LETTER TO THE EDITOR

NON-KETOTIC HYPERGLYCINAEMIAS

SIR:

We would like to report the recent use of halothane and fentanyl in a patient with non-ketotic hyperglycinaemia.

A white female infant approximately 58 hours old, birth weight 3100 grams, 40 weeks gestation, was admitted to our hospital with progressive unconsciousness and respiratory depression. Her mother was a 26-year-old white female primigravida who had a history of grand mal epilepsy and had been taking phenobarbitone 120 mg/day and phenytoin sodium 40 mg/day for many years. Approximately eight weeks before delivery the dose of these drugs was increased to 180 mg/day and 500 mg/day respectively for a severe attack of seizures. She had a normal spontaneous vaginal delivery at 40 weeks' gestation with the baby presenting as vertex ROA. The baby had good Apgar scores at birth (8 at one minute and 9 at five minutes). At approximately 12 hours of age, however, it was noticed that she had shallow respirations, was unresponsive and without a gag reflex. Her trachea was intubated and she was placed on a respirator and transferred to the University Hospital. A detailed diagnostic survey at our hospital revealed that she had non-ketotic hyperglycinaemia with elevated glycine levels in plasma and urine. She was weaned off the respirator, but remained comatose.

As a part of a discharge plan, it was decided that she have a gastrostomy to aid in feeding. A preoperative evaluation revealed that the child had satisfactory spontaneous respiration and responded with a shrill cry and generalized jerking movements to painful stimuli. She also had rather tense abdominal muscles. The muscle tension in her abdomen was unevenly distributed. Therefore, it was decided to use general anaesthesia. We could not find any previous reports of the use of general anaesthesia in patients with non-ketotic hyperglycinaemia. We found one report[1] where a ventricular shunt was placed, but the type of anaesthesia and anaesthetic management were not discussed. Non-ketotic hyperglycinaemia is an inborn error of metabolism resulting from a defect in the glycine cleavage enzyme system.[2] It is characterized biochemically by elevation of glycine in the blood, urine and cerebrospinal fluid.[2] Neurological deterioration is most probably the result of excess glycine, which functions as an inhibitory neuro-transmitter.[3]

With the above information, we arrived at the following conclusions:

(a) One of the normal uses of glycine in the body is in the synthesis of protoporphyrinogen and heme.[4] We were not sure whether the use of thiopentone in hyperglycine states would facilitate the conversion of glycine to the porphyrias or porphyrinurias.[5] Also, because she was already comatose, recovery from thiopentone would probably be delayed. So we decided not to use thiopentone.

(b) We felt that the abdominal muscle rigidity present in certain areas was related to excessive activity of some neuronal sites that were free of the effects of glycine. Therefore, it probably would be safe to use muscle relaxants, if necessary, and her muscles should relax with satisfactory levels of inhalational agents.

(c) It probably would be safe to use ketamine and fentanyl, but these agents would not provide the desired muscle relaxation.

(d) We concluded that halothane or enflurane and nitrous oxide could be used, because these agents would provide satisfactory anaesthesia and adequate muscle relaxation for gastrostomy. Furthermore, rapid elimination could be achieved through the lungs at the end of the operation.

The patient had nothing by mouth for six hours before the operation and was given intramuscular atropine 0.02 $mg \cdot kg^{-1}$ 30 minutes before induction. Anaesthesia was induced with a 70:30 nitrous oxide and oxygen mixture with one per cent halothane. Orotracheal intubation was successful; even without muscle relaxants it was not difficult. Anaesthesia was maintained with 60:40 nitrous oxide and oxygen mixture and 1.5–1.75 per cent halothane. Vital signs were stable during operation and there was adequate muscle relaxation for the gastrostomy. The operation lasted 45 minutes and the total anaesthetic time was one hour 15 minutes. She had spontaneous respiration at the end of the procedure and the trachea was extubated without complications. When she returned to the ward, she expressed pain by

means of a shrieky cry, for which she was given one intramuscular dose of fentanyl 20 $\mu g \cdot kg^{-1}$. She responded to this very nicely without depression of respiration or change in vital signs. She was discharged 48 hours later on a regular feeding schedule.

We think the above information will be of use to all anaesthesiologists.

K.A. Sami, M.D.
Assistant Professor
Director of Clinical Services
Department of Anesthesiology
Medical School
C596 Mayo Memorial Building, Box 294
420 Delaware Street S.E.
Minneapolis, Minnesota 55455

REFERENCES

1. KRIEGER, INGEBORG, EDWARD S. WINBAUM & ARTHUR B. EISENBREY. Cerebrospinal fluid glycine in non-ketotic hyperglycinemia. Effect of treatment with sodium benzoate and a ventricular shunt. *Metabolism 26*(5): 517–524 (1977).
2. ARNESON, DORA, LAWRENCE T. CHIEN, PHILIP CLANCE & R. SIDNEY WILROY. Strychnine therapy in non-ketotic hyperglycinemia. *Pediatrics 63*(3): 369–373 (1979).
3. APRISON, M.H., R.A. DAVIDOFF & R. WERMAN. Glycine: its metabolic and possible transmitter roles in nervous tissue. Handbook of Neurochemistry *3*: 381 (1970).
4. WALDENSTROM, JAN G.: Erythrocyte disorders – diseases related to abnormal heme or porphrin metabolism. Hematology, McGraw-Hill Book Company, 451–9 (1972).
5. DUNDEE, JOHN W., W.N.C. MCCLEERY & GEORGE MCLOUGHLIN. The hazard of thiopental anesthesia in porphyria. Anesthesia and Analgesia, *41*(5): 567 (September, October, 1962).