Hyperventilation Studies During Nitrous Oxide-Narcotic-Relaxant Anesthesia

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DELIBERATE passive hyperventilation has been used as an adjuvant to anesthesia to assure adequate ventilation, to reduce the amount of anesthetic agent or muscle relaxant required,[1, 2, 3] or to produce apnea and a quiescent operative field with minimal anesthesia.

Various objections to hyperventilation have been raised. Hypocapnia as a possible cause of hypotension and shock was promulgated by Henderson years ago[4] and subsequently refuted by Seevers.[5] Studies by Burnum and associates[6] in unanesthetized man again suggested hypocapnia as a cause of hypotension. Others have pointed to potentially adverse effects on the central nervous system because of cerebral vasoconstriction and possible cerebral hypoxia. Most of the data supporting this view have been obtained from conscious volunteers,[7, 8] but suggestive material has been secured in anesthetized dogs[9] and man.[10]

Metabolic disturbances also have been attributed to hyperventilation. Here again, most of the data have been gathered from unanesthetized man. Acute hyperventilation in awake volunteers has produced hypokalemia,[11] lowered inorganic phosphate, and increased urinary excretion of sodium and potassium.[12, 13] Prolonged passive hyperventilation of awake subjects resulted in metabolic acidosis.[14] Papadopoulos and Keats[15] observed a slight metabolic acidosis in patients maintained in respiratory alkalosis during barbiturate-nitrous oxide-oxygen-relaxant or cyclopropane-oxygen-relaxant anesthesia. Virtually no metabolic changes were reported by Robinson[16] in patients less actively hyperventilated during similar anesthesia. Finally, prolonged apnea following hyperventilation has been the concern of some anesthesiologists.[17]

To evaluate the possible effects of the modest hyperventilation frequently practiced, it is desirable to have more studies on the effects of prolonged passive hyperventilation as background information. A series of such studies has been undertaken in this clinic to assess the response to and recovery from this maneuver during different types of general anesthesia. As a corollary, control studies in which arterial P_{CO_2} was maintained at normal levels during otherwise similar anesthesia have been performed to better compare the effects of hyperventilation.

The purpose of the present study was to obtain data from patients anesthetized with a nitrous oxide-narcotic-relaxant technique with and without passive hyperventilation.

Methods

Patients ranged in age from 20 to 60 years and had no evidence of pulmonary dysfunction. Most patients were given premedication consisting of pentobarbital, 50–100 mg. intramuscularly, and atropine or scopolamine, 0.4–0.6 mg. one to one and one half hours before anesthesia. Some patients received meperidine, 50–100 mg. Anesthesia was induced with thiopental followed by succinylcholine, oxygenation, and endotracheal intubation. Eighty per cent nitrous oxide and 20 per cent oxygen were delivered from a demand nitrous-oxide-oxygen machine (manufactured by Anesthesia Equipment Ltd.). Its delivered concentration was within ± 1 volume per cent (v/v) of calibrated concentration as measured with a Pauling oxygen analyzer. The gases were introduced into a modified non-rebreathing head of the Jefferson ventilator.

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TABLE 1. Mean Changes and Standard Deviations in Arterial Blood Constituents During and After Anesthesia With and Without Hyperventilation

		Control	15 Minutes	2 Hours	End Anesth.	First Breath	15 Minutes	1 Hour	2 Hours
*p*H	H	7.41 ± .02	7.66 ± .05	7.63 ± .05	7.63 ± .05	7.49 ± .07	7.58 ± .03	7.56 ± .01	7.55 ± .04
	N	7.39 ± .02	7.38 ± .08	7.37 ± .02	7.38 ± .03	7.35 ± .05	7.32 ± .01	7.31 ± .01	7.33 ± .02
P_{CO_2} mm. Hg	H	37 ± 2.9	17 ± 2.6	15 ± 2.8	15 ± 2.8	26 ± 6.9	37 ± 6.2	38 ± 5.4	38 ± 5.7
	N	35 ± 1.2	36 ± 0.5	35 ± 3.9	34 ± 5.6	38 ± 8.8	41 ± 3.2	39 ± 3.7	40 ± 1.6
O_2 Sat. %	H	91 ± 3		94 ± 1.8	98 ± 1	95 ± 4.7	80 ± 11.3	91 ± 6.1	92 ± 4.6
	N	93 ± 2.8		97 ± 2.1	97 ± 1.2	97 ± 1.7	87 ± 4	91 ± 4.7	91 ± 3.3
HCO_3 mEq. liter	H	25 ± 2.3	20 ± 1.7	17 ± 2.1	17 ± 1.7	21 ± 3.8	22 ± 3.6	22 ± 2.8	21 ± 3.2
	N	23 ± 1.4	22 ± 1.6	21 ± 2	21 ± 1.6	22 ± 2.5	22 ± 1.8	21 ± 1.8	21 ± 1.5
BB	H	47 ± 2.2	46 ± 1.6	45 ± 1.7	45 ± 1.2	45 ± 3.2	44 ± 3.2	44 ± 2.6	43 ± 2.6
	N	45 ± 1.9	44 ± 2.1	44 ± 1.4	44 ± 1.1	44 ± 1.1	44 ± 1.2	43 ± 1.1	43 ± 1
Lactic Acid mEq. liter	H	2.6 ± .88	1 min. 3.8 ± .86	1.6 ± .91	1.5 ± 1.25			2.9 ± .05	3.6 ± 1.25
	N	2.7 ± .6	2.3 ± .6	2.3 ± .57	2.5 ± .73			3.1 ± 1.1	3.1 ± 1.1
Sodium mEq. liter	H	135 ± 9	135 ± 7.3	135 ± 7.0	138 ± 6.5			132 ± 2.0	131 ± 4.6
	N	141 ± 2.3	138 ± 3.2	138 ± 1.5	140 ± 1.9			139 ± 3.3	136 ± 1.1
Potassium mEq. liter	H	4.2 ± .21	4.2 ± .38	4.0 ± .17	3.9 ± .17			4.0 ± .52	4.0 ± .51
	N	4.1 ± .24	4.1 ± .31	4.1 ± .21	4.1 ± .26			4.1 ± .24	4.0 ± .28
Calcium mEq. liter	H	5.0 ± .6	5.5 ± .67	5.4 ± .6	5.3 ± .52			5.2 ± .63	5.4 ± .73
	N	5.6 ± .38	5.4 ± .75	5.2 ± .71	5.2 ± .61			5.3 ± .61	5.4 ± .42

H Hyperventilated patients
N Nonhyperventilated patients

Hyperventilation was accomplished by using controlled respiration at rates of 30–40 strokes per minute and tidal volumes of 500–700 ml., using positive pressures of 10–30 cm. of water. Five to 10 cm. of water negative pressure was used. An attempt was made to reach and maintain a low Pa_{CO_2} of at least 15 mm. of mercury. Meperidine (100–350 mg.) and *d*-tubocurare (30–57 mg.) were used in divided doses as necessary to provide analgesia and muscle relaxation, respectively.

At the termination of anesthesia, patients received 100 per cent oxygen for approximately five minutes. The ventilator was then stopped and the patient allowed to resume spontaneous respiration. If patients remained apneic for five to eight minutes, they were ventilated intermittently with oxygen even though it might further lengthen the time to spontaneous respiration. Edrophonium (10–40 mg.) and levallorphan (1–3 mg.) were given as necessary during the immediate postanesthetic period to counteract curare and meperidine, respectively.

A styletted needle was placed in the brachial artery prior to anesthesia and samples of blood were drawn anaerobically at various intervals during, and up to two hours following, anesthesia and hyperventilation. Whole blood *p*H and P_{CO_2} were determined within five minutes using a Beckman *p*H electrode and a Severinghaus P_{CO_2} electrode mounted in a constant temperature water bath at 37° C. An electrometer amplifier was used to read the determinations.[18] Oxygen saturation was determined photometrically.[19] Bicarbonate and buffer base were determined using the nomogram of Singer and Hastings.[20] Sodium and potassium were determined with the flame photometer attachment to the Beckman DU spectrophotometer. Calcium was determined by a modified Kingsley method.[21] Lactic acid was determined by the method of Barker and Summerson.[22] An eight-channel electroencephalogram was recorded in six hyperventilated patients. Normal saline, 500–1,000 ml., was used as the intravenous fluid; glucose was avoided to eliminate possible errors in lactic-acid determination. Hyperventilation was carried out in ten patients. Five patients served as controls by adjusting ventilation to maintain Pa_{CO_2} near the preoperative level. Patients included in the study received no blood transfusions.

Results

The mean duration of hyperventilation was 3.2 hours with a range of from 2 hours to

6 hours and 15 minutes. Several patients could not be included in the study because it was impossible to obtain a Pa_{CO_2} value below 20 mm. of mercury by hyperventilation. In the nonhyperventilated group, anesthesia lasted from 2 to 4.5 hours with a mean of 3.1 hours. Some studies of nonhyperventilated patients had to be discontinued because maintaining a normal Pa_{CO_2} and using 80 per cent nitrous oxide produced moderate hypoxia. Evidently, these patients had either altered ventilation-perfusion ratios, alveolar-capillary block, or lowered CO_2 production.

In all but one patient there were no adverse effects upon blood pressure during or following hyperventilation. In that patient and one control patient, moderate hypotension occurred shortly after induction but was reversed by a single intravenous injection of 2 mg. methoxamine.

Data obtained from arterial blood studies are presented in table 1, and depicted graphically in figures 1 and 2. Several patients demonstrated respiratory alkalosis preoperatively, which was probably due to stimulation from insertion of the arterial needle. Values for *p*H and Pa_{CO_2} reached their maximal changes usually within 15 minutes after the start of hyperventilation. The lowered Pa_{CO_2} values ranged from 12 to 20 mm. of mercury and were maintained at constant levels as long as hyperventilation was continued. The *p*H was elevated as expected. The arterial oxygen saturation of most patients improved with hyperventilation. In hyperventilated patients the period of apnea at the end of anesthesia ranged from 5 seconds to 10 minutes with a mean value of 3 minutes. During this time Pa_{CO_2} had risen an average of 11 mm. of mercury to a mean of 26 mm. of mercury, and the oxygen saturation fell only slightly (an average of 3 per cent, from 98 to 95). Thus, at the onset of spontaneous respiration, there was hypocapnia and normal oxygen saturation. Most patients responded to their names by opening their eyes at approximately the same time as the first breath was taken. The patient hyperventilated longest (6 hours 15 minutes) remained apneic for only 3 minutes. Her Pa_{CO_2} at the first breath was 24 mm. of mercury with an oxygen saturation of 94 per cent.

Fifteen minutes after cessation of controlled respiration, Pa_{CO_2} for hyperventilated patients was at the control preanesthetic value (36

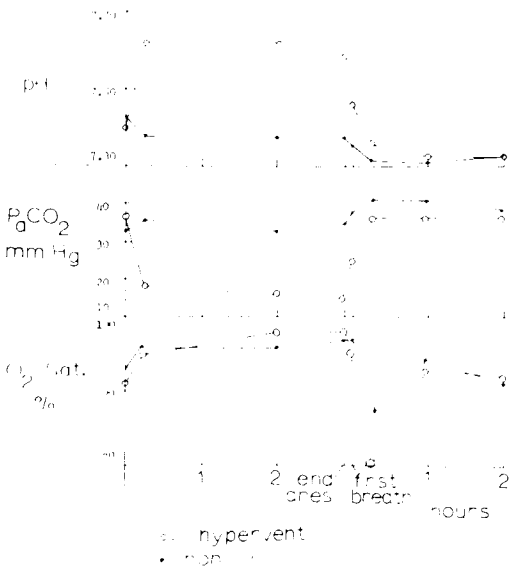

FIG. 1. Changes in *p*H and blood gases of arterial blood in patients undergoing N_2O-meperidine-curare anesthesia with and without hyperventilation.

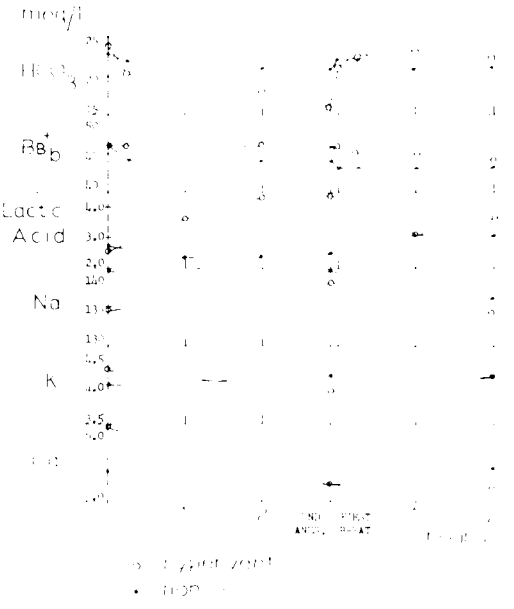

FIG. 2. Acid base and serum electrolyte changes in patients undergoing N_2O-meperidine-curare anesthesia with and without hyperventilation.

mm. of mercury). For nonhyperventilated patients the 15 minute postanesthesia sample (41 mm. of mercury) was above control (33 mm. of mercury), but still within normal limits. The *p*H for both groups was below the control value. The alarming finding of this study was that arterial oxygen saturations fell to a mean of 80 per cent (range 61–91 per cent) within 15 minutes after resumption of respiration in hyperventilated patients, while the Pa_{CO_2} values were normal. A similar decrease occurred in nonhyperventilated patients, but not to as marked a degree, mean 87 per cent (range 81–91 per cent). Both groups of patients would respond to questions and breathe deeply when asked to but tended to remain drowsy and appeared to be hypoventilating. Most patients were given nasal oxygen after the determination of oxygen saturation indicated hypoxia. Within two hours after the conclusion of anesthesia, values of Pa_{CO_2} and oxygen saturation were at the preoperative level without the benefit of nasal oxygen.

Bicarbonate levels dropped an average of 4 mEq. liter in the first fifteen minutes of hyperventilation, from 24 to 20 mEq. liter, and then decreased slowly during the remainder of the procedure to 15 mEq. liter. During the period of apnea, bicarbonate was quickly elevated 5 mEq. liter to a mean of 21 mEq. liter and remained at that level for the succeeding two hours after anesthesia. In nonhyperventilated patients, bicarbonate remained fairly constant throughout the entire study, but slightly depressed, 2 mEq. liter below control. Whole blood buffer base remained essentially unchanged throughout anesthesia and two hours postoperatively in both hyperventilated and nonhyperventilated patients.

Lactic acid levels in hyperventilated patients were gradually elevated from a preoperative mean of 2.3 mEq. liter to a high of 4.5 mEq. liter at the end of anesthesia. The level then receded during the first postoperative hour but was still slightly elevated at the second postoperative hour, approximately 1 mEq. liter above the preoperative value. In nonhyperventilated patients, lactic acid levels remained almost constant throughout anesthesia but were slightly elevated in the postoperative period, a mean of 0.4 mEq. liter.

There were no significant changes in serum sodium during the study. Most hyperventilated patients exhibited a mean decrease of potassium of 0.3 mEq. liter. Hyperventilated patients also exhibited a slight decline in serum calcium of 0.8 mEq. liter on the average. Nonhyperventilated patients exhibited no changes in serum potassium or calcium. The slight changes in lactic acid, sodium, potassium, and calcium for hyperventilated patients were not statistically significant at the .05 level.

In those patients monitored with the electroencephalograph, fast activity with low voltage consistent with light anesthesia was seen in each instance. Slow waves were not noted. (These observations have been published in greater detail in another communication.[7])

Discussion

The short period of apnea following hyperventilation (mean, 3 minutes) tends to rule out hyperventilation and lowered Pa_{CO_2} as a major cause of prolonged apnea after anesthesia. The fact that Pa_{CO_2} was low (mean 26 mm.) and oxygen saturation was normal (mean 95 per cent) indicates that neither hypercarbia nor hypoxemia are necessary for initiation of respiration following prolonged passive hyperventilation.

We have considered several possibilities to explain the fall in oxygen saturation 15 minutes after resumption of respiration. Although diffusion hypoxia from nitrous oxide is a possibility, one would not expect it to be present 15 minutes after the end of controlled respiration, especially since 100 per cent oxygen was given for five minutes prior to the termination of mechanical ventilation. Altered ventilation perfusion ratios from areas of atelectasis might explain the hypoxia and normal Pa_{CO_2}. Another possibility is that repletion of washed out carbon dioxide stores and lowered carbon dioxide production associated with narcotics keeps Pa_{CO_2} near normal despite hypoventilation. The hypoventilation causes hypoxia, which evidently in this situation is a poor respiratory stimulus, if at all. Further observations and measurements of alveolar ventilation are required to fully explain this phenomenon.

We would suggest that patients anesthetized with techniques similar to those used in this study receive routine supplemental oxygen for approximately one hour postoperatively.

Using the nitrous oxide-narcotic-relaxant technique, hyperventilation produces no significant acid-base disturbances. The elevation of lactic acid from 2.5 to 4.5 mEq. liter is of little clinical importance. Papadopoulos and Keats observed also that there was a slight metabolic acidosis with a slight rise of lactic acid during hyperventilation with barbiturate-nitrous oxide-relaxant anesthesia. The cause of elevation in lactic acid was suggested as having been caused by glucose infusion.[3] Our patients did not receive glucose but still exhibited a similar slight elevation of lactic acid.

Perhaps the chief objection to hyperventilation is possible cerebral hypoxia. Low oxygen tension in the cerebral cortex of hyperventilated dogs was reported by Sugioka.[9] However, the data have been questioned on the basis of function of the oxygen electrode.[7] Allen and Morris[10] have recently reported that cerebral damage may be caused by hyperventilation as measured by the critical flicker fusion test. Although the electroencephalogram may not be the most sensitive index of cerebral hypoxia, it was interesting that none of our patients showed evidence of the slow wave activity which has been interpreted by some as indicative of cerebral hypoxia during respiratory alkalosis in unanesthetized man. In the final analysis we are left with clinical evaluation of cerebral damage after hyperventilation. It is difficult to conceive of severe cerebral hypoxia having occurred in patients who have been hyperventilated and maintained at Pa_{CO_2} levels of 12–15 mm. of mercury for several hours and who then are able to carry on a conversation within ten minutes of the resumption of spontaneous respiration.

Summary

Ten patients, anesthetized with a nitrous oxide-narcotic-relaxant technique, hyperventilated from 2 to $6\frac{1}{2}$ hours with Pa_{CO_2} maintained at from 12 to 20 mm. of mercury, and then followed two hours following anesthesia, were compared with a nonhyperventilated control group. There were no great alterations in serum sodium, potassium, calcium, or in acid-base balance in either group. Hyperventilated patients resumed spontaneous respiration at subnormal Pa_{CO_2} levels and normal arterial oxygen saturations. In the postanesthesia period Pa_{CO_2} quickly returned to and remained at control levels. Arterial oxygen saturation fell and then returned to normal within two hours. Reasons for this observation are discussed. Lowered Pa_{CO_2} was not associated with hypotension during light anesthesia.

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INTRAVENOUS INDUCTION The induction characteristics of different intravenous anesthetics have been compared on the basis of almost 9,000 administrations. None of the newer thiobarbiturates (butalitone or methitural) offer advantages over the older drugs. None of the methylated thiobarbiturates are suitable for clinical use. The incidence of involuntary spontaneous muscle movement and tremor increases with dosage and is reduced by analgesic premedications. It is increased by "anti-analgesic drugs" of which promethazine and hyoscine are important. The non-barbiturate G 29303 compares favorably with thiopental for smoothness of induction and it produces less hypotension than any of the available barbiturates. (*Dundee, J. W.: Characteristics of Intravenous Induction of Anesthesia, Der Anaesthesist 11: 272 (Aug.) 1962.*)

BRONCHOSCOPY General anesthesia plus muscular relaxation with succinylcholine may safely be employed by using a modified Broyle's bronchoscope which has a notched plastic slide over the aperture. This allows an endobronchial instrument to be introduced when slide is drawn and maintains a sufficient fit when replaced around the instrument to allow ventilation of lungs with high flows through the side arm of the bronchoscope. (*Fluvog, J. T.: New Method of General Anesthesia in Bronchoscopy, Amer. Rev. Resp. Dis. 86: 275 (Aug.) 1962.*)