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IV Nembutal: Safe Sedation for Children Undergoing CT

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In a prospective study of 225 consecutive pediatric patients who required sedation for CT imaging, we monitored oral and nasal air flow, transcutaneous oxygen saturation, and cardiac rate and rhythm before and after the administration of IV Nembutal. In addition, the first 50 patients in this series had blood pressures mechanically monitored at 1-min intervals. There was no significant change in the cardiac rate, rhythm, or blood pressure in any patient. Seventeen episodes (7.5%) of transient oxygen desaturation to 80% of baseline or less occurred after sedation. The patterns of oxygen desaturation in this series can be explained by the following mechanisms: (1) hyperventilation leading to hypocapnia with resultant loss of the CO_2 stimulus of respiration (12 patients); (2) upper airway obstruction from pharyngeal muscle relaxation (three patients); (3) a shift in sensitivity of CNS CO_2 receptors (one patient); and (4) central apnea (one patient). Oxygen desaturation normalized spontaneously in 14 patients. In two patients, oxygen saturations returned to normal after modification of head position to optimize airway patency. In one patient, mild stimulation was required to interrupt transient apnea. All but one patient in whom desaturation occurred showed oxygen desaturation within the first 5 min after IV sedation.

At The Children's Hospital of Denver, IV Nembutal has been used in over 870 pediatric patients. No patient required resuscitation, intubation, or assisted ventilation. Only one patient required prolonged observation, and one patient demonstrated an idiosyncratic hyperactive response. The sedation failure rate was less than 1%. The average dose of sedation was reduced when compared with IM Nembutal because the rapid onset of activity after IV administration allowed titration of dose to patient response.

Some form of sedation is frequently required in pediatric imaging [1–3]. Nembutal, a short-acting barbiturate, has been recommended for sedation by numerous researchers [4, 5]. The clinical safety, effectiveness, and efficiency of IV administration of Nembutal have been documented previously [6]. Hesitancy on the part of some radiologists to use IV Nembutal sedation reflects a concern about its potential side effects, which include respiratory and cardiac depression. No direct antagonist to Nembutal exists, and, historically, IV sedation has not been commonly used by diagnostic radiologists.

This study was undertaken to evaluate the frequency and extent of potential cardiac and respiratory side effects associated with IV Nembutal sedation in pediatric patients who require sedation for CT.

Materials and Methods

IV Nembutal was used in 225 consecutive pediatric patients who required sedation for CT. Each patient was evaluated for the cardiac and respiratory side effects of Nembutal sedation. Sedation was administered by one of four pediatric radiologists. Each patient received a dose of 2–6 mg/kg IV Nembutal in the following prescribed manner (Fig. 1) [6]. A total dose of 5 mg/kg is loaded into a syringe. One half of the dose (2.5 mg/kg) is administered over approximately 30 sec. The patient is observed for disconjugate eye movement, a yawn, quiet sleep, or a slowed respiratory rate. If the patient remains active for 30 sec after the injection

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BEGIN WITH TOTAL DOSE OF 5 MG/KG NEMBUTAL
ADMINISTER ½ TOTAL DOSE
OBSERVE 30 SECONDS
ADMINISTER ½ OF THE REMAINING DOSE
OBSERVE 30 SECONDS
ADMINISTER REMAINDER OF DOSE IF NECESSARY
OBSERVE

Fig. 1.—Methods of IV Nembutal sedation.

a second dose of one half the remaining Nembutal is administered (1.25 mg/kg). The remaining dose (1.25 mg/kg) may be required if the patient does not quiet over the next 30–60 sec. Occasionally, 5 mg/kg is insufficient and an additional dose of 1 mg/kg may be administered, for a total dose of 6 mg/kg. If adequate sedation is not achieved no further drug is administered and the CT examination is terminated. If the patient awakens during the examination a repeat dose of half the original dose up to 3 mg/kg may be given in a manner similar to that described above after 30 min. Although IV Nembutal was used in the retarded adults who required sedation for CT, patients older than 16 years of age were excluded from this study.

All scans were performed on a Philips 310/350 Tomoscan unit with a scan time of 4.8 and 9.6 sec. Cardiac and respiratory rates were monitored with a Hewlett Packard 78801A neonatal monitor. Transcutaneous oxygen saturation was measured with either a Nellcor pulse oximeter or an Ohmeda 3700 pulse oximeter. A breath monitor designed with a thermistor intended to detect the difference in temperature between exhaled breath and ambient air was coupled to an oscilloscope and used to identify nasal and oral air flow. This was correlated with chest wall motion output from the Hewlett Packard monitor to help differentiate oxygen desaturation due to upper airway obstruction from desaturation caused by apnea. In the first 50 patients, a Dinamap pressure monitor mechanically registered blood pressures at 1-min intervals. The patients were also visually monitored by the CT technologists throughout the examination. All patients in whom sedation was contemplated were not given anything to eat or drink for 3 hr before the CT examination. All sedated patients were identified with a fluoroscent sticker placed on their outer clothing to facilitate the recognition of sedated patients by other hospital personnel. After the examination, patients were observed by their parents or guardians in the radiology waiting room until their level of consciousness was such that they could be safely discharged.

Results

The age distribution of those patients requiring sedation was similar to that of our earlier study [6]. In the present series, 25% of patients 6 weeks to 6 months of age, 30% of patients 6 months to 1 year of age, and 30% of patients 1 year to 3 years of age required sedation. Overall, 10% of all patients required sedation.

The dose of IV Nembutal ranged from 2–6.1 mg/kg (mean dose, 4.5 mg/kg). Two patients required additional sedation when they awakened after the painful stimulation of IV contrast administration. There were two sedation failures. There was no change in blood pressure in any of the patients evaluated. No cardiac arrhythmia or significant change in cardiac rate was observed.

TABLE 1: Etiology and Treatment of Oxygen Desaturation After IV Nembutal Sedation in 17 of 225 Patients

Etiology	No. of Cases	Characteristics	Treatment
Hyperventilation	12 (5%)	Early desaturation with rapid spontaneous recovery	None
Upper airway obstruction	3 (1.5%)	Noisy breathing, snoring	Alter head position
Altered CO_2 sensitivity	1 (0.5%)	Stabilized decrease in respiratory rate	None Nasal O_2
Central apnea	1 (0.5%)	Prolonged apnea, greater than 2 min	Mild stimulation

Oxygen desaturation to 80% of baseline or less occurred 17 times. The frequency and probable cause of oxygen desaturation are listed in Table 1. In 12 patients, the pattern of desaturation was similar. Transient oxygen desaturation occurred within the first 1–2 min after IV sedation and rapidly normalized spontaneously in the following 30–90 sec.

In three patients, desaturation was due to airway obstruction. This was recognized by audible snoring or noisy breathing and by decreased amplitude of the thermistor-measured air flow without change in the respiratory rate. In one patient, the episode resolved spontaneously. In two patients, oxygen saturation normalized when the head position was altered by turning the head to one side in order to reduce the effects of gravity, which contribute to airway collapse and obstruction when the tongue and hypopharyngeal muscles relax. This change in position helps to optimize airway patency.

The desaturation in one patient was accompanied by a more prolonged decrease in respiratory rate. The O_2 saturation stabilized at 75% with a drop in respiratory rate from a baseline of 30 breaths per minute to a respiratory rate of 15. The patient was audibly snoring but in no apparent distress. Following the 7-min examination, the patient's head was turned to the side and saturation immediately returned to 85%. A combination of partial airway obstruction and a decrease in CO_2 sensitivity caused by Nembutal was likely responsible for the desaturation in this case.

The final patient in whom oxygen desaturation was documented demonstrated a slowed respiratory rate with periods of apnea and intermittent sobbing and sighing. This is the only patient in whom cyanosis was visibly detectable. A nadir in O_2 saturation of 50% occurred at 5 min. Following mild stimulation, the patient began to cry and her oxygen saturation immediately began to normalize. Within 5 min, the patient's oxygen saturation was above 85% and remained so throughout and following the examination. There were no apparent adverse sequelae to the brief apneic period. This was the only patient in whom desaturation was clinically evident.

None of the sedated patients required resuscitation, assisted ventilation, or intubation. The increase in sensitivity to small and transient changes in oxygen saturation that can be identified with pulse oximetry allowed the recognition of subtle

saturation changes caused by Nembutal that would otherwise have been clinically undetectable.

The frequency, extent, and etiology of oxygen desaturation did not correlate with Nembutal dose, although the one patient in whom apnea resulted in cyanosis received 6.1 mg/kg. Three of the patients desaturated with doses of 2.5 mg/kg or less. The mean dose of those who desaturated was 3.4 mg/kg. The mean dose used in the series of 225 patients was 4.5 mg/kg. The variation in desaturation with age was not statistically significant. Although the length of time from IV administration of Nembutal to the lowest level of oxygen saturation observed in each patient was variable, all but one patient in whom significant desaturation occurred demonstrated a drop in O_2 saturation within the first 5 min after sedation. The one patient in whom desaturation was delayed normalized oxygen saturation spontaneously without intervention.

Discussion

We have now used IV pentobarbital sodium (Nembutal) sedation in a dose of 2–6 mg/kg in over 870 patients. We have had no complications from sedation. One patient exhibited a hyperactive response to this medication. None of the patients sedated have required resuscitation, assisted ventilation, or intubation. The mean interval from the time of sedation to discharge was 55 min, with only one patient requiring observation for longer than 2.5 hr. This patient was a mentally retarded male with mandibular hypoplasia, a mandibular fracture with osteomyelitis, parotid inflammation, and a retropharyngeal abscess. He had been hospitalized previously for apnea and airway obstruction. Oxygen desaturation after sedation normalized immediately by adjusting the head position to optimize airway patency. He was admitted to the pediatric ICU after the CT examination and was observed for 4 hr awaiting drainage of his abscess. At The Children's Hospital of Denver, the patient population is almost exclusively pediatric. Occasionally, however, retarded adults are imaged and they frequently require sedation. Although IV Nembutal is successfully used in these patients, patients older than 16 years of age were excluded from this pediatric study. In this prospective study, we found no cardiovascular change in either pulse, rhythm, or blood pressure. This is in agreement with others, who have noted few cardiovascular effects with barbiturates in hypnotic doses [7–10]. In hypnotic doses, the respiratory depression caused by barbiturates is similar to that of normal sleep [11–13]. Significant oxygen desaturation, defined as a drop in O_2 saturation to 80% of baseline or less, occurred 17 times after IV Nembutal sedation in 225 consecutive patients (7.5%) in whom sedation was required for CT examination.

Physiologic causes of desaturation to 80% have been described and are not uncommon. In fact, prolonged periods of oxygen saturations as low as 70% can be seen with lobar pneumonia [14]. While it is true that normal, awake individuals usually maintain a stable oxygen saturation of approximately 95%, it is not unusual to measure 15–20% saturation changes after hyperventilation, sighing, and sobbing, even in the nonsedated patient.

There appear to be at least four distinct mechanisms of oxygen desaturation after Nembutal sedation. These may occur individually or in combination. The most benign and readily reversible can be attributed to a short-term direct effect of barbiturates on the respiratory center coinciding with a low arterial pCO_2 caused by hyperventilation associated with crying. In the adult, drops in O_2 saturation accompanying apnea after hyperventilation can be seen; however, the degree of desaturation is compounded in children for two reasons: (1) the ratio of vital capacity to total lung capacity is greater in the child than in the adult; the hyperventilation associated with crying exaggerates the elimination of CO_2 seen with hyperventilation; and (2) the residual volume is much smaller in children than in adults and, as a result, the residual O_2 capacity of the lung is less. Because respiratory drive is CO_2 sensitive and relatively O_2 insensitive when oxygen saturations are above 75%, it is not unusual to see relatively large drops in oxygen saturation after hyperventilation in the pediatric patient. This appears to have been the mechanism of desaturation in 12 of the 17 patients in whom desaturation occurred. The pattern of desaturation was characteristic. In 1–2 min after sedation, as the patient calmed from crying during the venipuncture, the patient might yawn or sigh, the respiratory rate would slow, and oxygen saturation would drop. The desaturation then rapidly and spontaneously normalized over the next 30–90 sec. This appears to be an exaggerated response to hyperventilation, and an effect similar to that described after IV Pentothal administration, in which a brief period of apnea is followed by a return to normal breathing when the pCO_2 returns to normal [8, 15].

The second mechanism of desaturation relates to relaxation of the pharyngeal musculature with resultant airway obstruction. Patency of the oropharyngeal and hypopharyngeal airway is maintained by active tone of the tongue and pharyngeal musculature [16]. Muscle relaxation after sedation results in collapse of the airway and contributes to airway obstruction. By turning the head to the side, one diminishes the effects of gravity on the collapse of the upper airway and thus optimizes airway patency. Studies with ethanol and barbiturates have shown an incremental sensitivity to sedation in which pharyngeal musculature is more sensitive to sedation than either central respiratory centers or the phrenic nerve. Collapse of the pharyngeal and hypopharyngeal airway due to muscle relaxation results in obstruction. This, in combination with direct sedative effect on the respiratory musculature involved with breathing, causes a fall in the minute ventilation and subsequent hypoxia and hypercarbia [17, 18]. Desaturation on this basis occurred in three patients and was readily reversible with modification of head position. In one patient the desaturation corrected immediately by turning the head to one side. To prove that obstruction rather than stimulation was responsible for the recovery, the head was then turned to the original position and desaturation recurred. This was again normalized by turning the head and optimizing airway patency. Since the airway reflexes remain intact, even with relatively high doses of Nembutal, the maintenance of airway

patency with postural change or jaw thrust is probably preferable to placement of an oral or nasal airway, which is more apt to cause choking or laryngospasm.

The third mechanism of desaturation relates to a shift of CO_2 sensitivity. Barbiturates are nonselective CNS depressants; however, different structures in the brain demonstrate varying sensitivities to a given dose. The cerebral cortex and vestibular activating systems are the most sensitive. The medullary system is less sensitive, and direct effect on the circulatory and respiratory centers requires high concentrations of sedative [8]. Barbiturates shift the CO_2 sensitivity of CNS receptors and allow for an increase in the pCO_2 with concomitant decrease in O_2 saturation. Respiratory response to hypoxia is not appreciable until oxygen saturation drops below 50 ml of mercury, although there is interaction between the CO_2 and O_2 receptors at higher saturations. Thus, a barbiturate-induced decrease in sensitivity to CO_2 allows a steady-state decrease in oxygen saturation that is below normal but above that needed to induce the hypoxic respiratory drive. Additionally, both the hypoxic drive of ventilation and augmentation of the hypoxic drive due to hypercapnia are blunted by barbiturates [19]. The change in CNS CO_2 receptor sensitivity appears to have contributed to the desaturation in one patient in this series. In this patient, respiratory rate decreased from 30 breaths per minute to 15 breaths per minute, and O_2 saturations stabilized at 75%. Partial upper airway obstruction was also involved, because saturation improved from 75% to 85% immediately with change in head position after the examination.

The fourth cause of oxygen desaturation is probably related to a generalized CNS depression caused by Nembutal. This is certainly one of the most serious side effects of sedation. In the one patient who became apneic and cyanotic, this appeared to be the primary mechanism of desaturation. The hyperesthesia caused by Nembutal is advantageous when central apnea occurs. Only minimal painful stimulation is required to produce adequate agitation to reverse the apneic spell and restore the normal breathing pattern.

Although we have encountered no serious sedation-related complications in over 870 patients sedated with IV Nembutal, any effective form of sedation should be approached with caution. Nembutal carries the uncommon but serious risks of cardiac and respiratory depression as well as laryngospasm. No patient in our series has required resuscitation, ventilation, or intubation; however, we recommend that appropriate resuscitation equipment be easily accessible in the CT laboratory. Furthermore, we recommend that anyone responsible for sedation of any kind have the ability to resuscitate and maintain adequate cardiac and respiratory support. The cardiovascular effects of Nembutal are minimal at doses used for sedation. Most complications with IV Nembutal have followed dosages higher than those used for sedation when barbiturates were used as the sole pharmaceutical for anesthesia [8].

Nembutal is an effective sedative for CT imaging. Its hypnotic action is ideal, particularly when analgesia is not required. The advantages of IV administration result from its rapid onset of activity and the ability to reliably obtain adequate blood levels for sedation. Blood levels of Nembutal after IM or rectal administration are grossly unpredictable, and the delay in onset of sedation is a serious drawback [20, 21]. Fewer patients require sedation when the need for sedation can be individually evaluated while maintaining adequate CT throughput. With IV sedation, the sedative dose can be titrated to the patient's response. There has been an overall decrease in the average sedation dose after IV Nembutal when compared with IM injection. The immediate onset of sedation after IV administration of Nembutal is advantageous in that the radiologist responsible for sedation is most actively involved with the patient at the time when the patient is at greatest risk for the complications of sedation.

The pharmacokinetics of Nembutal allows approximately 60 min of sedation reflecting the alpha distribution phase of activity. The beta elimination phase is prolonged but of little clinical significance except in patients on long-term therapy [8]. Since Nembutal is bound to plasma albumin, dosage should be adjusted when sedating patients on chronic barbiturate therapy. Milligram per kilogram dosages in older patients can frequently be considerably less than those required for infants and young children. A total dose greater than 100 mg is rarely required. Barbiturates are contraindicated in patients with porphyria, a rare disease in the United States.

We have had no serious complications in over 870 patients sedated with IV Nembutal. No patients have required resuscitation, ventilation, or intubation. One patient demonstrated a paradoxical hyperactive response, an unusual idiosyncratic reaction.

In summary, there were no significant changes in cardiac rate, rhythm, or blood pressure after sedation with IV Nembutal. Significant oxygen desaturation occurred 17 times in 225 examinations (7.5%). In all but one of the patients, the desaturation occurred within the first 5 min after IV sedation. Fourteen of the 17 patients in whom significant oxygen desaturation was observed recovered spontaneously. In two, recovery was augmented by modifying the head position to optimize airway patency. One patient's O_2 saturation normalized after mild stimulation. IV Nembutal is a safe, effective, and efficient form of sedation for pediatric CT imaging.

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REFERENCES

1. Anderson RE, Osborn AG. Efficacy of simple sedation for pediatric computed tomography. *Radiology* **1977**;124:739–740
2. Mitchell AA, Louik C, Lacouture P, Slone D, Goldman P, Shapiro S. Risks to children from computed tomographic scan premedication. *JAMA* **1982**;247:2385–2388
3. Varner PD, Ebert JP, McKay RD, Nail CS, Whitlock TM. Methohexital sedation of children undergoing CT scan. *Anesth Analg* **1985**;64:643–645
4. Heinz RE. Techniques in imaging of the brain part 11: premedication and sedation. In: Rosenberg RN, ed. *The clinical neurosciences neuroradiol-*

ogy. New York: Churchill Livingstone, **1984**:204–206
5. Fitz CR, Rad K. Primary tumors in children. In: Lee SH, Rao K, eds. *Cranial computed tomography*. New York: McGraw-Hill, **1983**:295–297
6. Strain JD, Harvey LA, Foley LC, Campbell JB. Intravenously administered pentobarbital sodium for sedation in pediatric CT. *Radiology* **1986**;161:105–108
7. Elliott HW, Fisher CW, de Lappe A, Davis K. Botnik E. Propiomazine, pentobarbital, hydroxyzine, and placebo: double-blind comparison of sedation effects. *Anesthesiology* **1969**;31:233–236
8. Smith SE. Intravenous anaesthesia. In: Churchill-Davidson HC, ed. *A practice of anaesthesia*, 5th ed. Chicago: Year Book Medical, **1984**: 626–639
9. Smith SE. Sedative and hypnotic drugs. In: Churchill-Davidson HC, ed. *A practice of anaesthesia*, 5th ed. Chicago: Year Book Medical, **1984**: 642–645
10. Andersen TW, Gravenstein JS. Cardiovascular effects of sedative doses of pentobarbital and hydroxyzine. *Anesthesiology* **1966**;27:272–278
11. Richter JA, Holtman JR Jr. Barbiturates: their in vivo effects and potential biochemical mechanisms. *Prog Neurobiol* **1982**;18:275–319
12. Harvey SC. Hypnotics and sedatives. In: Gilman AC, Goodman LS, eds. *The pharmacological basis of therapeutics*, 6th ed. New York: Macmillan, **1980**:339–363
13. *Physicians desk reference*, 40th ed. Oradell, N.J.: Medical Economics, **1986**:533–535
14. Youmans WB, Siebens AA. Respiration. In: Brobeck JR, ed. *Best and Taylor's physiological basis of medical practice*, 9th ed. Baltimore: Williams & Wilkins, **1973**:6-41–6-62
15. Hugelin A. Mechanisms of respiratory control during sleep and wakefulness: implications in newborn sleep apnea. *Kyoto Symposia* **1982**;36: 625–630
16. Remmers JE. Obstructive sleep apnea: a common disorder exacerbated by alcohol. *Am Rev Respir Dis* **1984**;130:153–155
17. Bonora M, Shields GI, Knuth SL, Bartlett D Jr, St John WM. Selective depression by ethanol of upper airway respiratory motor activity in cats. *Am Rev Respir Dis* **1984**;130:156–161
18. Hwang JC, St John WM, Bartlett D Jr. Respiratory-related hypoglossal activity: influence of anesthetics. *J Appl Physiol* **1983**;55(3):785–792
19. Hirshman CA, McCullough RE, Cohen PJ, Weil JV. Hypoxic ventilatory drive in dogs during thiopental, ketamine, or pentobarbital anesthesia. *Anesthesiology* **1975**;43(6):628–634
20. Kanto J, Iisalo E, Kangas L, Valovirta E. A comparative study on the clinical effects of rectal diazepam and pentobarbital on small children. Relationship between plasma level and effect. *Int J Clin Pharmacol Ther Toxicol* **1980**;18(8):348–351
21. Gregory GA. Pharmacology. In: Gregory GA, ed. *Pediatric anesthesia*. New York: Churchill Livingstone, **1983**:315–333