Bull. Tokyo Med. Dent. Univ., 18: 189–212, 1971.

CLINICAL STUDIES ON INFLUENCE OF INTRAVENOUS INFUSION OF FAT EMULSION ON CHANGES IN ACID-BASE EQUILIBRIUM

BY

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ABSTRACT

The influence of intravenous administration of 10% fat emulsion and a 12% amino acid solution on the acid-base equilibrium was observed and the factors considered to influence the acid-base equilibrium were also studied.

Intravenous infusion of a 10% fat emulsion produced a slight acidotic response, but there was no significant difference or any clinical meaning to this.

By infusing a 10% fat emulsion, the blood acetone bodies did not increase in quantity but the blood free fatty acid (FFA) increased two to four times. The acidotic response stated above is considered to be caused by this FFA increase.

Intravenous injection of a 12% amino acid solution produced a marked shift towards metabolic acidosis. The mean value of the pH decreased by 0.03, the mean value of the base excess by 2.8 mEq/l, and the mean value of Pco_2 by 2.0 mmHg.

This phenomenon is regarded as being due to the physical and chemical nature of the amino acid solution.

INTRODUCTION

Administration of fat emulsion post-operatively is very interesting clinically from the point of supplying high calories, essential fatty acid and fat-soluble vitamins, and its protein-saving effect.

The experiment on parenteral feeding of fat started with the subcutaneous injection of milk by Menzel et al. in 1869. Yamakawa et al. developed Yanol (which contains butter-fat and liver oil) in 1920, and Higasa et al. developed Fatgen (which is composed mainly of sesame oil). Mayer et al. developed Lipomul. But for clinical use all were questionable and are not employed today because of the limitation in the amount which can be infused and side effects[1–3]. But finally a fat emulsion for clinical use was developed through the studies by Gayer and Wretlind in 1960 on Intralipid composed mainly of soya bean oil[4]. Recently in Japan also, a fat emulsion, similar to Intralipid, composed mainly of soya bean oil was developed and is being gradually used clinically[2,3,5–7].

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Received for publication, July 13, 1971.

These two emulsion are made of soya bean oil and egg yolk phospholipid emulsion. More than 75% of the ingredients of soya bean oil are linoleic acid and oleic acid. The osmotic pressure of the emulsion is made isotonic by adding glycerol. The soya bean oil composes 10% of the emulsion in quantity, 500 ml giving 550 calories[2,3,5–7].

Clinical, pathological and biochemical studies have been conducted on Intralipid by Wretlind et al.[4,8,9], Hallberg et al.[10,11] and Gruker et al.[12] and on Intrafat by Kimura et al.[2,3,5–7,13,14].

A few reports on the influence of intravenous infusion of fat emulsion on the acid-base equilibrium were made public in foreign countries. By using the fat emulsion developed in Japan the changes in the acid-base equilibrium were observed and the factors which influence the acid-base equilibrium were studied. Among those factors which act on the acid-base equilibrium of the fat emulsion for intravenous infusion, there are two main ones: one is the infusion itself and the other is the fat metabolism.

The problem of the infusion itself is divided into two parts: one is the pH and the other is the titrable acidity. In this paper, the latter will be mainly discussed.

With regard to the fat metabolism, the problems are the blood FFA and blood acetone bodies. In the case of FFA, Rudman reported that FFA is united with the $\oplus$ radical of albumin as $R\text{-}COO^-$, and that the H^+ of FFA released at this time possibly influences the blood pH[15]. In the case of blood acetone bodies the problem is the aceto-acetic acid formed during the course from acetyl CoA to aceto-acetyl CoA due to the acceleration of the fatty acid metabolism and the keto-acidosis brought about by the accumulated aceto-acetic acid in the blood[16].

From the point of view stated above, the behavior of the acid-base equilibrium during the intravenous injection of fat emulsion was observed clinically, and the results of the observation and some comments are presented here.

Material

Eight pre-operative cases and thirty three post-operative cases, a total of forty one cases were studied. All were treated in the Second Department of Surgery of Tokyo Medical and Dental University Hospital from October 1970 to April 1971. Twenty six of the cases were males and fifteen were females. The ages were between twenty three and sixty nine. The diagnoses were fourteen cases of gastro-duodenal ulcer, four cases of gastric cancer, nine cases of cholelithiasis, four cases of hemorrhoid and ten cases with other diseases (Tables 1 to 5).

Cases where the general condition were not favorable and cases with

Table 1. Group A

Case	Sex	Age	Diagnosis	Operation
1. K.K	m	36	Lipoma	Extirpation
2. N.S	m	57	Hemorrhoids	Radical operation
3. I.I	f	49	Hemorrhoids	Radical operation
4. I.T	f	46	Blind loop syndrome	———
5. K.H	f	63	Gastric cancer	———
6. H.K	m	55	Gastric ulcer	———
7. T.N	f	49	Goiter	———
8. M.T	m	29	Duodenal ulcer	———
9. M.S	f	47	Gastric ulcer	———
10. H.A	m	23	Diaphragmatic hernia	———

Table 2. Group B

Case	Sex	Age	Diagnosis	Operation
1. M.Y	m	27	Cholelithiasis	———
2. M.H	m	24	Inguinal hernia	Radical operation
3. H.T	m	23	Hemorrhoids	Radical operation
4. A.Y	f	35	Hemorrhoids	Radical operation
5. K.K	f	64	Tumor of submaxillary salivary gland	Extirpation

underlying diseases which influence the fat metabolism were excluded.

Methods

1. Method of nutritive infusion

In order to observe the changes in the acid-base equilibrium during the intravenous injection of fat emulsion, all of the cases were divided into five groups according to the formula used (Table 6). In the cases where the fat emulsion was added attention was paid to maintain the content of the fat at 1 g/kg/day.

Group A:

10% fat emulsion 500 ml

Group B:

10% xylitol 500 ml

Table 3. Group C

Case	Sex	Age	Diagnosis	Operation
1. S.H	m	61	Gastric cancer	Gastrectomy
2. H.T	m	69	Cholelithiasis	Cholecystectomy
3. Y.T	f	37	Cholelithiasis	Cholecystectomy
4. S.Y	m	33	Gastric ulcer	Gastrectomy
5. S.T	m	46	Gastric ulcer	Gastrectomy
6. A.M	f	59	Gastric ulcer	Gastrectomy
7. H.H	m	55	Cholelithiasis	Cholecystectomy
8. T.A	f	58	Cancer of cecum	Hemicolectomy
9. S.K	m	66	Gastric polyp	Gastrectomy
10. Y.A	m	49	Gastric ulcer	Gastrectomy

Table 4. Group D

Case	Sex	Age	Diagnosis	Operation
1. S.Y	m	58	Gastric cancer	Gastrectomy
2. M.I	m	34	Cholelithiasis	Cholecystectomy
3. H.A	m	65	Gastric ulcer	Gastrectomy
4. K.Y	m	39	Cholelithiasis	Cholecystectomy
5. S.S	m	25	Cholelithiasis	Cholecystectomy
6. H.T	m	37	Duodenal ulcer	Gastrectomy
7. U.S	f	56	Gastric ulcer	Gastrectomy
8. S.Y	m	58	Duodenal ulcer	Gastrectomy
9. I.Y	f	56	Gastric ulcer	Gastrectomy
10. M.T	m	51	Tumor of abdomen	Exploratory laparotomy
11. S.M	f	64	Gastric ulcer	Gastrectomy

Group C:

① Ringer's solution 500 ml
① 5% Glucose 500 ml
② 10 Fat emulsion 500 ml
② 10% Xylitol 500 ml

Table 5. Group E

Case	Sex	Age	Diagnosis	Operation
1. S.K	f	52	Gastric ulcer	Gastrectomy
2. H.Y	f	37	Cholelithiasis	Cholecystectomy
3. T.T	m	52	Cholelithiasis	Cholecystectomy
4. I.A	m	26	Tumor of esophagus	Extirpation
5. Y.S	m	34	Gastric cancer	Gastrectomy

Table 6. Comparison of five groups classified by contents of infusion

Group	10% Fat emulsion (*ml*)	Amino acid solution (*ml*)	5% Glucose (*ml*)	10% Xylitol (*ml*)	Ringer's solution (*ml*)	Total (*ml*)	Number of cases
A	500	—	—	—	—	500	10
B	—	—	—	500	—	500	5
C	500	—	500	500	500	2,000	10
D	500	500	—	500	500	2,000	11
E	—	—	500	1,000	500	2,000	5

Group D:

① Ringer's solution 500 ml
① 12% Amino acid solution 500 ml
② 10% Fat emulsion 500 ml
② 10% Xylitol 500 ml

Group E:

① Ringer's solution 500 ml
① 5% Glucose 500 ml
② 10% Xylitol 1,000 ml

The rate of infusion was 200 ml/hour in groups A and B. In groups C, D and E, ① was injected first followed by ②. The two solutions in both ① and ② were mixed simultaneously.

By this method and by this rate of infusion the intravenous infusion of fat emulsion has done safely[16], and by this rate of infusion glucose could be utilized efficiently[17], and there was also almost no renal leakage of amino acid[18].

2. Time and method of blood-drawing

In Groups A and B, blood was drawn before the infusion (B-1), im-

mediately after the infusion (0°), three hours after the infusion (3°) and five hours after the infusion (5°). In Groups C, D and E, blood was drawn before the infusion (B-1), just when the infusion of ① was completed (B-2), immediately after the infusion (0°), three hours after the infusion (3°) and before the infusion on the following day (17°).

Blood was obtained from the femoral artery using a syringe with 1 mg of heparin added per 5 ml of blood, and determinations of the acid-base equilibrium values were performed anaerobically[19].

3. Measurement of acid-base equilibrium

The acid-base equilibrium was measured by the Astrup micro-method[20,21]. The pH was measured by Radiometer, AME-9 type, and the Pco_2 and base excess (hereafter referred to as B.E.) were calculated using the Siggaard-Andersen curve nomogram[22-24].

4. Analysis of factors which influence the acid-base equilibrium

1) Measurement of pH and titrable acidity of the solutions

Employing the pH stat (Toa Denpa, Ltd., HS-2A type), the pH and titrable acidity of each solution used in this experiment were measured. For titration, 1/10 N NaOH (F=1.002, Muto Chemical, Ltd.) was used[16].

2) Quantitative measurement of blood FFA

Fat at the rate of 1 g/kg/day was injected using a 10% fat emulsion and the quantitative measurement of blood FFA was assayed by the method of Duncombe[25] (employing "NEFA-TEST WAKO" of Wako Chemical, Ltd.).

3) Quantitative measurement of blood acetone bodies

Fat at the rate of 1 g/kg/day was injected using a 10% fat emulsion and the quantitative measurement of blood acetone bodies was made according to Welk's[26,27] method modified by Greenberg & Lester[28-30].

Results

1. Values of acid-base equilibrium

1) Values of Groups A and B and comparison of these values

Table 7 shows the acid-base equilibrium values of Group A. The figures in parenthesis represent the differences in the values before and after the infusion. The mean and standard error of the values and the difference in the values before and after the infusion are shown in the lowest column. Figures 1, 2 and 3 show the mean and standard error of the difference in the values before and after the infusion.

The mean pH of Group A was as follows: at B-1, 7.395±0.0066; at 0°, 7.401±0.0054; and at 5°, 7.413±0.0064. The value five hours after the in-

Table 7. Values of Group A

No.	Measurement items	Measurement points before and after infusion			
		B−1	0°	3°	5°
1.	pH	7.395 (0)	7.409 (0.014)	7.380 (−0.015)	7.390 (−0.005)
	Pco_2*	41.0 (0)	37.0 (−4.0)	39.5 (−1.5)	39.5 (−1.5)
	B. E.**	+ 0.2 (0)	− 1.1 (−1.3)	− 1.6 (−1.8)	− 0.9 (−1.1)
2.	pH	7.399 (0)	7.369 (−0.030)	7.395 (−0.004)	7.405 (0.006)
	Pco_2	40.0 (0)	42.0 (2.0)	39.5 (−0.5)	40.5 (0.5)
	B. E.	0 (0)	− 0.7 (−0.7)	− 0.6 (−0.6)	+ 0.6 (0.6)
3.	pH	7.410 (0)	7.412 (0.002)	7.395 (−0.015)	7.401 (−0.009)
	Pco_2	42.0 (0)	38.0 (−4.0)	41.5 (−0.5)	42.5 (0.5)
	B. E.	+ 1.6 (0)	− 0.5 (−2.1)	+ 1.8 (0.2)	+ 1.5 (−0.1)
4.	pH	7.383 (0)	7.415 (0.032)	7.445 (0.062)	7.440 (0.057)
	Pco_2	42.5 (0)	38.0 (−4.5)	36.5 (−6.0)	37.5 (−5.0)
	B. E.	+ 0.5 (0)	− 0.2 (−0.7)	+ 1.0 (0.5)	+ 1.3 (0.8)
5.	pH	7.381 (0)	7.381 (0)	7.378 (−0.003)	7.398 (0.017)
	Pco_2	42.0 (0)	42.0 (0)	44.0 (2.0)	43.0 (1.0)
	B. E.	− 0.1 (0)	+ 0.1 (0.2)	+ 1.1 (1.2)	+ 1.8 (1.9)
6.	pH	7.381 (0)	7.390 (0.009)	7.391 (0.010)	7.410 (0.029)
	Pco_2	43.0 (0)	42.5 (−0.5)	45.5 (2.5)	44.0 (1.0)
	B. E.	+ 1.0 (0)	+ 0.7 (−0.3)	+ 2.5 (1.5)	+ 3.0 (2.0)
7.	pH	7.438 (0)	7.430 (−0.008)	7.448 (0.010)	7.438 (0)
	Pco_2	41.0 (0)	40.2 (−0.8)	38.0 (−3.0)	40.5 (−0.5)
	B. E.	+ 3.0 (0)	+ 2.2 (−0.8)	+ 2.0 (−1.0)	+ 2.6 (−0.4)
8.	pH	7.365 (0)	7.392 (0.027)	7.405 (0.040)	7.393 (0.028)
	Pco_2	43.5 (0)	42.2 (−1.3)	41.0 (−2.5)	42.0 (−1.5)
	B. E	− 0.3 (0)	+ 0.6 (0.9)	+ 1.0 (1.3)	+ 0.6 (0.9)
9.	pH	7.380 (0)	7.402 (0.022)	7.420 (0.040)	7.450 (0.070)
	Pco_2	46.0 (0)	42.0 (−4.0)	40.0 (−6.0)	35.5 (−10.5)
	B. E	+ 1.7 (0)	+ 1.2 (−0.5)	+ 1.2 (−0.5)	+ 0.8 (−0.9)
10.	pH	7.421 (0)	7.412 (−0.009)	7.397 (−0.024)	7.405 (−0.016)
	Pco_2	38.5 (0)	39.0 (0.5)	42.0 (3.5)	41.0 (2.5)
	B. E	+ 0.3 (0)	+ 0.2 (−0.1)	+ 1.0 (0.7)	+ 0.8 (0.5)
Mean and S.E.	pH	7.395±0.0066 (0)	7.401±0.0054 (0.006±0.0058)	7.405±0.0074 (0.010+0.0085)	7.413±0.0064 (0.017±0.0086)
	Pco_2	42.0±0.61 (0)	40.3±0.63 (−1.6±0.67)	40.8±0.8 (−1.2±0.99)	40.6±0.77 (−1.4±1.1)
	B. E.	0.8±0.31 (0)	0.3±0.29 (−0.54±0.245)	0.9±0.36 (0.15±0.328)	1.2±0.33 (0.42±0.318)

( ) : Difference in values before and after infusion
* : Pco_2 (mmHg)
** : B.E. (mEq/l blood)

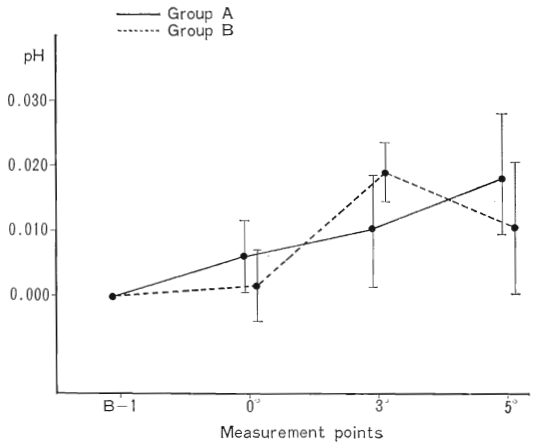

Fig. 1. pH of Groups A and B. Mean and S.E. of changes in values before and after infusion.

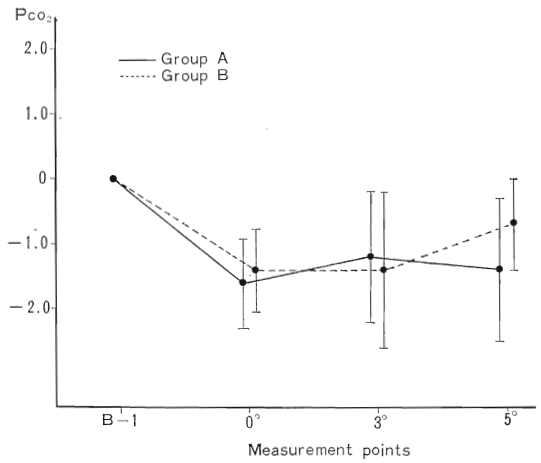

Fig. 2. Pco_2 of Groups A and B. Mean and S.E. of changes in values before and after infusion.

fusion (5°) was the highest, being 7.413±0.0064 and higher than at B-1 by 0.018±0.0086. The mean Pco_2 was: at B-1, 42.0±0.61; and at 0°, 40.3±0.63, the latter being lower than at B-1 by 1.6±0.67 mmHg. The mean B.E. was: at B-1, +0.8±0.31 mEq/l; and at 0°, +0.3±0.29 mEq/l, the latter being lower by 0.54±0.245 mEq/l. The value at 5° was higher than that at B-1 by 0.42±0.318 mEq/l.

Table 8 and Figures 1, 2 and 3 show the acid-base equilibrium values of Group B and the mean and standard error of the difference in the values before and after the infusion. The mean pH of Group B was as follows:

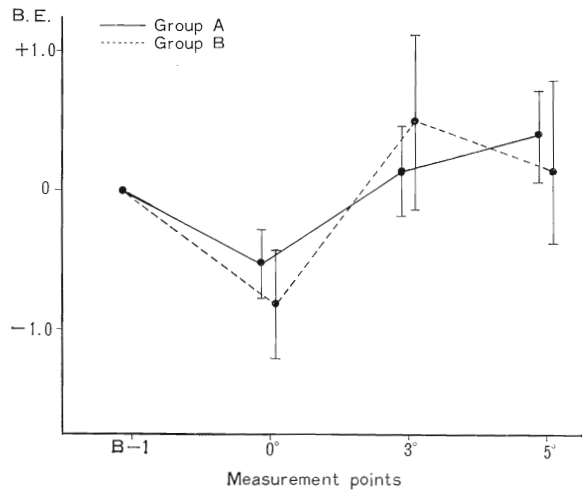

Fig. 3. B.E. of Groups A and B. Mean and S.E. of changes in values before and after infusion.

Table 8. Values of Group B

No.	Measurement items	Measurement points before and after infusion			
		B−1	0°	3°	5°
1.	pH	7.403 (0)	7.393 (−0.010)	7.405 (0.002)	7.395(−0.008)
	Pco_2*	41.5 (0)	42.5 (1.0)	40.5 (−4.5)	42.0 (0.5)
	B. E.**	+ 1.2 (0)	+ 1.1 (−0.1)	+ 0.6 (−0.6)	+ 0.7 (−0.5)
2.	pH	7.408 (0)	7.395 (−0.013)	7.430 (0.022)	7.400(−0.008)
	Pco_2	42.5 (0)	40.5 (−2.0)	38.0 (−4.5)	42.0 (−0.5)
	B. E.	+ 2.2 (0)	0 (−2.2)	+ 0.9 (−1.3)	+ 1.1 (−1.1)
3.	pH	7.390 (0)	7.409 (0.019)	7.412 (0.022)	7.420(0.030)
	Pco_2	42.5 (0)	40.0 (−2.5)	44.0 (1.5)	44.0 (1.5)
	B. E.	+ 1.0 (0)	+ 0.5 (−0.5)	+ 3.2 (2.2)	+ 3.5 (2.5)
4.	pH	7.390 (0)	7.398 (0.008)	7.408 (0.018)	7.435(0.045)
	Pco_2	42.5 (0)	39.5 (−3.0)	44.0 (1.5)	39.5 (−3.0)
	B. E.	+ 0.8 (0)	− 0.6 (−1.4)	+ 3.0 (2.2)	+ 2.0 (1.2)
5.	pH	7.380 (0)	7.385 (0.005)	7.412 (0.032)	7.375(−0.005)
	Pco_2	45.5 (0)	45.0 (−0.5)	41.0 (−4.5)	43.5 (−2.0)
	B. E.	+ 1.5 (0)	+ 1.6 (0.1)	+ 1.5 (0.0)	+ 0.2 (−1.3)
Mean and S.E.	pH	7.394±0.0045 (0)	7.396±0.0035 (0.002±0.0053)	7.413±0.0039 (0.019±0.0044)	7.405±0.0093 (0.011±0.0099)
	Pco_2	42.9±0.61 (0)	41.5±0.91 (−1.4±0.65)	41.5±1.02 (−1.4±1.2)	42.2±0.7 (−0.7±0.73)
	B.E.	1.3±0.22 (0)	0.5±0.35 (−0.82±0.38)	1.8±0.48 (0.5±0.65)	1.5±0.52 (0.16±0.66)

( ) : Difference in values before and after infusion
* : Pco_2 (mmHg)
** : B.E. (mEq/l blood)

at B-1, 7.394±0.0045; at 0°, 7.396±0.0035; and at 3°, 7.413±0.0039. The value at 3° was the highest, being higher than that at B-1 by 0.0019±0.0014. The mean Pco_2 was as follows: at B-1, 42.0±0.61 mmHg; and at 0°, 41.5± 0.90 mmHg. The value at 0° was the lowest, being lower than that at B-1 by 1.4±0.65 mmHg. The mean B.E. was as follows: at B-1, +1.3±0.22 mEq/l; at 0°, +0.5±0.35 mEq/l; and at 3°, +1.8±0.48 mEq/l. The value at 0° was the lowest, being lower than that at B-1 by 0.82±0.36 mEq/l.

Summary of 1)

With regard to the changes in pH, Pco_2 and B.E. of Group A, pH showed little variation but B.E. showed a tendency to be low in most cases. The value of B.E. was +0.8 mEq/l before the infusion, becoming +0.3

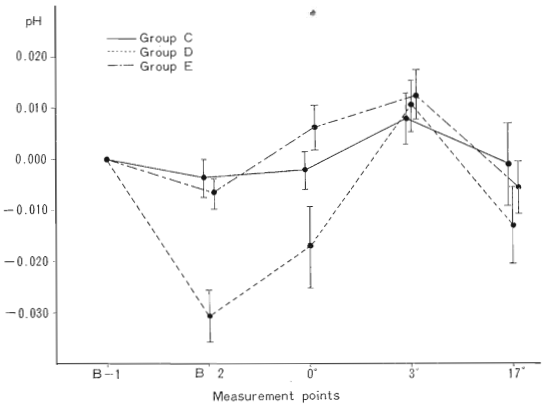

Fig. 4. pH of Groups C, D and E. Mean and S.E. of changes in values before and after infusion.

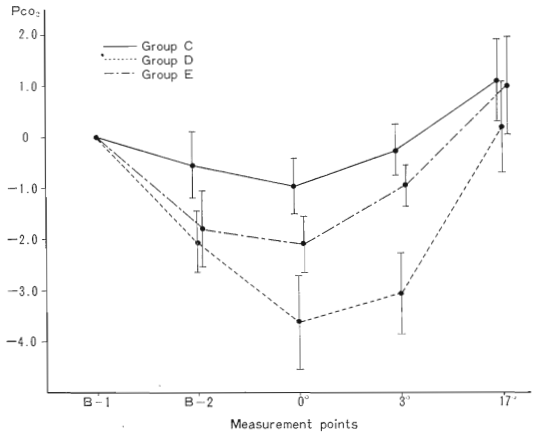

Fig. 5. PCO_2 of Groups C, D and E. Mean and S.E. of changes in values before and after infusion.

Table 9. Values of Group C

No.	Measurement items	Measurement points before and after infusion				
		B−1	B−2	0°	3°	17°
1.	p H	7.371 (0)	7.375(0.004)	7.385(0.014)	7.410(0.039)	7.428(0.057)
	Pco_2*	40.5 (0)	40.0 (−0.5)	39.5 (−1.0)	39.5 (−1.0)	38.0 (−2.5)
	B.E.**	0 (0)	− 0.8 (−0.8)	− 1.0 (−1.0)	+ 0.5 (0.5)	+ 1.0 (1.0)
2.	p H	7.452 (0)	7.469(0.017)	7.461(0.009)	7.455(0.003)	7.462(0.010)
	Pco_2	35.5 (0)	34.5 (−1.0)	35.5 (0)	35.0 (−0.5)	34.0 (−1.5)
	B.E.	+ 0.5 (0)	+ 1.0 (0.5)	+ 0.7 (0.2)	+ 0.3 (−0.2)	+ 0.2 (−0.3)
3.	p H	7.450 (0)	7.440(−0.010)	7.445(−0.005)	7.470(0.020)	7.450(0)
	Pco_2	38.0 (0)	39.5 (1.5)	37.0 (−1.0)	37.5 (−0.5)	39.5 (1.5)
	B.E.	+ 2.0 (0)	+ 2.5 (0.5)	+ 1.0 (−1.0)	+ 3.1 (1.1)	+ 3.0 (1.0)
4.	p H	7.428 (0)	7.425(−0.003)	7.429(0.001)	7.452(0.024)	7.440(0.012)
	Pco_2	40.5 (0)	39.0 (−1.5)	37.5 (−3.0)	38.0 (−2.5)	41.0 (0.5)
	B.E.	+ 2.0 (0)	+ 1.2 (−0.8)	+ 0.6 (−1.4)	+ 2.1 (0.1)	+ 3.4 (1.4)
5.	p H	7.430 (0)	7.410(−0.020)	7.402(−0.028)	7.420(−0.010)	7.440(0.010)
	Pco_2	41.5 (0)	42.5 (1.0)	42.5 (1.0)	41.5 (0)	40.0 (−1.5)
	B.E.	+ 3.0 (0)	+ 2.2 (−0.8)	+ 2.0 (−1.0)	+ 2.4 (−0.6)	+ 2.6 (−0.4)
6.	p H	7.430 (0)	7.435(0.005)	7.429(−0.001)	7.432(0.002)	7.400(−0.030)
	Pco_2	39.0 (0)	34.5 (−4.5)	39.0 (0)	40.0 (1.0)	42.0 (3.0)
	B.E.	+ 1.5 (0)	− 0.5 (−2.0)	+ 1.2 (−0.3)	+ 2.2 (0.7)	+ 1.0 (−0.5)
7.	p H	7.455 (0)	7.445(−0.010)	7.465(0.010)	7.455(0)	7.420(−0.035)
	Pco_2	37.5 (0)	38.0 (0.5)	38.0 (0.5)	37.5 (0)	40.5 (3.0)
	B.E.	+ 2.0 (0)	+ 2.0 (0)	+ 3.0 (1.0)	+ 2.0 (0)	+ 1.8 (−0.2)
8.	p H	7.445 (0)	7.448(0.003)	7.440(−0.005)	7.460(0.015)	7.451(0.006)
	Pco_2	40.5 (0)	38.5 (−2.0)	36.5 (−4.0)	38.5 (−2.0)	41.0 (0.5)
	B.E.	+ 3.1 (0)	+ 2.0 (−1.1)	+ 0.8 (−2.3)	+ 3.0 (−0.1)	+ 4.0 (0.9)
9.	p H	7.390 (0)	7.389(−0.001)	7.390(0)	7.395(−0.005)	7.385(−0.005)
	Pco_2	37.5 (0)	35.0 (−2.5)	34.5 (−3.0)	37.0 (−0.5)	39.5 (2.0)
	B.E.	− 2.0 (0)	− 3.8 (−1.8)	− 3.5 (−1.5)	− 2.1 (−0.1)	− 1.2 (0.8)
10.	p H	7.415 (0)	7.395(−0.020)	7.400(−0.015)	7.395(−0.020)	7.385(−0.030)
	Pco_2	36.0 (0)	39.5 (3.5)	37.0 (1.0)	39.5 (3.5)	42.5 (6.5)
	B.E.	− 1.2 (0)	− 0.6 (0.6)	− 1.3 (−0.1)	− 0.6 (0.6)	+ 0.3 (1.5)
Mean and S.E.	pH	7.427±0.0083 (0)	7.423±0.0090 (−0.004±0.0035)	7.425±0.0087 (−0.002±0.0038)	7.434±0.0084 (0.008±0.0051)	7.426±0.0083 (−0.0005±0.0008)
	Pco_2	38.7±0.62 (0)	38.1±0.80 (−0.55±0.68)	37.7±0.68 (−0.95±0.54)	38.4±0.5 (−0.25±0.49)	39.8±0.73 (1.2±0.80)
	B.E.	1.1±0.52 (0)	0.52±0.59 (−0.57±0.28)	0.35±0.55 (−0.7±0.29)	1.29±0.51 (0.2±0.15)	1.6±0.49 (0.5±0.23)

( ) : Difference in values before and after infusion
* : Pco_2 (mmHg)
** : B.E. (mEq/l blood)

Table 10. Values of Group D

No.	Measurement items	Measurement points before and after infusion				
		B−1	B−2	0°	3°	17°
1.	p H	7.460(0)	7.430 (−0.030)	7.465 (0.005)	7.459 (−0.001)	7.460 (0)
	Pco_2*	35.0 (0)	32.0 (−3.0)	30.5 (−4.5)	32.0 (−3.0)	36.5 (1.5)
	B. E.**	+ 0.5 (0)	− 2.0 (−2.5)	− 1.2 (−1.7)	− 0.7 (−1.2)	+ 2.0 (1.5)
2.	p H	7.391(0)	7.382 (−0.009)	7.411 (0.020)	7.405 (0.014)	7.425 (0.034)
	Pco_2	43.8 (0)	42.0 (−1.8)	35.5 (−8.3)	34.0 (−9.8)	40.0 (−3.8)
	B. E.	+ 1.5 (0)	0. (−1.5)	− 1.5 (−3.0)	− 2.5 (−4.0)	+ 1.8 (0.3)
3.	p H	7.390(0)	7.345 (−0.045)	7.400 (0.010)	7.430 (0.040)	7.395 (0.005)
	Pco_2	34.5 (0)	32.5 (−2.0)	35.5 (1.0)	33.0 (−1.5)	39.0 (4.5)
	B. E.	− 3.0 (0)	− 6.8 (−3.8)	− 2.2 (0.8)	− 2.0 (1.0)	− 1.0 (2.0)
4.	p H	7.400(0)	7.362 (−0.038)	7.350 (−0.050)	7.410 (0.010)	7.370 (−0.030)
	Pco_2	38.0 (0)	38.5 (0.5)	40.0 (2.0)	37.0 (−1.0)	39.5 (1.5)
	B. E.	− 1.0 (0)	− 3.0 (−2.0)	− 3.0 (−2.0)	− 1.0 (0)	− 2.0 (−1.0)
5.	p H	7.410(0)	7.390 (−0.020)	7.410 (0)	7.421 (0.011)	7.421 (0.011)
	Pco_2	42.5 (0)	43.0 (0.5)	35.5 (−7.0)	37.0 (−5.5)	37.0 (−5.5)
	B. E.	+ 2.0 (0)	+ 1.2 (−0.8)	− 2.0 (−4.0)	− 0.5 (−2.5)	0 (−2.0)
6.	p H	7.432(0)	7.390 (−0.042)	7.430 (−0.020)	7.421 (−0.012)	7.405 (−0.027)
	Pco_2	39.0 (0)	40.0 (1.0)	36.0 (−3.0)	40.0 (1.0)	42.0 (3.0)
	B. E.	+ 1.8 (0)	− 0.5 (−2.3)	− 0.5 (−2.3)	+ 1.0 (−0.8)	+ 1.8 (0)
7.	p H	7.412(0)	7.411 (+0.001)	7.412 (0)	7.440 (0.028)	7.390 (−0.022)
	Pco	41.5 (0)	35.5 (−6.0)	38.5 (−3.0)	36.5 (−5.0)	42.5 (1.0)
	B. E.	+ 1.5 (0)	− 2.0 (−3.5)	0. (−1.5)	+ 1.8 (0.3)	+ 1.0 (−0.5)
8.	p H	7.420(0)	7.355 (−0.065)	7.380 (−0.040)	7.425 (0.005)	7.381 (−0.039)
	Pco_2	37.0 (0)	34.5 (−2.5)	35.0 (−2.0)	33.5 (−3.5)	40.5 (3.5)
	B. E.	+ 0.4 (0)	− 5.8 (−5.4)	− 4.0 (−3.6)	− 2.0 (−1.6)	− 1.0 (−0.6)
9.	p H	7.442(0)	7.420 (−0.022)	7.402 (−0.040)	7.430 (−0.012)	7.381 (−0.061)
	Pco_2	40.5 (0)	36.5 (−4.0)	36.0 (−4.5)	36.0 (−4.5)	41.8 (1.3)
	B. E.	+ 3.0 (0)	− 0.5 (−3.5)	− 2.1 (−5.1)	0 (−3.0)	− 0.5 (−3.5)
10.	p H	7.460(0)	7.432 (−0.028)	7.422 (−0.038)	7.485 (0.025)	7.461 (0.001)
	Pco_2	41.0 (0)	38.0 (−3.0)	35.2 (−5.8)	37.5 (−3.5)	38.5 (−2.5)
	B. E.	+ 5.0 (0)	+ 1.0 (−4.0)	− 1.2 (−6.2)	+ 4.8 (−0.2)	+ 4.0 (−1.0)
11.	p H	7.410(0)	7.375 (−0.035)	7.360 (−0.050)	7.415 (0.005)	7.389 (−0.021)
	Pco_2	40.5 (0)	38.0 (−2.5)	35.5 (−5.0)	36.0 (−4.5)	38.5 (−2.0)
	B. E.	+ 1.0 (0)	− 2.5 (−3.5)	− 5.0 (−6.0)	− 2.2 (−3.2)	− 1.2 (−2.2)
Mean and S.E.	pH	7.421±0.0072 (0)	7.390±0.0086 (−0.03±0.0051)	7.404±0.0092 (−0.17±0.0077)	7.431±0.0067 (0.01±0.0046)	7.407±0.0090 (−0.014±0.0077)
	Pco_2	39.4±0.86 (0)	37.3±1.03 (−2.1±0.60)	35.7±0.67 (−3.6±0.89)	35.7±0.67 (−3.1±0.80)	39.6±0.57 (0.2±0.92)
	B. E.	1.1±0.60 (0)	−1.9±0.74 (−2.81±0.42)	−2.1±0.42 (−3.1±0.61)	−0.3±0.46 (−1.4±0.47)	−0.63±0.46 (−0.63±0.46)

( ) : Difference in values before and after infusion
* : Pco_2 (mmHg)
** : B.E. (mEq/l blood)

Table 11. Values of Group E

No.	Measurement items	Measurement points before and after infusion				
		B−1	B−2	0°	3°	17°
1.	p H	7.468(0)	7.465 (−0.003)	7.479 (0.011)	7.392 (0.024)	7.440 (−0.028)
	Pco_2*	42.5 (0)	38.5 (−4.0)	39.0 (−3.5)	40.0 (−2.5)	40.5 (−2.0)
	B.E.**	+ 6.2 (0)	+ 3.5 (−2.7)	+ 5.0 (−1.2)	+ 6.2 (0)	+ 3.0 (−3.2)
2.	p H	7.415(0)	7.412 (−0.003)	7.430 (0.015)	7.442 (0.027)	7.412 (−0.003)
	Pco_2	42.5 (0)	42.0 (−0.5)	39.0 (−3.5)	41.0 (−1.5)	44.0 (1.5)
	B.E.	+ 2.2 (0)	+ 2.0 (−0.2)	+ 1.2 (−1.0)	+ 3.5 (1.3)	+ 3.2 (1.0)
3.	p H	7.480(0)	7.460 (−0.020)	7.470 (−0.010)	7.488 (0.008)	7.450 (−0.030)
	Pco_2	41.0 (0)	38.5 (−2.5)	39.5 (−1.5)	40.5 (−0.5)	45.5 (4.5)
	B.E.	+ 6.5 (0)	+ 3.1 (−3.4)	+ 4.1 (−2.4)	+ 6.7 (0.2)	+ 7.7 (1.2)
4.	p H	7.410(0)	7.405 (−0.005)	7.415 (0.005)	7.412 (0.002)	7.439 (0.029)
	Pco_2	41.0 (0)	38.5 (−2.5)	39.5 (−1.5)	41.2 (0.2)	42.0 (1.0)
	B.E.	+ 1.2 (0)	− 0.5 (−1.7)	0 (−1.2)	+ 1.5 (0.3)	+ 4.0 (2.8)
5.	p H	7.410(0)	7.410 (0)	7.420 (0.010)	7.410 (0)	7.415 (0.005)
	Pco_2	39.0 (0)	39.5 (0.5)	38.5 (−0.5)	38.5 (−0.5)	39.0 (0)
	B.E.	0. (0)	+ 0.5 (0.5)	0 (0)	+ 0.5 (0.5)	+ 0.8 (0.8)
Mean and S.E.	pH	7.437±0.0138 (0)	7.430±0.0118 (−0.006±0.0032)	7.443±0.0118 (0.006±0.0033)	7.449±0.0159 (0.012±0.0050)	7.431±0.0067 (−0.005±0.0098)
	Pco_2	41.2±0.58 (0)	39.4±0.06 (−1.8±0.76)	39.1±0.17 (−2.1±0.54)	40.2±0.43 (−0.96±0.42)	42.2±1.04 (1.0±0.95)
	B.E.	3.2±1.19 (0)	1.7±0.68 (−1.5±0.66)	2.1±0.94 (−1.2±0.34)	3.7±1.1 (0.46±0.20)	3.7±1.0 (0.52±0.89)

( ) : Difference in values before and after infusion
* : Pco_2 (mmHg)
** : B.E. (mEq/l blood)

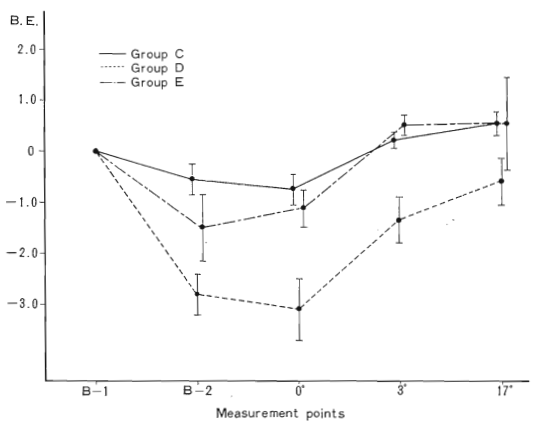

Fig. 6. B.E. of Groups C, D and E. Mean and S.E. of changes in values before and after infusion.

mEq/l after the infusion. It became lower by an average of 0.54 mEq/l. Pco_2 showed a similar tendency to become low. The value of Pco_2 became lower by an average of 1.6 mmHg from 42.0 mmHg before the infusion to 40.3 mmHg after the infusion. The B.E. values after the fat infusion were not significantly different from the values before the infusion. But the Pco_2 value after the fat infusion was significantly different from the value before the infusion at $p<0.05$.

With regard to the changes in pH, Pco_2 and B.E. of Group B, there was no significant difference between the values before and after the infusion.

In comparing Groups A and B, pH, Pco_2 and B.E. showed similar changes, there being no significant difference between the two groups.

2) Values of Groups C, D and E and comparison of these values

Tables 9, 10 and 11 and Figures 4, 5 and 6 show the values of the acid-base equilibrium of Group C and the changes in the values at B-1. The mean pH before the infusion (B-1) of Group C was 7.427±0.0008. The mean pH immediately after the infusion of a mixture of 5% glucose and Ringer's solution (B-2) was 7.423±0.009. The mean pH immediately after the infusion of a mixture of xylitol and fat emulsion (0°) was 7.425± 0.009. The mean pH three hours after the infusion (3°) was 7.434±0.008. This value was the highest, being higher than that at B-1 by 0.008±0.005. The mean pH before the infusion on the following day (17°) was 7.426± 0.008. The mean Pco_2 was as follows: at B-1, 38.7±0.62 mmHg; at 0°, 37.7±0.08 mmHg; and at 3°, 38.4±0.55 mmHg. The value at 0° was the lowest being lower than that at B-1 by 0.94±0.54. The mean B.E. was as follows: at B-1, 1.1±0.52 mEq/l; at 0°, 0.35±0.55 mEq/l; and at 3°, 1.3±0.5 mEq/l. The value at 0° was the lowest, being lower than that at B-1 by 0.74±0.27 mEq/l.

The mean pH of Group D was as follows: at B-1, 7.421±0.007; at 0° (after the infusion of xylitol and fat emulsion), 7.404±0.009; and at 3°, 7.431±0.007. The value at B-2 was the lowest, being lower than that at B-1 by 0.030±0.051. The mean Pco_2 was as follows: at B-1, 39.4±0.86 mmHg; at B-2, 37.3±1.03; at 0°, 35.7±0.67 mmHg; and at 17°, 39.4±0.57 mmHg. The value at 0° was the lowest, being lower than that at B-1 by 3.64±0.67 mmHg. The value at 3° was also lower than that at B-1 by 3.1±0.8 mmHg. The mean B.E. was as follows: at B-1, 1.1±0.6 mEq/l; at B-2, −1.9±0.74 mEq/l; at 0°, −2.1±0.42 mEq/l; at 3°, −0.3±0.038 mEq/l; and at 17°, 0.4±0.52 mEq/l. The value at 0° was the lowest, being lower than that at B-1 by 3.14±0.61 mEq/l. At 3° this value returned almost to the level at B-1.

The mean pH of Group E was as follows: at B-1, 7.437±0.014; at B-2 (after the infusion of Ringer's solution and glucose), 7.430±0.00118; at 0°

(after the infusion of xylitol), 7.443±0.0118; and at 3°, 7.449±0.016. The value at B-2 was lower than that at B-1 by 0.006±0.003, but the value at 3° was higher than that at B-1 by 0.012±0.05. The mean Pco_2 was as follows: at B-1, 41.2±0.58 mmHg; at B-2, 39.4±0.061 mmHg; at 0°, 39.1±0.70 mmHg; and at 3°, 40.2±0.43 mmHg. The value at 0° was lower than that at B-1 by 2.1±0.54 mmHg and at 3° it returned to the level at B-1. The mean B.E. was as follows: at B-1, 3.2±1.19 mEq/l; at B-2, 1.7±0.68 mEq/l; at 0°, 2.1±0.94 mEq/l; and at 3°, 3.7±1.1 mEq/l. The value at B-2 was lower than that at B-1 by 1.5±0.66 mEq/l, and at 3° at returned to the level at B-1.

Summary of 2)

The mean pH of Group C varied before and after the infusion. The mean B.E. at B-2 was lower than that at B-1 by 0.57 mEq/l and at 0° by 0.74 mEq/l. The mean Pco_2 at B-1 was lower than that at B-2 by 0.6 mmHg and at 0° by 0.95 mmHg. There was no significant difference in these values. The mean pH of Group D at B-2 was lower than that at B-1 by 0.03. This difference was significant at $p<0.05$. The mean Pco_2 at B-1 was lower than that at B-2, 0° and 3° by 2–3.5 mmHg, the difference being significant at $p<0.01$. That is to say, the value did not return to the level at B-1 even after three hours after the infusion. The mean B.E. at B-1 fell from that at B-2 by 2.8 mEq/l and by 3.14 mEq/l at 0°, the difference being significant at $p<0.01$. The value at B-1 returned to the level at 3°. The mean pH of Group E at B-1 rose by 0.01 at 0° and 3°, the difference being significant at $p<0.05$. The mean Pco_2 at B-1 decreased by 1.5 mEq/l at B-2, but on the other hand at 0° it became higher than that at B-2 by 0.4 mEq/l.

Next, Group C (infusion of fat emulsion), Group D (infusion of amino acid solution) and Group E (infusion of xylitol solution) were compared. In comparing Groups C and E, the values of pH, Pco_2 and B.E. showed no significant difference.

In comparing Groups C and D, the pH values at B-2 were significantly different at $p<0.01$. The Pco_2 values at 0° and 3° were significantly different at $p<0.05$ and at $p<0.01$, respectively. The B.E. values at B-2 and 0° were significantly different at $p<0.01$ and at $p<0.05$, respectively.

In comparing Groups D and E, the pH values at B-2 were significantly different at $p<0.05$ but there was no significant difference between the values of B.E. and Pco_2.

2. Factors which influence acid-base equilibrium

1) pH and titrable acidity of the solution.

Table 12 shows the pH and titrable acidity of the solution used in this experiment. The pH values of Ringer's solution, 5% glucose, 10% xylitol

Table 12. pH and titrable acidity of infused solutions

Infusion solution	Lot No.	pH	Titrable acidity
5% Glucose	Lot. 6302	4.30	0.410
	Lot. 6303	4.40	0.430
Ringer's solution	Lot. 7045	5.59	0.374
	Lot. 7046	5.66	0.376
10% Xylitol	ocssafag	5.71	0.323
	octasag4g	6.19	0.299
Amino acid solution	AN 210	5.74	34.753
	AK 300	5.61	35.060
10% Fat emulsion	BA 220	7.39	0.292
	BC 020E	7.31	0.294

Table 13. FFA values (mEq/l plasma)

Case	Sex	Age	B	0°	3°	17°
1.	m	46	0.74	4.26	1.44	0.41
2.	f	59	0.68	3.37	2.54	1.28
3.	f	58	0.82	2.97	2.19	0.87
4.	m	55	1.00	2.29	1.31	0.89
5.	f	31	0.46	0.83	0.36	0.38
6.	m	56	0.94	1.32	0.24	——
Mean and S.E.			0.773 ±0.072	2.507 ±0.480	1.347 ±0.347	0.766 ±0.150

and 10% fat emulsion were all between 4.5 and 7.39, and the values of the titrable acidity were between 0.29 and 0.43, being close to 0.

As for the amino acid solution, the pH was 5.7, while the titrable acidity was between 33 ml and 35 ml, being 150 times higher than that of 5% glucose.

Titrable acidity is the amount of 1/10 N NaOH required to adjust the pH of 100 ml of the solution to 7.4[16]. Therefore, the H^+ concentration of the fat emulsion was 0.24 mEq/l and that of the amino acid solution about 34 mEq/l.

2) Changes in blood FFA

Blood FFA rose distinctly immediately after the infusion (0°) of fat emulsion, 1 g/kg/day. The values of the blood FFA were 0.77 mEq/l before the infusion (B), 2.51 mEq/l immediately after the infusion (0°), 1.35 mEq/l three hours after the infusion (3°), and 0.77 mEq/l before the infusion on the following day (17°). The value at 17° returned to the level at B, but the value at 0° was about four times higher than at B (Table 13 and Figure 7).

3) Changes in blood acetone bodies

Table 14 and Figure 8 show the changes in the blood acetone bodies by the infusion of fat emulsion, 1 g/kg/day. The values of the blood acetone bodies were as follows: at B, 2.54 mg/dl; at 0°, 1.74 mg/dl; at 3°, 2.38 mg/dl; and at 17°, 6.52 mg/dl, the curve showing a U shape. The value was high during the starvation periods. B and 17°, but there was no rise in the values of the blood acetone bodies after the infusion of fat emulsion[29,30].

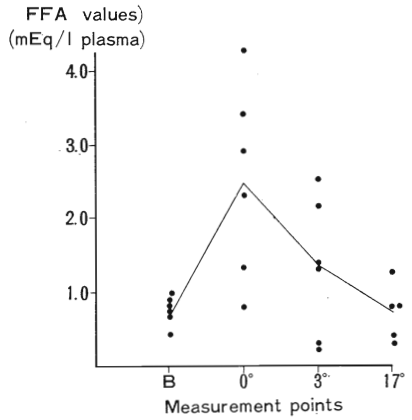

Fig. 7.

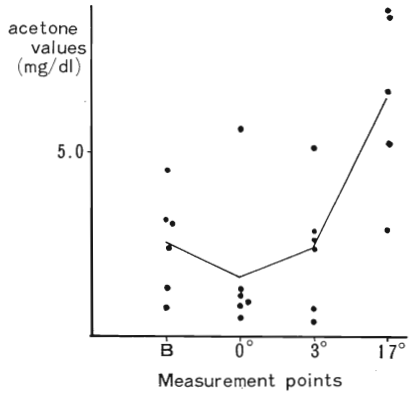

Fig. 8.

Table 14. Blood acetone body values (mg/dl)

Case	Sex	Age	B	0°	3°	17°
1.	m	46	3.13	1.08	2.90	6.69
2.	f	59	3.09	0.98	5.11	5.19
3.	m	58	1.38	5.60	2.66	8.94
4.	m	55	4.49	0.97	2.45	8.89
5.	f	31	2.31	1.24	0.75	2.90
6.	m	56	0.75	0.54	0.38	——
Mean and S.E.			2.52 ±0.501	1.74 ±0.71	2.38 ±2.38	6.52 ±6.52

Discussion

The normal values of the acid-base equilibrium reported by Astrup are as follows: pH, 7.35–7.42; Pco_2, 34–45 mmHg; and base excess, −2.3 to +2.3 mEq/l. Pco_2 expresses the respiratory factor, B.E. the metabolic factor and pH expresses both the Pco_2 and B.E.[20]

The concept of base excess was introduced by Astrup as the metabolic factor of acid-base equilibrium, as stated above. On the other hand, from the difference in the Pco_2-bicarbonate curve between the *in vitro* and *in vivo* experiments Schwarz et al.[31,32] raised some questions regarding the concept of B.E. In this paper the acid-base equilibrium values were interpreted accordingly to Astrup's opinion.

In summing up the changes in the acid-base equilibrium of Group A to which 10% fat emulsion was infused intravenously, the pH rose by an average of 0.006 from 7.395 to 7.401, B.E. decreased by an average of 0.5 mEq/l from 0.8 mEq/l, and Pco_2 decreased by an average of 1.6 mmHg from 42.0 mmHg to 40.3 mmHg. This slight decrease of B.E. and Pco_2 is considered to be a mild acidotic response. That is to say, a decrease of 0.5 mEq/l in B.E. represents a tendency of metabolic acidosis but the B.E. returned to the level before infusion at 3°. The Pco_2 of Group C decreased slightly after the infusion of fat emulsion. All these variations were within the normal range with no significant difference or clinical meaning.

There are a few other reports on the influence of fat emulsion on the changes in the acid-base equilibrium, but they are not uniform.

Rabbits and dogs were infused with several kinds of solutions by Sommerkamp et al. and especially the influence which fat emulsion has on the acid-base equilibrium was studied. He reported as follows: The standard bicarbonate (S.B.) showed a pronounced reduction by the fat infusion without any correlation to the quantity of the fat or the rate of the infusion. In the dog, S.B. decreased by 1.9 mval/l in the group infused with fat emulsion, and by 2.0 mval/l in the group not infused with fat emulsion[33]. Steinberethner et al. injected only the fat emulsion using 10% Intralipid and 20% Intralipid and observed the changes in the acid-base equilibrium. In the group infused with 20% Intralipid, only the S.B. decreased on the average from 26 mval/l to 23 mval/l, and at the same time compensatory respiratory alkalosis occurred[34].

The results with 10% fat emulsion, as stated above, agree with those obtained by the author.

Furthermore, there is another report in which fat emulsion was administered to the infant at the rate of 0.5 to 1.5 g of fat/kg/hour. During the short period after the infusion, metabolic acidosis appeared. It occurred

in the infant more frequently than in the experiment by Steinbereithner in the adult[35].

According to these reports and the author's observation, the following conclusion can be made. When the fat emulsion is administered at the rate of 1 g of fat/kg/day, or when the concentration of the fat emulsion infused was about 10%, the reduction in the value of S.B. (or B.E.) was not observed. If the quantity of the fat increase more than 1 g/kg/day, or if a fat emulsion of a high concentration is infused, the value of S.B. seemed to decrease.

When the fat emulsion is infused intravenously, factors such as titrable acidity of the fat emulsion, temporary increase in the blood FFA and increase in the blood acetone bodies are related to the acid-base equilibrium.

Table 12 shows the pH and titrable acidity of the solutions used in this experiment. The pH of the 10% fat emulsion was between 7.31 and 7.39 and the titrable acidity 0.29.

Incidentally, the pH and the titrable acidity of the other fat emulsions were: pH of 10% Intralipid, 6.0, and titrable acidity, 0.39; pH of 20% Intralipid, 6.8, and titrable acidity, 0.15; and pH of Lipofundin, 5.5, and titrable acidity, 0.23[34].

The titrable acidity of the solution means the mEq of the H^+ concentration of the solution. Therefore, the H^+ concentration of the 10% fat emulsion was 0.29 mEq/l. Even if 1,000 ml of the 10% fat emulsion were infused, only 0.29 mEq/l of H^+ enters the vein. Considering that the HCO_3^- concentration of the total extracellular fluid is 300 mEq[16], the H^+ concentration of the fat emulsion, as stated above, has no effect on the blood pH and, consequently, has no influence on the acid-base equilibrium.

The blood FFA is united with the $\oplus$ radical of the albumin in the form of $R\text{-}COO^-$. As the liberated H^+ acts on HCO_3^-, temporary increase of FFA influences the blood pH[15].

According to Rudman, he observed that the intravenous injection of 2 mg of ACTH in the rabbit caused a 6 to 10-fold increase in the plasma FFA, which was accompanied by marked hyperventilation and reduction in the blood pH of 0.05 to 0.25, plasma HCO_3^- concentration of 10 to 16 mEq/l and in the plsma Pco_2 of 7 to 22 mmHg. The reduction of the latter two is regarded as the phenomenon of metabolic acidosis and compensatory alkalosis[15].

The blood FFA immediately after the infusion of 10% fat emulsion increased about four times the value determined before the infusion. In the case where the fat emulsion was infused during the operation, the blood FFA showed an increase from 0.76 mEq/l to 1.53 mEq/l[13].

A temporary increase in the blood FFA influenced the acid-base equilibrium even in the case when the rate of the blood FFA metabolism was high[16]. According to the author's results, the blood FFA after the infusion

of fat emulsion increased about four fold the value determined before the infusion. In spite of this, there was little change in the pH. Yet, the slight reduction in the B.E. and Pco_2 observed in most of the cases in Group A was considered to be due to this temporary increase in the blood FFA.

In the case of the blood acetone bodies, accumulation of aceto-acetic acid in the blood formed during the course from acetyl CoA to aceto-acetyl CoA influences the acid-base equilibrium[16].

Table 14 and Figure 8 show that the value of the blood acetone bodies was the highest during the starvation period before the infusion and that the infusion of fat emulsion did not result in higher values.

Yamada et al. reported that they infused fat using a 10% fat emulsion at the rate of 2 g/kg into dogs and studied the changes in the ketone bodies. They stated that they did not observe any great changes[2,5].

There is another report that no abnormal ketone metabolism was observed by the tube feeding of fat emulsion at the rate of 1.5 g/kg/day, of glucose at the rate of 5.0 g/kg/day and of protein at the rate of 1.5 g/kg/day[36].

There was no significant difference in the changes in the blood acid-base equilibrium by the infusion of 10% fat emulsion, and the changes in the blood acetone bodies by the infusion of fat emulsion at the rate of 1 gm/kg/day showed no influence on the acid-base equilibrium.

There is, however, an opinion by Steinbereithner et al. that the marked reduction of S.B. by infusion of fat emulsion of high concentration is brought about by an increase of blood ketone bodies. But, in regard to this opinion, it should be discussed together with the changes in blood FFA.

Also there is another report that this increase in blood ketone bodies is not always due to a direct effect of the fat emulsion but due also to the patient's nutritive condition. This report also states that by adding 25% glycerin as an antiketogen substance the "kohlenhydratmangel ketose" can be controlled to the minimum[34].

As observed in the changes in the acid-base equilibrium of Group D, a marked shift towards metabolic acidosis was caused by infusion of amino acid solution. When 500 ml of a 12% amino acid solution was given intravenously, the pH decreased by 0.030 ± 0.005, the B.E. by 2.8 ± 0.42 mEq/l and Pco_2 by 2.0 ± 0.60 mmHg. The B.E. returned to the level before the infusion three hours after the infusion. But the Pco_2 decreased by 3.19 ± 0.8 mmHg from that before the infusion even three hours after the infusion. This decrease in the B.E. and Pco_2 values was considered to be obviously metabolic acidosis and compensatory respiratory alkalosis. The decrease in the values of pH, B.E. and Pco_2 showed a significant difference at $p<0.01$ compared with the values before the infusion and also a significant differ-

ence at $p<0.05$ compared with the decrease in the values of the groups infused with fat and the xylitol.

The pH of the 12% amino acid solution was 5.7 and the titrable acidity 34.8 ml. Not only the titrable acidity of the 12% amino acid solution but also the HCl, which is liberated from the amino acids and administered as hydrochloride, influences the acid-base equilibrium. Therefore the H^+ concentration of the 12% amino acid solution reaches as high as about 144 mEq/l. The marked shift towards metabolic acidosis by infusion of the amino acid solution was considered to greatly influence the H^+ concentration of the solution.

There is also the opinion that the physiological post-operative metabolic acidosis is due to the intravenous injection of amino acids in the early post-operative days, being caused by the breakdown of the ketoplastic amino acids[37].

But it can be easily concluded theoretically that the physical and chemical nature of the amino acid solution greatly influences the marked shift towards metabolic acidosis. There is the opinion that parenteral feeding with a combination of carbohydrates, fat and amino acid results in a marked shift of the acid-base balance towards metabolic acidosis, which can be minimized by taking adequate measures as buffering and reduction of Cl ions[38].

The variations in the acid-base equilibrium influenced by the intravenous xylitol infusion were similar to those of fat emulsion. Of the changes caused by xylitol, the pH and Pco_2 decreased by 1.42 ± 0.65 mmHg. Sato et al. reported that a slight decrease in excess bicarbonate induced by 5% xylitol infusion was observed, and this may be considered to be due to the increase of lactic acid without increase in pyruvic acid[39].

Conclusion

Changes in the acid-base equilibrium were observed by intravenous infusion of fat emulsion at the rate of 1 g/kg/day. These changes were compared with those caused by infusion of amino acid solution or xylitol and also compared with the results of fat emulsion. Furthermore, the factors during intravenous infusion of fat emulsion which influence acid-base equilibrium were studied.

1. The variations described below, which were caused by the fat emulsion infused intravenously, were observed.

1) A mild acidotic response appeared immediately after the infusion of the fat emulsion. The B.E. decreased by an average of 0.5 mEq/l, and Pco_2 by an average of 1.6 mmHg. By this decrease it is considered that there

is a slight shift towards metabolic acidosis and compensatory respiratory alkalosis as compared to the values determined before the infusion.

2) All of the variations described in 1) are within the normal range and show no significant difference or clinical meaning.

3) The variations described in 1) were considered to be caused by a temporary increase of blood FFA.

4) There was no increase in the quantity of the blood acetone bodies which would have influenced the acid-base equilibrium.

2. The variations caused by infusion of a 12% amino acid solution at the rate of 1.2 g/kg/day were observed.

1) A marked shift towards metabolic acidosis appeared after the intravenous amino acid infusion. The pH decreased by 0.03, B.E. by 2.81 mEq/l and Pco_2 by 2.0 mmHg immediately after the infusion, showing obvious metabolic acidosis and compensatory respiratory alkalosis as compared with the state of the acid-base equilibrium before the infusion. This change continued to be present for seven hours after the infusion.

2) The variations described above are considered to be due to the physical and chemical nature of the amino acid solution. (The fat emulsion employed in this clinical experiment was 10% Intrafat manufactured and provided by the Daigo Nutritive Chemical, Ltd.)

Acknowledgement

The author wishes to express his appreciaiton to Professor Eisuke Hamaguchi and Assistant Professor Nobuyoshi Kimura, 2nd Department of Surgery, Tokyo Medical and Dental University, School of Medicine, for their continuous guidance and encouragement, and to Dr. S. Fujiwara for his cooperation. The author also wishes to thank the staff members of the 2nd Department of Surgery for their cooperation.

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