BIOCHEMICAL CHANGES IN THE CEREBROSPINAL FLUID AND BLOOD DURING PERITONEAL DIALYSIS FOR URAEMIC ACIDOSIS*

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In certain pathological states, the cerebrospinal fluid (CSF) does not always reflect the varied biochemical changes which may occur in the blood. A good example is metabolic acidosis, in which a constant pH is maintained in the CSF despite acidity of the blood.[1] In addition, clinical manifestations of cerebral dysfunction are often absent in this condition.[2] On the other hand, cerebral dysfunction frequently develops in uraemic patients undergoing correction of their metabolic acidosis by haemodialysis.[3] This has puzzled various workers and has led them to study the biochemical content of the CSF before and during haemodialysis.[4,5] We are unaware of any published results of similar studies in patients undergoing peritoneal dialysis, and present our findings in this regard.

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PATIENTS AND METHODS

Specimens of arterial blood and spinal CSF were obtained from 14 patients with uraemic acidosis undergoing peritoneal dialysis. These specimens were collected immediately before and after dialysis. Not more than 10 minutes elapsed between obtaining the samples of blood and CSF. Peritoneal dialysis was carried out continuously for an average period of 72 hours.

Sodium, potassium, chloride, bicarbonate and urea levels in the blood and CSF and protein levels in the CSF were measured in all 14 cases, and creatinine, uric acid and fasting sugar levels in the blood and CSF in 11 cases. In addition, CSF and anaerobically-collected arterial blood from 8 of the cases were biochemically analysed at the bedside by means of the micro-Astrup apparatus.

In the laboratory, urea, creatinine, uric acid and sugar values were determined by means of the auto-analyser,

and flame photometry was used for the sodium and potassium estimations. The chloride content was ascertained according to the method of Schales and Schales,[6] the CSF protein according to the method of King and Haselwood[7] and the actual bicarbonate according to Van Slyke's volumetric method.

RESULTS

The detailed results are listed in the accompanying tables. The average values obtained are given, together with P values and the standard error of the mean.

Organic Substances

Urea values (Table I) were elevated both in the serum and in the CSF before dialysis, the serum value averaging 27·8 mg./100 ml. (P = 0·002) more than that of the CSF. Both values were decreased by dialysis and the final urea concentration in the serum averaged 11·9 mg./100 ml. (P = 0·02) less than that in the CSF. Predialysis levels of creatinine and uric acid were similarly elevated in the serum and CSF, much more so in the former. Dialysis reduced the concentrations of both these substances, although the final levels remained higher in serum than CSF. The glucose content of the serum and CSF increased during dialysis, being higher in the serum throughout the procedure, but the serum-CSF differences were statistically insignificant. The protein content of the CSF, whether normal or raised beforehand, was reduced by an average of 8·9 mg./100 ml. by dialysis.

Electrolytes

Before dialysis the serum levels of sodium (Table II) were in the low normal range, but the CSF levels were below normal. Both the blood and CSF levels increased during dialysis, though the CSF levels were higher throughout. Predialysis potassium levels were normal in the serum and CSF, but were decreased by the procedure, the serum level by an average of 0·6 mEq./litre and the CSF by an average of only 0·2 mEq./litre. The chloride content of both the serum and CSF was on the low side of normal before dialysis and was further decreased by this procedure. However, the CSF chloride content exceeded that of the serum throughout by 22·9 - 24·5 mEq./litre.

Acid-base Balance

Before dialysis the mean pH of the blood was abnormally low at 7·31, but the pH of the CSF showed the normal value of 7·33 (Table III). Dialysis increased the blood pH markedly to an average alkalotic figure of 7·5, but only increased the CSF pH to 7·34. The predialysis carbon dioxide tensions (PCO_2) in the blood and CSF were below normal levels, the CSF PCO_2 exceeding that of the blood by 5·7 mm.Hg as opposed to the normal discrepancy of 9·6 mm.Hg. Dialysis resulted in an increase in blood and CSF PCO_2, with the final value of the CSF exceeding that of the blood by 10·3 mm.Hg. The amount of actual bicarbonate (Table II) was decreased in both blood and CSF before dialysis, but to a slightly greater extent in the

TABLE I. CHANGES IN BLOOD AND CSF LEVELS OF VARIOUS ORGANIC SUBSTANCES DURING PERITONEAL DIALYSIS (AVERAGE VALUES IN MG./100 ML.)

Substance	No. of cases examined	Blood				CSF				Before dialysis		After dialysis	
		Normal	Pre	Post	Difference	Normal	Pre	Post	Difference	Blood > CSF	CSF > Blood	Blood > CSF	CSF > Blood
Urea	14	20–45	277·8	91·0	−186·8 (40·07) P < ·001	20–45	250·0	102·9	−147·1 (33·47) P < ·001	27·8 (7·64) P = ·002	—	—	11·9 (5·18) P = ·02
Creatinine	11	0·7–1·7	17·1	7·4	− 9·7 (2·49) P = ·001	0·6–1·3	5·4	3·6	−1·8 (0·86) P = ·02	11·7 (2·21) P < ·001	—	3·8 (0·51) P < ·001	
Uric acid	11	3·0–7·5	12·0	6·4	−5·6 (1·21) P < ·001	0·2–0·9	1·8	0·8	−1·0 (0·43) P = ·02	10·2 (1·45) P < ·001	—	5·6 (0·60) P < ·001	—
Fasting sugar	11	80–120	123·8	141·0	+17·3 (8·35) P = ·058	50–90	84·6	112·4	+27·8 (7·27) P < ·001	39·2 P = NS	—	28·7 P = NS	—
Protein	14	—	—	—	—	15–45	48·8	39·9	−8·9 (4·99) P = ·015	—	—	—	—

Normal values obtained from our laboratory. Pre = predialysis; Post = postdialysis; NS = not significant; + = increased during dialysis; − = decreased during dialysis. Standard error of the mean is given in brackets.

TABLE II. CHANGES IN BLOOD AND CSF LEVELS OF VARIOUS ELECTROLYTES DURING PERITONEAL DIALYSIS (AVERAGE VALUES IN mEq./LITRE)

Substance	No. of cases examined	Blood				CSF				Before dialysis		After dialysis	
		Normal	Pre	Post	Difference	Normal	Pre	Post	Difference	Blood > CSF	CSF > Blood	Blood > CSF	CSF > Blood
Sodium	14	134–144	135·1	144·6	+9·5 (2·09) P < ·001	148·5 ±2·8	144·5	148·5	+4·0 (2·08) P = ·05	—	9·4 (2·59) P < ·001	—	3·9 (1·25) P = ·002
Potassium	14	3·5–5·0	4·5	3·9	−0·6 (0·23) P = ·01	2·88 ±0·15	3·1	2·9	−0·2 (·09) P = ·05	1·4 (0·12) P < ·001	—	1·0 (0·16) P < ·001	—
Chloride	14	95–106	97·6	94·5	−3·1 (3·42) P = 0·1	120–130	122·1	117·4	−4·7 (2·81) P = ·09	—	24·5 (3·24) P < ·001	—	22·9 (1·27) P < ·001
Actual bicarbonate	14	20–26	14·6	25·7	+11·1 (1·61) P < ·001	20–35	15·8	20·9	+5·1 (1·42) P < ·001	—	1·2 (0·86) P = 0·1	4·8 (0·57) P < ·001	—

See footnote to Table I. Normal values for CSF sodium and potassium values obtained from Bradbury *et al.*[8] Other values obtained from our laboratory.

TABLE III. CHANGES IN BLOOD AND CSF ASTRUP VALUES DURING PERITONEAL DIALYSIS (AVERAGE VALUES)

Electrochemical value	No. of cases examined	Blood				CSF				Before dialysis		After dialysis	
		Normal	Pre	Post	Difference	Normal	Pre	Post	Difference	Blood > CSF	CSF > Blood	Blood > CSF	CSF > Blood
pH	8	7·414 ±·023	7·31	7·5	+0·19 (·03) P < ·001	7·311 ±0·026	7·33	7·34	+0·01 (0·02) P = NS	—	0·02 (0·03) P = NS	0·16 (0·03) P < ·001	—
PCO_2 mm.Hg	8	38·3 ±1·3	26·6	35·6	+9·0 (1·85) P < ·001	47·9 ±5·7	32·3	45·9	+13·6 (2·83) P < ·001	—	5·7 (2·22) P = ·01	—	10·3 (3·18) P = ·001
Base excess mEq./litre	8	—	−11·6	+3·5	+15·1 (2·31) P < ·001	—	−8·7	−1·6	+7·1 (1·18) P < ·001	—	2·9 (1·62) P = ·05	5·1 (1·12) P < ·001	
Standard bicarbonate mEq./litre	8	—	15·5	26·9	+11·4 (1·63) P < ·001	—	16·7	22·9	+6·2 (1·09) P < ·001	—	1·2 (1·13) P = NS	4·0 (1·08) P < ·001	
Total CO_2 mEq./litre	8	—	14·2	27·5	+13·3 (1·92) P < ·001	—	17·0	24·8	+7·8 (1·21) P < ·001	—	2·8 (1·16) P = ·01	2·7 (1·2) P = ·02	

See footnote to Table I. Normal values for pH and PCO_2 obtained from Posner and Plum.[2] NS = not significant.

blood. It increased in both during dialysis, especially in the blood, where the final level exceeded that of the CSF by an average of 4·8 mEq./litre. The values for base excess, standard bicarbonate and total CO_2 content followed more or less the same pattern as those for the actual bicarbonate.

DISCUSSION

The discussion which follows rests on the assumption that lumbar CSF is representative of the over-all CSF composition.

Organic Substances

The findings during haemodialysis by other investigators[3,5,9] have been confirmed by our results during peritoneal dialysis, in that the urea level is higher in the blood than the CSF before dialysis and higher in the CSF than the blood after dialysis; this implies passive diffusion of urea across the blood-brain barrier. Presumably this and the subsequent osmotic gradient across the blood-brain barrier could lead to cerebral oedema, which Kennedy *et al.*[3,5] regard as the cause of cerebral dysfunction during dialysis. Contrasting with this are the parallel changes throughout dialysis in the serum and CSF concentrations of uric acid, creatinine and sugar. This and their consistently higher levels in the serum suggest that they diffuse with difficulty across the blood-brain barrier into the CSF, especially creatinine and uric acid.

Electrolytes

The relative constancy of the potassium content of the CSF compared with that of the serum, found here during dialysis, has also been noted by Bradbury and his coworkers.[8] This independence of CSF potassium suggests its exact control by an active transport system across the blood-brain barrier. Sodium levels, on the other hand, increase correspondingly in both blood and CSF during dialysis. The persistently higher level of CSF sodium is considered by Bradbury *et al.*[8] to indicate active secretion of sodium ions by the choroid plexus, subject to a measure of control from the serum sodium level. Our findings during peritoneal dialysis indicate that this mechanism continues to function in both metabolic acidosis and alkalosis. CSF and serum chloride values decreased correspondingly during dialysis, indicating the dependence of the former upon the latter. The CSF values appear not to have been affected by the observed increase in actual bicarbonate in the CSF, implying that the chloride shift mechanism may not operate across the blood-brain barrier. Since the CSF protein content decreased during dialysis, it would also be difficult to implicate the Donnan equilibrium as a cause of the decreasing level of CSF chloride.

Acid-base Balance

The constancy of the CSF pH, despite considerable relative acidosis or alkalosis of the blood, demands an explanation. Since carbon dioxide can diffuse freely across the blood-brain barrier, it seems likely that the pH of the CSF is maintained by a shift of bicarbonate or hydrogen ions one way or the other, as the CSF lacks other buffers such as haemoglobin. The changes in bicarbonate content found in the present study favour its diffusion rather than its active transport across the blood-brain barrier (compare with urea). Regrettably, our findings do not permit conclusions regarding the possible active secretion of hydrogen ions by the choroid plexus, or the effect of hydrogen ions on the blood-brain barrier's permeability to bicarbonate.

SUMMARY

Changes in the biochemical content of CSF and blood of 14 patients with uraemic acidosis undergoing peritoneal dialysis are recorded. The results indicate that the CSF pH and potassium levels are maintained actively, independent of serum levels; sodium and chloride are actively secreted into the CSF, the amount, however, being dependent on their respective blood concentrations; creatinine and uric acid diffuse with great difficulty into the CSF; urea and bicarbonate levels in the CSF vary relatively to their serum levels, according to simple diffusional gradients. The relatively slow diffusion of urea out of the CSF during dialysis may well cause the cerebral dysfunction sometimes encountered.

The protective nature of the blood-brain barrier against certain metabolic changes in the blood is confirmed, but some of the physiological mechanisms involved have yet to be elucidated.

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