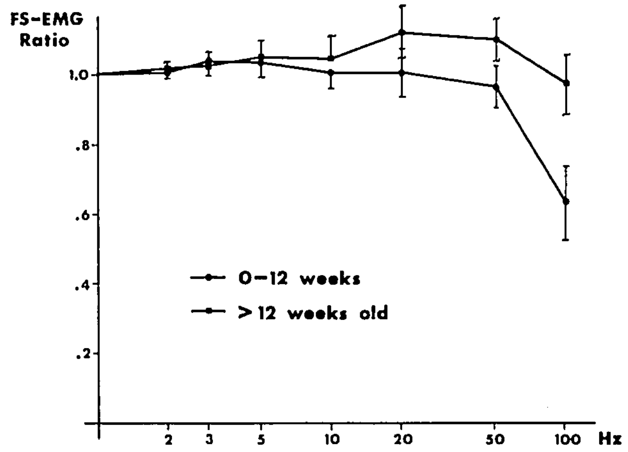

FIG. 1. Mean normalized frequency sweep electromyogram (FS-EMG) control response curves from surgical patients less than and older than 12 weeks of age. The ordinate represents FS-EMG amplitudes at points corresponding to various stimulation rates as ratios of the initial (*i.e.*, 1 Hz) amplitude. In the high-frequency (50–100 Hz) region, the younger infants had rapid declines in their responses that were not found in the infants older than 12 weeks of age.

of the CMAP is measured after each stimulus pulse and is continuously displayed on a strip-chart recorder. This provides a response curve that is a profile of the muscle's ability to sustain neuromuscular transmission across a wide range of excitation rates. In order to standardize the data, the amplitudes of the FS-EMG responses at 2, 3, 5, 10, 20, 50, and 100 Hz were normalized to the amplitude of the initial (*i.e.*, 1 Hz) response. The ratios at these individual frequencies were used to compute mean response curves.

The electrodes were inserted as soon as the patients were asleep (2 to 3 min after administration of methohexital). Control FS-EMGs were recorded before administration of any additional anesthetic or muscle relaxant. Seventy per cent nitrous oxide in oxygen was administered to 17 of the 25 subjects using an Ayre's T-piece in an open-loop system. The FS-EMG was recorded at 2-min intervals. After administration of nitrous oxide for at least 6 min, additional anesthetics and/or muscle relaxants were administered as needed for surgical anesthesia. Myoneural function continued to be monitored throughout the surgical procedure. At its termination the electrodes were removed.

The mean FS-EMG response profiles were obtained by calculating the mean for each of the normalized ratios at frequencies corresponding to 2, 3, 5, 10, 20, 50, and 100 Hz. Statistical inferences are based on Student's *t* test.

The slope, or decline of the high-frequency (>50 Hz) response was estimated by the difference between the FS-EMG ratios at 50 and 100 Hz. These data for the slope were plotted versus percentage changes from control in the amplitudes of the FS-EMG responses after administration of nitrous oxide. A least-squares linear regression technique was used to fit these data to a straight line.

Results

The 25 subjects studied could be divided into two groups according to chronologic age, since myoneural function in those children less than 12 weeks old differed measurably from that in those more than 12 weeks of age (fig. 1). Two examples of FS-EMG tracings recorded from patients are shown in figure 2. The amplitudes of responses recorded from infants less than 12 weeks old tended to decrease as the stimulation frequency approached 100 Hz. However, the high-frequency ($50 < f \leq 100$ Hz) responses obtained from the older group diminished only slightly with increasing stimulation frequency. At a stimulation rate of 100 Hz, the mean (±SE) FS-EMG level dropped to a normalized value of 0.643 ± .068 in the younger group, whereas in the older children the normalized ratio was 0.974 ± .078. The difference between the high-frequency FS-EMG responses of the two groups was statistically significant ($P < 0.01$).

The children in the two groups also responded differently following administration of nitrous oxide. After 6 min of administration of 70 per cent nitrous oxide the mean FS-EMG response of the younger children was depressed, while that of the older group had not changed (fig. 3). Within each age group there were individual variations, and there was no clearly delineated change in the FS-EMG response to nitrous oxide at 12 weeks of age. Those individuals (regardless of age) whose control FS-EMG response curves

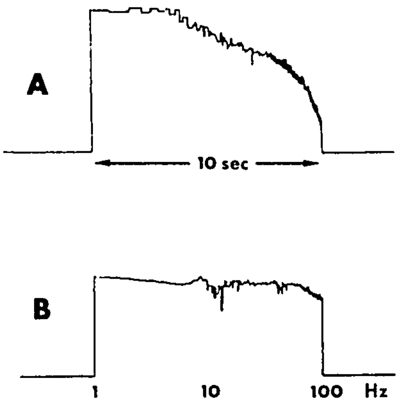

FIG. 2. Tracings of the frequency sweep electromyogram (FS-EMG) responses from the tibialis anterior muscles of a 1-day-old infant (*A*) and a 4-month-old infant (*B*) premedicated with methohexital.

dropped off most steeply at the higher frequencies tended to have their responses most depressed by nitrous oxide (fig. 4). The reductions of FS-EMG amplitudes in the younger group after nitrous oxide administration were due to decreases in the amplitudes of the recorded compound muscle action potentials.

All of the patients in the younger group were subject to failure of neuromuscular transmission at high frequencies of stimulation, and their FS-EMG amplitudes decreased during nitrous oxide anesthesia. The responses obtained from the older group of children were more varied, but typically their FS-EMG amplitudes did not decrease during frequency sweep stimulation, and after nitrous oxide, the FS-EMG responses were unchanged or slightly increased. The mean (±SE) percentage change in FS-EMG amplitude after nitrous oxide administration for the older group was +7.3 ± 3.8 per cent, compared with −23.0 ± 3.45 per cent for the younger group. This difference was statistically significant, $P < 0.01$.

The response obtained from the one child studied who was developmentally below average was like that of a much younger child. The FS-EMG showed a marked decline (*i.e.*, negative slope) at stimulation frequencies greater than 50 Hz, and the response was depressed (23 per cent) during nitrous oxide anesthesia.

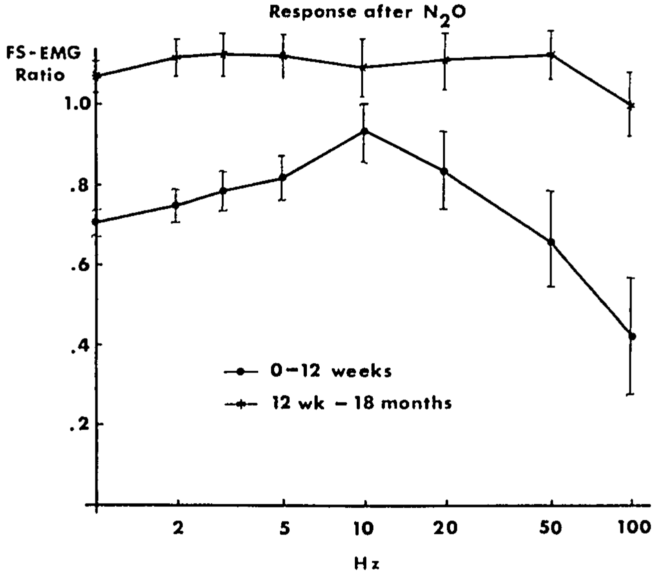

FIG. 3. Mean normalized frequency sweep electromyogram (FS-EMG) response curves obtained from children after 6 min of N_2O–O_2 (5:2 l/min) anesthesia. The FS-EMG ratios after N_2O administration are expressed as fractions of their control amplitudes. In the younger group N_2O decreased FS-EMG amplitude but it did not produce any statistically significant changes in the responses of the older children.

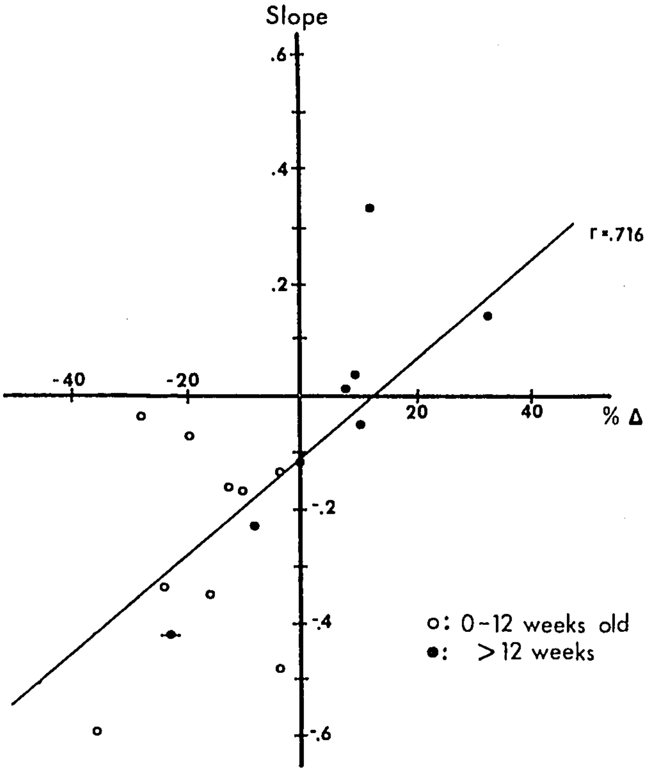

FIG. 4. Correlation between the slope of the frequency sweep electromyogram (FS-EMG) response curve in the region between 50 and 100 Hz and percentage change in the amplitude of the 1-Hz FS-EMG response after N_2O administration. Least-squares regression was used to fit these data to a linear curve. The data point for the 20-month-old infant who was within the lower fifth percentile for growth and development is also shown (–●–). The response obtained from this patient is characteristic of that from a much younger infant.

Discussion

The results of this study demonstrate a measurable, age-dependent difference between the myoneural function of infants less than 12 weeks old and that of older children and adults. By 12 weeks of age the FS-EMG response pattern has become adult-like. The diminished FS-EMG response in the high-frequency region of the younger infants indicates that these infants were unable to maintain a tetanic contracture because of failure in neuromuscular transmission. These results are consistent with those of other investigators who have shown, by measuring EMG[17] and force[4] at fixed frequencies, that the response to tetanic stimulation is not well sustained in the newborn. Two of the children in the older group had FS-EMG responses similar to those of much younger infants. We feel that this may indicate that their neuromuscular junctions had not yet reached a level of development commensurate with their chronologic ages. These results suggest that the infant neuromuscular junction continues to develop after birth; during this period of myoneural development, the infant is more susceptible to neuromuscular fatigue than is an older child or an adult.

It is well known that a margin of safety exists for neuromuscular transmission, and that this margin of safety is frequency-dependent. The failure of neuromuscular transmission that we observed in the FS-EMG responses obtained from the younger infants provokes speculation that the margin of safety in the newborn is less than that in more mature individuals.

During this period of myoneural development, the infant's already limited neuromuscular reserves may be further compromised by nitrous oxide anesthesia. Consequently, the adequacy of neuromuscular transmission is an important anesthetic consideration, particularly in management of the newborn, since even a slight reduction in neuromuscular function may diminish the patient's respiratory capacity. We recommend that neuromuscular transmission be monitored in these patients (even when muscle relaxants are not used), and that such monitoring include assessment of the patients' responses to tetanic stimulation at frequencies of 50 to 100 Hz.

References

1. Stead AL: The response of newborn infants to muscle relaxants. Br J Anaesth 27:124–130, 1955
2. Sabawala PB: The response of newborn human intercostal muscle to muscle relaxants, Progress in Anesthesiology. Edited by TB Boulton, R Bryce-Smith, MK Sykes et al. Amsterdam, Excerpta Medica, 1968, pp 1137–1143
3. Bennett EJ, Ignacio A, Patel K, et al: Tubocurarine and the neonate. Br J Anaesth 48:687–689, 1976
4. Churchill-Davidson H, Wise R: The response of the newborn infant to muscle relaxants. Can Anaesth Soc J 11:1–6, 1964
5. Walts L, Dillon J: The response of newborns to succinylcholine and *d*-tubocurarine. ANESTHESIOLOGY 31:35–38, 1969
6. Fischbach GD, Frank E, Jessell TM, et al: Accumulation of acetylcholine receptors and acetylcholinesterase at newly formed nerve–muscle synapses. Pharmacol Rev 30:411–428, 1978
7. Gregory GA, Eger EI II, Munson ES: The relationship between age and halothane requirements in man. ANESTHESIOLOGY 30:488–491, 1969
8. Waud BE, Waud DR: Effects of volatile anesthetics on directly and indirectly stimulated skeletal muscle. ANESTHESIOLOGY 50:103–110, 1979
9. Goudsouzian NG, Donlon JV, Savarese JJ, et al: Re-evaluation of dosage and duration of action of *d*-tubocurarine in the pediatric age group. ANESTHESIOLOGY 43:416–425, 1975
10. Cook DR: Neonatal anesthetic pharmacology: a review. Anesth Analg (Cleve) 53:544–548, 1974
11. Kelly SS, Roberts PV: The effect of age in the safety factor in neuromuscular transmission in rats. Br J Anaesth 49: 217–221, 1977
12. Redfern PA: Neuromuscular transmission in new-born rats. J Physiol (Lond) 209:701–709, 1970
13. Juntunen J, Teräväinen H: Structural development of the myoneural junction in the human embryo. Histochemie 32:107–112, 1972
14. Koenigsberger MR, Patten B, Lovelace RE: Studies of neuromuscular function in the newborn: a comparison of myoneural function in the full term and the premature infant. Neuropaediatrie 4:350–361 1973
15. Gerber HR, Johansen SH, Mortimer JT, et al: Frequency sweep electromyogram and voluntary effort in volunteers after *d*-tubocurarine. ANESTHESIOLOGY 46:35–39, 1977
16. Mortimer JT, Yodlowski EH: Frequency sweep analysis of neuromuscular junction continuity. J Med Eng Technol 3:242–247, 1979
17. Koenig J: Morphogenesis of motor endplates 'in vivo' and 'in vitro.' Brain Res 62:361–365, 1973