Acetate and Bicarbonate in the Correction of Uraemic Acidosis

H. E. ELIAHOU,* B.A., M.D.; P. H. FENG,† M.R.C.P. GLASG.; U. WEINBERG,‡ M.D.; A. IAINA,‡ M.D.; E. REISIN,‡ M.D.

British Medical Journal, 1970, 4, 399-401

Summary: Uraemic acidosis was readily corrected by the infusion of sodium acetate solution, which gave comparable results to equivalent amounts of sodium bicarbonate infusion. Preliminary data suggest that this was true even in severe liver disease.

Introduction

When administered intravenously, sodium acetate affords a readily procurable source of fixed base (Mudge *et al.*, 1949). In spite of the fact that it can be used as an effective buffer in metabolic acidosis (Cash *et al.*, 1969), its use has not become widespread. This is probably due to the availability of the other commonly used buffers, lactated Ringer's solutions and sodium bicarbonate solution, which can be readily administered parenterally. Watten *et al.* (1969), however, clearly showed that sodium acetate solution approached bicarbonate in its ability to restore blood pH and plasma bicarbonate in patients suffering from metabolic acidosis of acute cholera. Sodium acetate solution is more stable, less expensive, and easier to manufacture and has a longer shelf-life than the other available buffers, especially bicarbonate. All these points favour its use routinely in the treatment of metabolic acidosis (Watten *et al.*, 1969) and no doubt prompted Watten *et al.* (1969) and Cash *et al.* (1969) to use it, especially when needed in large quantities. Furthermore, sodium acetate can effectively replace sodium bicarbonate in the preparation of dialysate fluid for haemodialysis (Mion *et al.*, 1964) as well as for peritoneal dialysis (Boen *et al.*, 1964) because of its rapid conversion to bicarbonate (Schwartz and Waters, 1962; Earnest *et al.*, 1968). Another useful point is that acetate solutions are less liable to bacterial contamination when compared with dialysate solutions containing lactate in peritoneal dialysis (Richardson and Borchardt, 1969).

This study was undertaken to compare the efficacy of intravenous sodium bicarbonate and sodium acetate solutions in the correction of acidosis in patients suffering from chronic uraemia due to end-stage kidney failure.

Patients and Methods

Fifteen patients suffering from terminal renal failure and on maintenance haemodialysis were investigated. The studies were undertaken at least three days after the end of the last haemodialysis and just before the onset of the next haemodialysis. An infusion of 200 ml. of a solution containing 178.4 mEq of acetate in the form of sodium acetate was given at a constant rate of about 40 drops per minute. Just before the next haemodialysis session the same patients were given 200 ml. of sodium bicarbonate solution containing 178.4 mEq of bicarbonate§ at the same rate as the acetate solution.

Unoccluded venous blood samples were taken immediately before infusion (A), immediately after infusion (B), one hour later (C), and three hours after infusion (D). pH was measured with a capillary microelectrode (pH meter 27 Radiometer, Copenhagen). Total carbon dioxide content was determined by the Natelson microgasometer. Blood PCO₂ was calculated from the Henderson-Hasselbalch equation, assum-

ing a pK' of 6.10. A carbon dioxide solubility coefficient of 0.03 was used.

Results

There were no untoward effects in any of the patients during or after the infusions of acetate and bicarbonate solutions.

pH.—The rise in blood pH after the infusion of acetate as well as of bicarbonate is significant in each group (Table I). There is a linear relationship between the initial pH values and those immediately after and three hours after the

TABLE I.—Detailed Results of Blood pH after Acetate and Bicarbonate Administration

Case No.	Blood pH							
	Acetate				Bicarbonate			
	A	B	C	D	A	B	C	D
1	7.28	7.40	7.37	7.35	7.34	7.43	7.42	7.42
2	7.28	7.41	7.39	7.42	7.33	7.43	7.41	7.43
3	7.26	7.31	7.36	7.41	7.30	7.34	7.36	7.45
4	7.25	7.42	7.40	7.42	7.35	7.47	7.47	7.45
5	7.25	7.36	7.36	7.35	7.27	7.37	7.35	7.39
6	7.27	7.35	7.34	7.40	7.24	7.35	7.37	7.36
7	7.34	7.45	7.44	7.41	7.32	7.39	7.41	7.41
8	7.25	7.35	7.35	7.40	7.36	7.41	7.41	7.49
9	7.30	7.36	7.37	7.37	7.37	7.41	7.41	7.39
10	7.19	7.33	7.31	7.28	7.25	7.35	7.34	7.38
11	7.32	7.41	7.41	7.41	7.37	7.48	7.44	7.47
12	7.27	7.36	7.37	7.40	7.32	7.43	7.39	7.45
13	7.28	7.35	7.37	7.35	7.32	7.38	7.40	7.36
14	7.33	7.49	7.47	7.45	7.33	7.48	7.47	7.41
15	7.18	7.32	7.30	7.30	7.24	7.31	7.32	7.30
n	15	15	15	15	15	15	15	15
$\bar{X}$	7.268	7.378	7.373	7.381	7.313	7.401	7.397	7.410
S.D.	0.043	0.049	0.036	0.046	0.043	0.050	0.048	0.047
P	—	<0.005	<0.005	<0.005	—	<0.005	<0.005	<0.005

A = Initial. B = Immediately after the end of the infusion. C = One hour after the end of the infusion. D = Three hours after the end of the infusion.

$\bar{X}$ = Mean. S.D. = Standard deviation. P = Significance of the changes between A and each of the following periods.

infusion of either bicarbonate or acetate. The regression lines with the least square method were calculated and plotted (Figs. 1 and 2).

Total CO₂.—The rise in total CO₂ after the infusion of acetate as well as of bicarbonate is significant in each group (Table II). There is a linear relationship between the initial total CO₂ values and those immediately after and three hours

TABLE II.—Detailed Results of Blood Total CO₂ after Acetate and Bicarbonate Administration

Case No.	Total CO ₂ (mM/l.)							
	Acetate				Bicarbonate			
	A	B	C	D	A	B	C	D
1	16	20.2	20	19.8	16.6	21	19.8	20.2
2	18.5	23.8	23.1	23.4	18.6	24.5	21.7	21.4
3	16.9	19.7	20.6	21.1	18.6	24.0	21.5	21.5
4	16.2	22.6	20.6	20.6	17.9	23.1	21.9	21.9
5	13.8	19.0	19.0	19.2	13.6	17.3	16.2	15.3
6	15.6	20.4	21.5	22.5	16.5	19.9	20.2	19.3
7	18.9	23.2	23.8	23.1	21.4	28	27.4	27.4
8	17.5	22.5	23.5	24.2	22	24.8	24.5	24.7
9	13.6	19.2	19.9	19.9	17.3	23.7	22.8	21.9
10	12.7	16.8	16.8	16.8	13.5	16.8	17	17.2
11	19.4	25.4	25.4	24	18.3	21.6	22.7	22.3
12	16.6	18.2	21	22.2	15.5	19.8	19.6	17.6
13	16.8	22.2	23.3	21.1	18.7	25.2	23.3	23.8
14	17	24.8	24	24	21.4	29.5	29.5	27
15	11	14.4	14.4	14.6	15	19.1	19.5	18
n	15	15	15	15	15	15	15	15
$\bar{X}$	16.033	20.827	21.127	21.100	17.660	22.473	21.840	21.300
S.D.	2.280	2.952	2.827	2.666	2.559	3.532	3.398	3.385
P	—	<0.005	<0.005	<0.005	—	<0.005	<0.005	<0.005

* Director, Department of Nephrology, Tel-Hashomer Government Hospital, Tel-Hashomer, Israel.

† W.H.O. Fellow, Senior Registrar, General Hospital, Singapore 11.

‡ Physician, Department of Nephrology, Tel-Hashomer Government Hospital, Tel-Hashomer, Israel.

§ Four ampoules of sodium bicarbonate, each containing 44.6 mEq. of bicarbonate in 50 ml., as supplied by Abbott Laboratories.

FIG. 1.—Blood pH immediately after the infusion of equivalent amounts of acetate and bicarbonate. For acetate, S.E.E. = 0.033, $r = 0.738$ ($P < 0.005$). For bicarbonate, S.E.E. = 0.31, $r = 0.786$ ($P < 0.005$).

FIG. 3.—Total CO₂ immediately after the infusion of equivalent amounts of acetate and bicarbonate. For acetate, S.E.E. = 1.420, $r = 0.877$ ($P < 0.005$). For bicarbonate, S.E.E. = 1.334, $r = 0.926$ ($P < 0.005$).

FIG. 2.—Blood pH three hours after the infusion of equivalent amounts of acetate and bicarbonate. For acetate, S.E.E. = 0.032, $r = 0.715$ ($P < 0.005$). For bicarbonate, S.E.E. = 0.032, $r = 0.728$ ($P < 0.005$).

FIG. 4.—Total CO₂ three hours after the infusion of equivalent amounts of acetate and bicarbonate. For acetate, S.E.E. = 1.121, $r = 0.918$ ($P < 0.005$). For bicarbonate, S.E.E. = 1.012, $r = 0.954$ ($P < 0.005$).

after the infusion of either bicarbonate or acetate. The regression lines with the least square method were calculated and plotted (Figs. 3 and 4).

PCO₂.—After the infusion of acetate as well as of bicarbonate these changes are not significant in either group (Table III).

Analysis of variance comparing the pairs of regression lines obtained after bicarbonate and acetate administration, for pH and total CO₂, showed that the common variances of the two regression lines of acetate and bicarbonate may be regarded as equal and their slopes parallel and identical, because the tests quotients did not attain the significance limits ($P > 0.005$).

TABLE III.—Detailed Results of PCO₂ after Acetate and Bicarbonate Administration

	Partial Pressure CO ₂ (mm. Hg.)							
	Acetate				Bicarbonate			
	A	B	C	D	A	B	C	D
No. of cases	15	15	15	15	15	15	15	15
Mean values	33.79	35.98	36.78	36.28	35.11	38.00	37.34	36.87
S.D.	4.246	2.783	2.792	3.191	4.420	3.399	3.700	4.432
P	—	> 0.05	> 0.01	> 0.05	—	> 0.01	> 0.05	> 0.05

Patients with Liver Disease.—Three non-acidotic patients with severe liver disease were tested with small amounts of sodium acetate intravenously (100 ml. containing 89.2 mEq of acetate). One suffered from cirrhosis, one from chronic hepatitis with splenomegaly, and the third from acute severe jaundice following prolonged extracorporeal circulation for cardiac surgery. All three had high serum bilirubin levels (11–12.9 mg/100 ml.) and high transaminase levels (168, 240, and 1,370 units respectively). In all three there was a significant increase in pH and total CO_2 . The mean rise in pH was 0.093 and the mean rise in total CO_2 was 3.06 mM/l.

Discussion

The results obtained in correcting acidosis due to uraemia in this study compare favourably with those obtained by Cash *et al.* (1969) and Watten *et al.* (1969) in acute acidosis caused by cholera. Thus our study further confirms the conclusions reached by these authors that acetate-containing solutions can be used as an alternative to solutions containing bicarbonate. In a preliminary study of three patients with liver disease acetate solutions have also proved effective in

raising the blood pH and total CO_2 . There were no significant changes in the serum osmolality, serum electrolytes, and blood pressure of the patients with the doses used.

The ready availability of sodium acetate and the ease of its preparation obviously make its use practicable when it is needed in large quantities for the treatment of many patients simultaneously.

Our thanks are due to our biochemists, Messrs. R. Sylten and Y. Nakash, who performed the biochemical determinations.

REFERENCES

- Boen, S. T., Mion, C. M., Curtis, F. K., and Shlipetar, G. (1964). *Transactions. American Society for Artificial Internal Organs*, 10, 409.
 Cash, R. A., Toha, K. M. M., Nalin, D. R., Huq, Z., and Phillips, R. A. (1969). *Lancet*, 2, 302.
 Earnest, D. L., Sadler, J. H., Ingram, R. H., and Macon, E. J. (1968). *Transactions. American Society for Artificial Internal Organs*, 14, 434.
 Mion, C. M., Hegstrom, R. M., Boen, S. T., and Scribner, B. H. (1964). *Transactions. American Society for Artificial Internal Organs*, 10, 110.
 Mudge, G. H., Manning, J. A., and Gilman, A. (1949). *Proceedings of the Society for Experimental Biology and Medicine*, 71, 136.
 Richardson, J. A., and Borchardt, K. A. (1969). *British Medical Journal*, 3, 749.
 Schwartz, W. B., and Waters, W. C. (1962). *American Journal of Medicine*, 32, 831.
 Watten, R. H., Gutman, R. A., and Fresh, J. W. (1969). *Lancet*, 2, 512.

Spirolactone Diuresis in Patients with Cirrhosis and Ascites

RONALD C. EGGERT,* M.D.

British Medical Journal, 1970, 4, 401–403

Summary: Increased aldosterone levels with consequent or diuretic-potentiated electrolyte abnormalities are an important consideration when patients with cirrhosis and ascites undergo diuresis. A simple clinical method using the urinary Na/K ratio as a guide to spironolactone dosage is outlined. Patients with a ratio greater than 1 responded well to 100 mg. of spironolactone a day; those when it was one or less responded well to 200 to 1,000 mg. a day.

Administration of spironolactone alone (11 patients) or as the main diuretic (three patients) was a safe and effective means of inducing sustained uncomplicated diuresis in all these patients.

Introduction

Most patients with cirrhosis and ascites have increased aldosterone secretory rates (Coppage *et al.*, 1962; Ames *et al.*, 1965) which vary considerably from patient to patient. Decreased hepatic inactivation of aldosterone has also been found in cirrhotics (Coppage *et al.*, 1962). These factors cause increased effective aldosterone levels and often lead to sodium retention and appreciable potassium depletion (de Deuxchaisnes *et al.*, 1961; Casey *et al.*, 1965). Further potassium depletion occurs if thiazides or more potent natriuretic agents are given, as these drugs increase the amount of sodium presented to the distal tubule where increased aldosterone levels facilitate the exchange of sodium for potassium; severe electrolyte disturbances may result and may be related to the development of hepatic encephalopathy (Lieberman and Reynolds, 1965; Sherlock *et al.*, 1966).

The spiro lactones are competitive inhibitors of mineralocor-

ticoids (Liddle, 1957). In human studies their natriuretic and potassium-retaining effects can be titrated against the level of circulating mineralocorticoid, the urinary Na/K ratio being used as a guide to effectiveness (Ross, 1962). In most clinical studies of diuresis in patients with cirrhosis fixed and relatively small doses of spiro lactones usually combined with other types of diuretics have been used (Gantt and Ecklund, 1962; Sherlock *et al.*, 1966). If we assume wide variations in aldosterone secretory rates in such patients with ascites, it is reasonable to expect a varying requirement for an aldosterone antagonist during diuresis.

This study was undertaken to assess the value of spironolactone in the treatment of ascites in cirrhosis, the urinary Na/K ratio being used to titrate individual dose. The design was simplified so that it could be conveniently and inexpensively applied in varying clinical situations. Another objective was to use measures, particularly diet, to which the patients could easily adhere after discharge.

Patients and Methods

Fourteen patients with cirrhosis due to chronic alcoholism and persistent ascites were admitted to the general medical wards of the University of Minnesota Hospitals or the St. Paul-Ramsey Hospital. The diagnosis of cirrhosis was based on history, physical examination, and laboratory tests of hepatic function and was confirmed in six cases by liver biopsy.

The patients were observed in hospital for 3 to 54 days before beginning the diuretic regimen. Serious complications, such as infection or haemorrhage, were not present at the time diuresis was undertaken. The patients were maintained on bed rest and weighed daily. The daily diet was not rigidly controlled and contained 45–90 mEq of sodium and 40–80 mEq of potassium. Fluid was restricted to 1 litre per day. Twenty-four-hour urine samples were collected daily until

* Instructor in Medicine, Department of Medicine, University of Minnesota Hospitals, Minneapolis, Minnesota 55455.