Generalized Seizures Associated with Nitrous Oxide in an Infant

Marcelo Lannes, M.D.,* Joëlle F Desparmet, M.D.,† Benjamin G. Zifkin, M.D., F.R.C.P.C.,‡

Despite evidence showing cerebral excitatory actions of nitrous oxide and the increased motor activity associated with its use,¹ ² ³ ⁴ electroencephalographic (EEG)-documented electrical seizure activity after N₂O administration have been lacking.

We present a case of tonic clonic seizures after exposure to nitrous oxide in oxygen occurring in an otherwise healthy child coming for an elective orthopedic procedure.

Case Report

A 7-month-old, 9.6-kg, girl was admitted for reduction of hip dysplasia during general anesthesia. History was unremarkable; developmental milestones were appropriate for her age, and the family history was negative for epilepsy. Results of the physical examination were normal. Preoperative hemoglobin was 114 g/l.

The infant had been breast fed 6 h before coming to the operating room. After monitoring of heart rate and oxygen saturation was established, the patient was given 50% and then 70% N₂O in oxygen by mask while intravenous cannulation was attempted. The patient was calm, had her eyes open, and was breathing smoothly; SaO₂ was 100%. While the hand was being examined for possible intravenous placement sites, the patient started to seize; first she exhibited quivering of the lips, then eye-rolling, and finally tonic clonic movements, starting at the upper limbs and then generalizing to include the whole body. Inspired oxygen concentration was immediately increased to 100%, and ventilation was assisted by mask.

Just as the patient started to seize, intravenous access was achieved. Blood glucose by chemstrip was between 2 and 4 mmol (36-72 mg/dl). A bolus dose of dextrose in water was given (total dose, 1.75 g) followed by a continuous infusion of 10% dextrose in water at 40 ml/h. Within approximately 1 min, the seizures stopped, and the patient began crying. Oxygen saturation had dropped to the mid-80s when the patient started seizing; but was 100% as soon as the abnormal movements ceased.

The surgical procedure was canceled, and the patient was transferred to the postanesthesia care unit (PACU). She slept for 45 min and was sent to the ward when fully awake. In the PACU, serum glucose and serum electrolytes levels were normal. The neurologic examination and a diagnostic 16-channel EEG done the same day showed no abnormalities. The neurology consultant believed that the most likely diagnoses were either a "convulsive syncope from pain or a generalized seizure secondary to hypoglycemia."

The patient was brought back to the operating room 1 week later for the same procedure. The child was given breast milk 5 h and dextrose in water 2 h before the scheduled time of surgery. No


* Anaesthesia Resident, McGill University.
† Associate Professor of Anaesthesia, McGill University.
‡ Neurologist, EEG Laboratory, Montreal Children’s Hospital and Département des Sciences Neurologiques, Hôpital du Sacré-Cœur de Montréal, Faculty of Medicine, University of Montréal.

Received from the Department of Anaesthesia and EEG Laboratory, Montreal Children’s Hospital, McGill University, Montreal, Canada. Submitted for publication September 27, 1996. Accepted for publication May 19, 1997.

Address reprint requests to Dr. Desparmet: Department of Anaesthesia, Montreal Children’s Hospital, 2300 Tupper Street, Montreal, H3H 1P3, Canada.

CASE REPORTS

Fig. 1. Baseline electroencephalograph before administration of nitrous oxide. Paper speed, 30 mm/s. Time constant was 0.16 s, sensitivity, 10 μV/mm; high and low frequency filters were 70 Hz and 10 Hz, respectively. The electrodes were placed at F3, F4, T3, T4, C3, C4, Cz, P3, P4, O1, and O2 (International 10-20 system).

Premedication was used. In the operating room, usual monitors were applied, and the patient was given 70% nitrous oxide and 1.5% halothane by mask. While an attempt was being made to establish intravenous access, the patient again showed convulsive activity with generalized tonic clonic movements. Inspired oxygen concentration was switched to 100% with halothane at 0.77%. By the time venous cannulation was achieved (30 s later), the seizures had stopped spontaneously. Blood glucose concentration at the time of the seizure was 4.6 mmol/l (85 mg/dl). Dextrose in water (2.5 g) was given intravenously; the trachea was intubated after muscle relaxation with suxamethonium, and the case proceeded uneventfully. Anesthesia was maintained with halothane in oxygen only. The patient was transferred to the ward the next day after a short stay in recovery room and was discharged home the next day.

At this time, the hypothesis for a causative role of nitrous oxide in this child’s seizures was raised. Because the patient was scheduled for a cast change 4 weeks later, it was decided that continuous EEG monitoring would be used.

The patient was admitted from home, having received breast milk 7 h before induction. No premedication was given. The EEG was continuously monitored using a 10-channel Grass model. Routine monitors were applied, and a baseline EEG before induction was recorded (fig. 1). No abnormalities were seen.

Nitrous oxide in oxygen by mask was then started at 20% and increased in a stepwise manner by 10–20% every 5 min while venous cannulation was attempted. At an inspired concentration of 50%, the child stopped crying and was breathing quietly without reacting to the attempts at venous cannulation. Approximately 11 min after the beginning of nitrous oxide and 2 min after the concentration had increased to 70%, the EEG showed high amplitude rhythmic theta activity initially over the temporal region followed by high amplitude alpha and theta rhythmic activity plus lower amplitude beta activity over both hemispheres (fig. 2). The child’s arms were hyperextended, and the eyes deviated upward. The nitrous oxide was immediately discontinued, and 100% oxygen plus 1.2% halothane was given by mask.

The EEG showed high amplitude continuous rhythmic spikes and beta frequency activity, maximum over both anterior regions and both temporal regions, which lasted for approximately 10 s before becoming diffuse. Generalized clonic movements were then observed. The clonic phase lasted approximately 20 s and was followed by a relative flattening of the EEG (fig. 3A) and then by high amplitude delta activity and later by a diffuse beta activity overlying moderate amplitude polymorphous delta activity, which lasted for the remainder of the recording (fig. 3B). The duration of the seizure was approximately 60 s. Spontaneous breathing was assisted with the adequacy of the ventilation being assessed by precordial auscultation and end tidal CO2 tracings. SaO2 was never below 98%.

The case then proceeded uneventfully. The patient had a normal examination in the recovery room and was feeding normally. She was discharged home after a 2 h observation period.

Discussion

The administration of nitrous oxide may increase motor activity with clonus and opisthotonus even in clinically used concentrations.1 When nitrous oxide is used as the sole anesthetic agent in hyperbaric conditions, abdominal muscle rigidity, catatonic movements of extremities, periods of muscular hyperactivity alternating with periods of muscle relaxation, clonus, and opisthotonus have been described.2 Nevertheless, no seizure activity was noted when cerebral electrical activity was monitored. Mice exposed to different concentrations of nitrous oxide in a hyperbaric chamber, even for short durations, exhibited convulsion-like movements (grazing, jerking, forward pointing of the ears) when they were lifted by the tail after removal from nitrous oxide.3,6

Although the administration of N2O is associated with characteristic EEG effects, including a fast oscillatory activity in the frontal areas, no seizure activity has been described.1,3,7 One case has been reported of a 5-year-old boy who developed seizure-like movements on induction of anesthesia, once with nitrous oxide and the other with nitrous oxide and halothane; induction with halothane alone failed to elicit the same reaction.8 EEG was not recorded. Another case report described seizures during induction of anesthesia with nitrous oxide and isoflurane. The epileptiform nature of the abnormal movements was documented by EEG monitoring, although the seizures were attributed to isoflurane.9

The patient described in the present report had three episodes of seizures, all of them when exposed to ni-
trous oxide. Hypoglycemia was thought initially to be the etiology because of the results of the first blood glucose, but this seemed less likely after the second episode when seizures occurred despite the administration of dextrose in water 2 h before induction and the normal blood glucose level. Based on the \( \text{SpO}_2 \) monitoring, the ease of ventilation and the \( \text{ETCO}_2 \) readings (always above 30), it would appear that neither hypoxemia nor hypocapnia played a role in triggering the seizures.

In summary, we present a case of seizures associated with nitrous oxide use in a healthy infant. No other factors could be significantly implicated in the production of this child’s seizures.

**Fig. 3.**A. Electroencephalographic tracing at the end of the seizure shortly before cessation of motor activity. B. Post-ictal tracing. Patient receiving halothane and oxygen.

Anesthesiology, V 87, No 3, Sep 1997
References


