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Electroencephalograms in children during isoflurane anesthesia

YUKAKO KITAHARA[1], OSAMU FUKATSU[1], and FUJINORI NOZAKI[2]

[1] Department of Anesthesia, Tokyo Metropolitan Hachioji Children's Hospital, 4-33-13 Daimachi, Hachioji-City. Tokyo, 193 Japan
[2] Department of Anesthesia, Yokohama Rosai Hospital for Labour Welfare Corporation, 3211-1 Kozukuemachi, Kohoku-ku Kanagawa, 222 Japan

Abstract: The electroencephalograms (EEG) of 55 children under isoflurane anesthesia were studied to elucidate any change in pattern with age. The children ranged from 1 month to 14 years of age were divided into six age groups. The standard minimum alveolar concentration (MAC) was determined in each group. Anesthesia was induced using the slow induction method, and EEG was recorded at isoflurane concentrations of 1.5 MAC in 100% oxygen, 1.0 MAC in 100% oxygen, and 1.0 MAC under administration of 66% nitrous oxide in oxygen. Ventilation was controlled mechanically (end-tidal CO_2 35–40 mmHg).

At 1.5 MAC, the incidences of burst suppression in the groups of 6 months to 6 years of age were significantly less than in groups older or younger than that age ($P < 0.05$). Except for infants less than 6 months of age, the mean values of maximum amplitude at 1.0 MAC were two to three times of those in adults. Children 3–6 years of age showed the highest value of 427.0 ± 83.5 μV.

Key words: Children, EEG, Isoflurane

Introduction

Electroencephalogram (EEG) is widely used to monitor central nervous system function during anesthesia and the effect of inhalational anesthetics on the EEG of adults has been studied in depth [1,2]. However, because EEG waves vary with age in children, basic changes in EEG patterns among children under general anesthesia have not yet been established.

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Isoflurane is a commonly used volatile anesthetic agent in pediatric anesthesia and in this study the effects of isoflurane on the EEG patterns of infants and children were studied, with and without nitrous oxide.

Materials and methods

Fifty-five children scheduled for elective surgery under general anesthesia were selected for our study. All were born after full-term pregnancies and had medical histories of normal growth and development, with no convulsive diseases. Written informed consent from the children's parents and institutional approval were obtained prior to the study.

The children were from 1 month to 14 years of age, and were divided into the following six age groups: Group A ($n = 9$) 1–6 months; group B ($n = 8$) 6–12 months; group C ($n = 11$) 1–3 years; group D ($n = 10$) 3–6 years; group E ($n = 9$) 6–10 years; and group F ($n = 8$) 10–14 years. All subjects were premedicated with intramuscular atropine sulfate 0.02 mg·kg^{-1}, 30 min before anesthesia. Lead II ECG and noninvasive blood pressure (Pulsemate BX-5, Nippon Colin, Tokyo, Japan) were monitored. Anesthesia was induced with inhalation of 2%–3% of isoflurane carried with a mixture of 66% N_2O and 33% oxygen. After induction, a 22-G teflon catheter was inserted into a cubital or a saphenous vein and intubation was facilitated by vecuronium bromide (0.08 mg·kg^{-1}). Ventilation was adjusted to maintain an end-tidal CO_2 of 35–40 mmHg, and during the course of the study the end-tidal CO_2 level and anesthetic concentrations were measured (Datex Capnomac, Datex, Helsinki, Finland). Body temperature was kept between 36.5° and 37.5°C, using a warming blanket.

Disk electrodes were placed on the right and left frontal regions to detect the EEG. The conventional technique was used to record the EEG, setting the time

constant at 0.3 s and the high-cut filter at 25 Hz. The EEG was measured on both frequency and amplitude using a compressed spectral array analyzer (EEG Trend monitor, Nihon Koden, Tokyo, Japan) and the frequencies were divided into δ (1–4 Hz), θ (4–8 Hz), α_1 (8–10 Hz), α_2 (11–13 Hz) and β (14 Hz), the proportions of their waves were expressed as a percentage. As previous studies showed [3,4], reverse arousal is indicated by slow waves caused by noxious stimuli; thus we observed the occurrence of this phenomenon during operation. We defined "burst suppression" as the EEG pattern that contained bursting slow waves and continuous electrical silence (including total silence) of over 3.0 s.

Using data from a previous study [5] which reported minimum alveolar concentration (MAC) as being different between age groups, we determined MAC to be 1.87% in group A, 1.80% in group B, 1.60% in groups C and D, and 1.50% in groups E and F. At these MACs the procedure was as follows: (1) 10 min were allowed to obtain EEG at 1.5 MAC in 100% oxygen; (2) then, the concentration of isoflurane was reduced to 1.0 MAC in 100% oxygen and EEG was obtained according to the same protocol; and (3) nitrous oxide (66%) was added in oxygen with 1.0 MAC of isoflurane. Five min later, EEG was recorded again and the operation was started under these anesthetic concentrations.

Results were expressed as means ± SD. The differences between means of selected groups were assessed by analysis of variance or Student's *t*-test. The descriptive data were represented by percentage proportion, and differences among groups were assessed by chi-square analysis. $P < 0.05$ was considered significant.

Results

EEG at 1.5 MAC

Table 1 shows the values obtained from 6 groups at 1.5 MAC of end-tidal isoflurane. The incidences of burst suppression were rather low (from 27.3% to 10.0%) in groups B, C, and D. There were significant differences in the incidences between high- and low-occurrence groups. Specifically, the incidence of

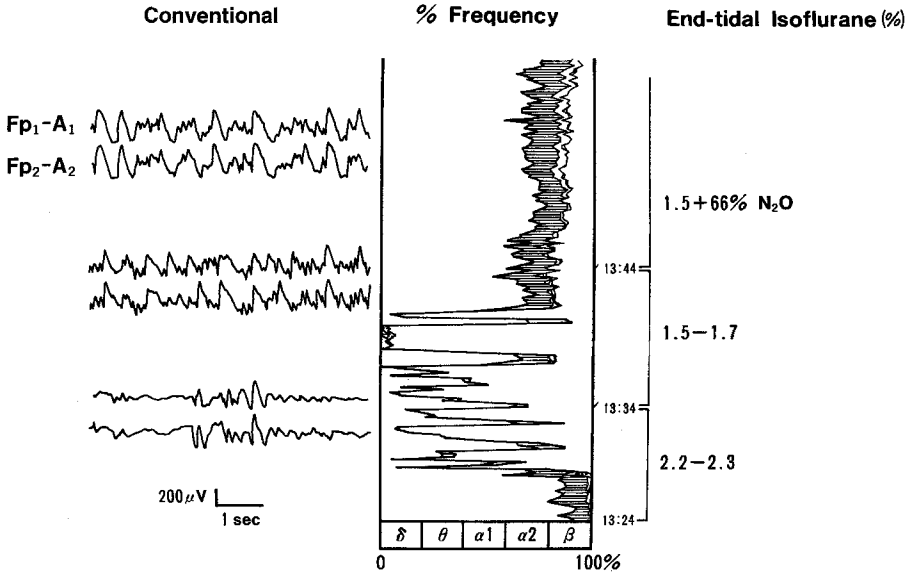

Fig. 1. EEG of a 12-year-old child. Burst suppression was observed shortly after reaching an expiratory isoflurane concentration of 1.5 MAC, which was maintained after the inspiratory concentration was reduced

Table 1. Comparison of groups A–F at 1.5 MAC end-tidal isoflurane

Age	A 1–6 months	B 6–12 months	C 1–3 years	D 3–6 years	E 6–10 years	F 10–14 years
Number of patients (*n*)	9	8	11	10	9	8
Number of subjects showing burst suppression/*n*	7/9	2/8	3/11	1/10	6/9	6/8
Percentage	77.8	25.0*	27.3*	10.0**	66.7	75.0
End-tidal isoflurane (%)	2.82 ± 0.02	2.73 ± 0.03	2.43 ± 0.03	2.45 ± 0.04	2.26 ± 0.03	2.27 ± 0.04
End-tidal CO_2 (mmHg)	36.2 ± 1.8	35.7 ± 2.2	37.6 ± 1.5	35.8 ± 1.2	35.9 ± 1.2	36.9 ± 1.4
Mean arterial pressure (mmHg)	44.8 ± 4.3+	56.5 ± 3.6	58.0 ± 4.2	59.5 ± 5.5	61.7 ± 4.5	61.8 ± 3.3

* $P < 0.05$ *vs* groups A,F; ** $P < 0.01$ *vs* group A,F; $P < 0.05$ *vs* group E; + $P < 0.01$ *vs* other groups.

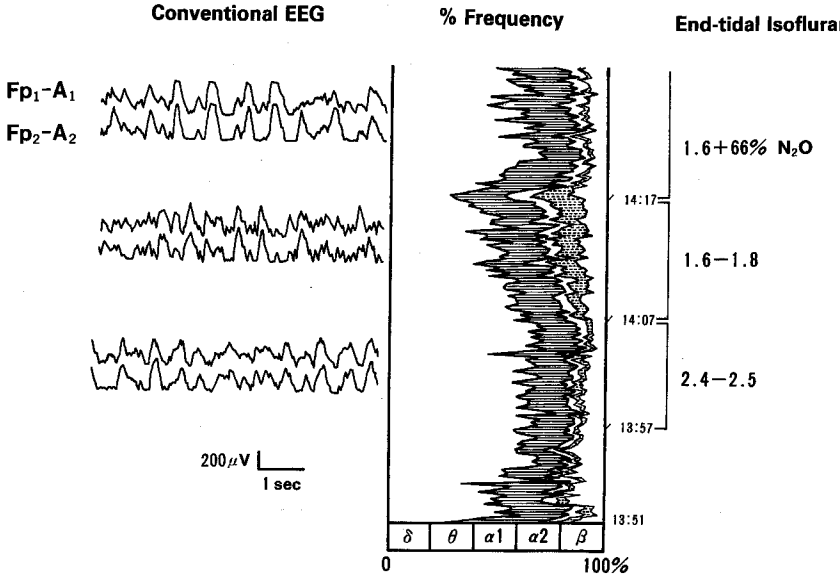

Fig. 2. EEG of a 4-year-old child. There was no electrical silence even during the expiratory isoflurane concentration of 1.5 MAC for 10 min

burst suppression in patients between 6 months and 6 years of age (6 out of 29 cases, 20.7%) was lower than in other patients (19 out of 26 cases, 73.1%) ($P < 0.001$).

Two typical time sequences are illustrated in Figs. 1 and 2; conventional EEGs are shown in the left column, distributions of 5 spectrum EEG in the central column, and anesthetic concentrations in the right column. Figure 1 shows burst suppression once the end-tidal isoflurane level exceeded 1.5 MAC in a 12-year-old patient, while Fig. 2 shows that no occurrence was observed in a 4-year-old patient throughout the whole study period.

EEG at 1.0 MAC

Table 2 shows that at 1.0 MAC none of the 6 groups showed burst suppression but waves of 8–20 Hz were superimposed on high-voltage slow waves. Significant differences in maximum peak-to-peak voltage were noted between groups; the highest value was 427.0 ± 83.5 μV in group D and the lowest was 168.9 ± 54.6 μV in group A ($P < 0.005$).

Amplitude and frequency of superimposed waves showed a tendency to increase with age. Figure 3 depicts typical EEGs at 1 MAC isoflurane in infants under 1 year of age.

EEGs following N_2O supplementation

The amplitude of slow components of EEG increased temporarily in all patients and the amplitude of superimposed waves decreased after supplementation of 66% N_2O (Figs. 1 and 2). Skin incision or peritoneal traction caused reverse arousal in 9 out of 55 patients (16.4%).

Table 2. Comparison of groups A–F at 1.0 MAC end-tidal isoflurane

Age	A 1–6 months	B 6–12 months	C 1–3 years	D 3–6 years	E 6–10 years	F 10–14 years
Number of patients (n)	9	8	11	10	9	8
Number of subjects showing burst suppression/n	0/9	0/8	0/11	0/10	0/9	0/8
Maximum peak-to-peak voltage (μV)	168.9 ± 54.6*	251.3 ± 51.3	303.6 ± 94.3	427.0 ± 83.5*	325.6 ± 72.5	316.3 ± 99.7
Average frequency of superimposed waves (Hz)	8.9 ± 1.9	12.8 ± 1.6	11.6 ± 1.8	11.3 ± 1.6	11.1 ± 1.0	11.4 ± 1.4
End-tidal isoflurane (%)	1.88 ± 0.03	1.79 ± 0.04	1.65 ± 0.03	1.67 ± 0.02	1.53 ± 0.04	1.50 ± 0.03
End-tidal CO_2 (mmHg)	35.4 ± 1.5	36.7 ± 2.3	36.2 ± 1.6	36.8 ± 1.8	35.6 ± 2.5	35.2 ± 1.9
Mean arterial pressure (mmHg)	54.7 ± 4.3	60.6 ± 4.9	62.4 ± 2.5	60.4 ± 5.1	71.3 ± 2.9	65.0 ± 3.6

* $P < 0.05$ *vs* groups.

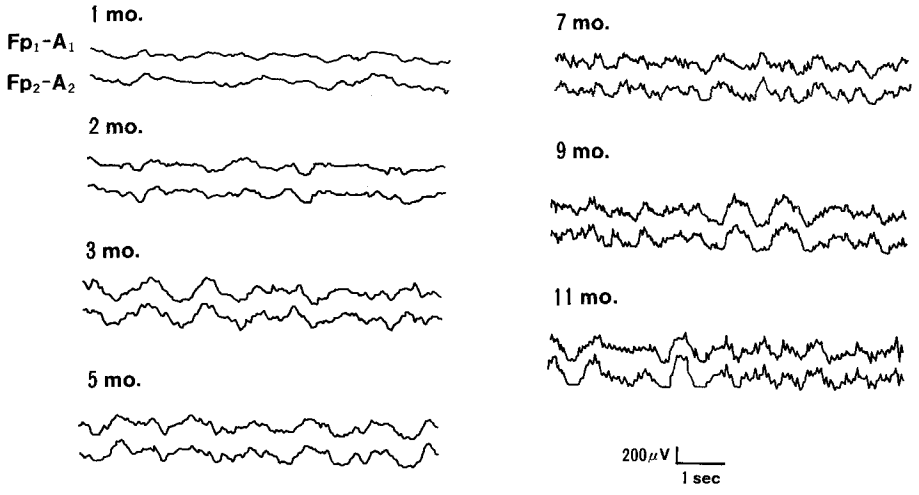

Fig. 3. EEG of infants under 1 year of age at 1.0 MAC end-tidal isoflurane. The amplitude of superimposed waves increased with age in months

Discussion

The present study demonstrated several characteristics in EEG when children received isoflurane anesthesia with and without N_2O. There was a difference in the incidence of burst suppression at 1.5 MAC between age groups. Groups A, E, and F showed higher numbers, but groups B, C, and D showed low incidence. The occurrence in adults was reported to be 50% [2].

We can speculate the following reasons for these differences. Firstly, the metabolic activities of the brain between different age groups varies. A study using a single photon emission computed tomography[6]found that the high cerebral blood flow (CBF) in children 1–5 years of age to be between 90 and 100 ml·100 g^{-1}·min^{-1}. High CBF and metabolic rate has also been reported by Mehta et al. [7] and Kennedy and Sokoloff [8] in children. CBF was reported to decrease abruptly with growth between 5 and 20 years of age [6]. On the other hand, CBF in neonates reported was as low as 40 ml·100 g^{-1}.min^{-1} [9,10]. There have been no investigations on oxygen consumption in neonates. However, animal experiments suggest a lower metabolic rate in neonates than infants [11,12].

Secondly, hemodynamic changes should be considered as a cause of high incidence of burst suppression of EEG in group A. In Table 1, MAP in group A was lower than those in the other groups. However, Hernandez et al. [13] reported that autoregulation of CBF was maintained between 97 and 27 mmHg of mean arterial pressure (MAP) in newborn dogs, but between 150 and 70 mmHg in the adult animals [14]. The MAP of 44.8 mmHg in the present study might not support the hypothesis that declines in CBF caused a high incidence of burst suppression.

Thirdly, the sites of electrodes might have caused the suppression of EEG. Eger et al. [2] used temporal leads in adults, while the authors adopted frontal leads because of the area's predominance of EEG activity under anesthesia [15]. The amplitudes of the EEGs obtained from the frontal, temporal, and occipital regions in children are known to be 2 and 3 times of those in adults [16], disproving the specific changes in the frontal lobe.

EEGs in infants and children showed a wide range of responses to isoflurane anesthesia with and without N_2O. Infants and children between 6 months and 6 years of age showed a low incidence of burst suppression compared to other age groups among infants and children. The mechanism of the above response was not clarified.

In conclusion, the authors found that EEGs in children during isoflurane anesthesia differ greatly with growth. The phenomenon of burst suppression was frequently seen in infants under 6 months and in children over 6 years of age at 1.5 MAC isoflurane.

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