Acid-Base Equilibrium During Cyclopropane Anesthesia and Operation in Infants

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The effect of endotracheal cyclopropane anesthesia and operation on acid-base equilibrium in 30 unsedated infants was determined by preanesthetic and operative arterial blood analyses for *p*H, P_{CO_2}, and CO_2. Anesthesia was administered via a nonrebreathing system, respirations spontaneous. The depth of anesthesia was correlated with the clinical signs of light anesthesia, the EEG, and in 10 cases with an arterial concentration of cyclopropane between 7 and 15 mg./100 ml.

Because of hyperventilation, the result of crying, most of the infants had a mild respiratory alkalosis before anesthesia. In addition, infants with pyloric stenosis exhibited a slight metabolic alkalosis preoperatively. There was no evidence of a respiratory acidosis during anesthesia and operation, and there was no change in the metabolic component of the acid-base equilibrium.

STUDIES of the arterial blood carbon dioxide have demonstrated that respiratory acidosis occurs during cyclopropane anesthesia in premedicated adults [1, 2] with spontaneous respiration and in children [3] with assisted respiration. The question arises as to whether the acid-base equilibrium is also disturbed during cyclopropane anesthesia in infants. The fact that the abdominal muscles are weak in infants [4] evoked the possibility that the degree of anesthetic depression required for surgery might be less in infants than in adults. This factor led to the belief that respiratory acidosis may not occur during operation in the unsedated infant anesthetized with cyclopropane. This study, therefore, was designed to determine the status of the acid-base equilibrium during surgical anesthesia with cyclopropane in infants.

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Procedure

Thirty infants who were scheduled for elective operation, ranging in age from one week to 26 weeks and without evidence of cardiorespiratory disease, were selected for this study. A control sample of arterial blood for the determination of blood gases was drawn in 17 of the patients one hour after premedication with 0.12 to 0.15 mg. of atropine sulfate. The tracheas of the infants were intubated without anesthesia, and anesthesia induced with 20 to 30 per cent cyclopropane in oxygen using a nonrebreathing system (Stephen-Slater Valve). The inspired cyclopropane concentration was adjusted to maintain a light surgical level of anesthesia as indicated by the electroencephalograph and by the following clinical signs: eyeballs centrally fixed, pupils usually constricted, grasp reflex weak, and flexor tone of arms present but diminished. During operation an arterial blood sample was drawn 45–60 minutes after the induction of anesthesia. Respiration was spontaneous throughout the operation. Rectal temperature was maintained between 98.6° and 99.6° F. by use of a heating pad placed beneath the infant. No blood or other intravenous fluid was administered.

Methods

Brachial or radial arteries were used for sampling. The dead space of a 5 ml. siliconized glass syringe and a 25-gauge needle were filled with heparin. The needle was guided into the artery and 3 to 4 ml. of blood withdrawn. Arterial blood could be distinguished from the venous because it could be aspirated readily whereas venous blood would not flow freely in the absence of a tourniquet.

*p*H and P_{CO_2} of the arterial blood were measured by means of a Sanz-Metrom capillary *p*H electrode and a Severinghaus P_{CO_2} electrode usieng an Epsco Blood Parameter

TABLE 1. Preoperative and Operative Values for *p*H, P_{CO_2} and CO_2 Content during Pyloromyotomy

Case	Age (wks.)	Wt. (kg.)	*p*H	P_{CO_2}* (mm. Hg)	CO_2 (mEq./liter)
			—	—	—
1	7	3.3	7.44	26.0	17.9
			7.48	38.7	27.9
2	4	3.9	7.47	38.2	28.1
			7.50	30.9	24.3
3	3	3.4	7.50	31.0	24.4
			7.55	27.3	24.0
4	5	3.7	7.48	38.9	29.3
			7.45	31.5	22.2
5	2	3.6	7.38	39.8	24.0
			—	—	—
6	5	4.4	7.43	36.0	24.2
Mean ± S.D.			7.49	32.1	24.6
Preoperative			±0.04	±4.7	±2.4
During Operation			7.45	35.0	24.7
			±0.04	±4.3	±4.0

* P_{CO_2} values are calculated. There was no significant difference between calculated and measured values for P_{CO_2}.

Analyzer. The *p*H meter was calibrated against two known buffer solutions (National Bureau of Standards) and had a minimal drift of 0.002 *p*H unit in thirty minutes. Arterial CO_2 content was measured in 12 patients using duplicate 0.03 ml. samples in a Natelson Micro-gasometer, Model 600. Using CO_2 content and the *p*H, the P_{CO_2} of the blood was calculated from the Henderson-Hasselbalch equation and compared with the value determined by the P_{CO_2} electrode. In 11 patients in whom the CO_2 content was not measured, it was calculated from *p*H and P_{CO_2} using the Henderson-Hasselbalch equation. In 7 cases arterial P_{O_2} was also determined using a Radiometer type E5044 P_{O_2} electrode with a Sanborn amplification and read-out system. Arterial cyclopropane concentrations were measured in 10 cases using a Perkin-Elmer gas chromatograph.[5]

The acid-base data were analyzed according to the recommendations of Schartz & Relman.[6]

Results

The results are tabulated in tables 1 and 2. The data of the infants with pyloric stenosis are presented separately because of preexisting metabolic alkalosis in most instances.

The values for CO_2 content obtained by direct measurment did not differ from the CO_2 content obtained by substituting *p*H and P_{CO_2} in the Henderson-Hasselbalch equation in cases 7–18. Therefore, in case 19-30, CO_2 content was determined by the latter method.

Of all the values for P_{CO_2} determined during operation, only one was high enough to indicate respiratory acidosis, case 19 with a P_{CO_2} of 48 mm. of mercury. The P_{CO_2} increased during operation in nine out of 12 infants in whom both preanesthetic and operative determinations were made (table 2) but with the one exception, did not exceed the normal range. An analysis of paired data in these 12 cases revealed no significant differences for P_{CO_2} ($P > 0.4$), *p*H ($P > 0.5$) or CO_2 content ($P > 0.5$).

Arterial P_{O_2} was ascertained during anesthesia in seven patients and averaged 434 mm. of mercury. The mean arterial concentration of cyclopropane for a group of 10 patients was 10.4 ± 2.7 mg./100 ml.

Discussion

Respiratory acidosis was not observed during operation in these infants as demonstrated by the fact that the arterial P_{CO_2} did not increase significantly. Evidently, respiration was not depressed during surgery under light cyclopropane anesthesia. A low average arterial P_{CO_2} (32 mm. of mercury) obtained in the preoperative state was the result of crying in some of the infants during arterial puncture. This mild respiratory alkalosis persisted during operation in many of the infants. The wide variation in the *p*H and P_{CO_2} values obtained in the control and the surgical states is most likely the result of the variable intensity of stimulus arising from either needle puncture or operation, affecting ventilation. The failure to give opiates or barbiturates for premedication, the decrease of respiratory dead space afforded by endotracheal intubation and respiratory stimulation during light anesthesia by operation presumably were factors that aided in maintaining a slightly hypocarbic state.

Freeman *et al.*[7] who measured end-expiratory

TABLE 2. Preoperative and Operative Values for Arterial *p*H, P_{CO_2} and CO_2 Content*

Case	Age (wks.)	Wt. (kg.)	*p*H	P_{CO_2} (mm. Hg)	CO_2 (mEq./liter)	P_{O_2} (mm. Hg)	Cyclopropane (mg./100 ml.)
			—	—	—		
7	8	4.2	7.38	32.3	19.0		
			7.47	26.8	19.0		
8	8	4.2	7.43	31.6	21.2		
			—	—	—		
9	4	3.9	7.40	38.2	23.1		
			—	—	—		
10	14	5.0	7.38	32.6	20.2		
			—	—	—		
11	26	8.6	7.35	30.8	19.0		
			7.46	25.5	18.5		
12	10	5.7	7.43	27.5	19.6		
			7.50	29.0	23.0		
13	6	4.7	7.47	30.1†	22.2		
			—	—	—		
14	10	7.3	7.48	26.2	18.7		
			7.46	24.6	19.1		
15	1	3.0	7.43	27.9	18.8		
			7.41	34.7	23.0		
16	1	2.6	7.48	26.5	22.2		
			—	—	—		
17	26	7.9	7.42	28.1	18.3		
			—	—	—		
18	13	5.6	7.33	38.1	20.3		
			—	—	—		
19	8	3.6	7.34	48.0	25.1†		
			—	—	—	—	—
20	7	3.6	7.40	38.0	22.8†	457	8.4
			7.36	36.8	20.2†	87	—
21	8	5.2	7.41	32.0	19.7†	424	9.3
			7.38	36.0	20.7†	94	—
22	5	5.2	7.45	28.7	19.4†	481	7.3
			7.37	37.0	20.8†	91	—
23	15	6.2	7.37	37.1	20.8†	468	7.1
			—	—	—	—	—
24	8	4.8	7.39	37.6	22.1†	366	12.5
			7.38	37.0	21.7†		—
25	6	4.5	7.35	40.1	21.5	362	13.4
			7.41	31.3	19.3†		—
26	15	6.2	7.41	31.4	19.3†		9.3
			7.41	33.0	20.3†		—
27	8	3.9	7.33	43.0	22.0†		10.0
			7.47	38.0	26.8†		—
28	6	3.9	—	—	—		—
			7.47	31.0	21.9†		—
29	6	4.5	7.40	41.0	24.6†		15.2
			—	—	—	—	—
30	5	4.3	7.42	38.1	24.0†	478	11.2
Average:	9.3	4.7					
Mean ± S.D. Preoperative			7.43±.05	32.4±4.7	21.1±2.3	91± 3.6	—
During Operation			7.40±.05	34.1±6.1	21.0±2.0	434±51.2	10.4±2.7

* Preoperative values were not obtained in every case.

† Calculated by Henderson-Hasselbalch equation.

Most of these infants had inguinal herniorrhaphies; infants 16 and 21 had colostomies performed for congenital megacolon; 17 and 18 had repair of extrophy of bladder, and infant 15 had an anoplasty.

P_{CO_2}, found no evidence of respiratory acidosis in infants breathing spontaneously during endotracheal cyclopropane anesthesia. Bunker *et al.*,[3] however, using arterial blood or "arterialized" capillary blood found that respiratory acidosis occurred in 4 infants studied during operation under cyclopropane anesthesia, although assisted respiration was the technique used. It is surprising that respiratory acidosis occurred in the presence of assisted respiration; perhaps respiratory dead space was increased by the use of a to and fro absorption system without intubation. Bunker did not observe respiratory acidosis in spontaneously breathing infants anesthetized with ether.

The absence of respiratory acidosis during surgical anesthesia implies that the work of breathing must be increased to maintain a normocarbic state in the face of the increased respiratory resistance of the anesthetized state. Tachypnea * associated with surgical stimulation during light general anesthesia, an increase in airway resistance due to a decreased diameter of the airway in intubated infants [8] and a decrease in lung compliance related to a decrease in tidal volume [9] are factors contributing to the increased work of respiration. Current studies in this laboratory show that the work of spontaneous respiration is increased 2 to 4 times in anesthetized infants. During prolonged procedures, controlled respiration may be the method of choice to decrease the fatiguing effect of increased work of breathing.

Light cyclopropane anesthesia is sufficient for abdominal surgical procedures because in most infants abdominal muscle relaxation is adequate at this depth. The light level of anesthesia was confirmed by the presence of flexor tone of the arms,[10] EEG level 3 and arterial cyclopropane concentrations of 7–15 mg./100 ml., averaging 10.4 mg./100 ml. In adults it is unlikely that abdominal surgical relaxation would occur unless the arms were completely relaxed. This difference reflects the predominance of flexor tone in the infant under four months of age.[11] This tone is controlled by subcortical centers which presumably are not depressed by levels of anesthesia necessary to produce good operating conditions. The abdominal muscles are relatively weak in the infant under six or seven months of age because of lack of exercise and development before he is able to raise himself to the sitting position.[4]

It has been reported that the plasma CO_2 content and *p*H are normally lower in infants than in adults.[12, 13] In addition, the lowering of the CO_2 content by hyperventilation may explain our observation of the low mean value for plasma CO_2, 21 mEq./liter, as compared to the usual values of 26 mEq./liter in adults. The plasma CO_2 content was not significantly changed from the control in the infants studied during anesthesia. Therefore, it is reasonable to state that there were no metabolic changes in acid base equilibrium.

Patients with pyloric stenosis had a combined respiratory and metabolic alkalosis preoperatively, the respiratory component indicated by the slightly low P_{CO_2} and the metabolic component by the slightly elevated CO_2 content. Consequently *p*H values as high as 7.55 were recorded. In this group P_{CO_2} returned toward normal during operation and *p*H decreased, but remained higher than in the patients without pyloric stenosis.

Summary

Arterial *p*H, P_{CO_2} and CO_2 were obtained in infants under 6 months of age during cyclopropane anesthesia and operation with spontaneous respiration. Light surgical levels of anesthesia were maintained and correlated with the EEG, the presence of flexor tone in the arm and with an average blood cyclopropane concentration of 10.4 mg./100 ml. *p*H, P_{CO_2} and CO_2 during surgical anesthesia were not changed significantly from those of the preoperative state. Respiratory acidosis did not occur during operation under light cyclopropane anesthesia in unsedated infants. There was no change in the metabolic component of acid-base equilibrium.

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COLON SURGERY The only important contraindications to colon surgery are active heart failure, complete heart block or a recent (within three months) myocardial infarct. In patients undergoing major abdominal surgery, an intravenous infusion of lactated Ringer's solution should be started at least two hours prior to induction of anesthesia. An hour or two of intravenous therapy is often judicious before emergency surgery of the colon. Reduction in the operative and immediate postoperative morbidity and mortality of patients undergoing large excisional surgical procedures has been affected by the use of a transfusion blood warmer, elimination of the empiric administration of calcium salts and an appreciation of the magnitude of extracellular fluid loss during extensive surgery. (*Lipton, B.: Anesthesia for Surgery of the Anorectum and Colon, Surg. Clinics N. Amer. 45: 1317 (Oct.) 1965.*)

ETHACRYNIC ACID An unsaturated ketone derivative of aryloxyacetic acid is a new diuretic agent whose administration orally or intravenously leads to marked urine flow and increased excretion of sodium, chloride and potassium. Its onset of action is prompt when given intravenously with appreciable effect within minutes and maximum effect within 30 minutes. Fifteen patients suffering from acute pulmonary edema superimposed on chronic congestive heart failure were given a single 50 mg. dose of the drug intravenously. All but one showed rapid onset of diuresis with striking reduction of pulmonary edema. Adverse reactions were limited to a single case of phlebitis at the site of improper injection. It is a valuable agent in the management of severe pulmonary edema. (*Rosenberg, B., Dobkin, G., and Rubin, R.: Intravenous Use of Ethacrynic Acid in the Management of Acute Pulmonary Edema, Amer. Heart J. 70: 333 (Sept.) 1965.*)