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Effects of Chronic Hypoxia on Kidney Function

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Renal disfunctions which appear in the chronic respiratory insufficient patient are analysed, as well as the participation of the arterial blood hypoxemia in their genesis. Renal clearances of Na, K, Cl, Ca, Mg and Pi, and those of urea and creatinine, were lower in 36 patients having chronic hypoxemia than in 15 normosemic controls, showing significant statistical differences for Na, K, Cl, Ca and urea. The correlations between the clearances of these substances and the pO_2 arterial blood levels had a greater statistical significance than can be established with pCO_2 or $[H^+]$ levels. Thus, the existence of a causal dependency between renal disfunction and hypoxemia may be deduced.

Key words: Hypoxemia, Renal clearances.

Different authors through animal experimentation (1, 3, 8, 17, 26) have been concerned with hypoxia effects on kidney function; likewise with human beings, considering as experimental situations the effects of acute (10, 13, 14, 29) and chronic (6, 7, 24) respiratory failure. Diuresis and natriuresis decrease is a common feature; morphostructural kidney changes have at times been described (1, 2, 4, 7).

Renal functional disturbances have been considered by some as a direct hypoxemic consequence, but because hypoxemia is frequently associated to hypercapnia and acidosis, other investigators have debated which of these changes could really be the primary source, or at least, the most important one in renal difunction (14, 21-23).

In this direction, a comparison between laboratory data from a control sample of healthy subjects and those of chronic respiratory insufficiency (CRI) affeced patients, in whom renal clearance of sodium, potassium, chloride, calcium, magnesium and inorganic phosphate were determined, along with the urea and creatinine metabolites, could de elucidative.

Materials and Methods

Measurements were made on 51 subjects, 36 of them had CRI and 15 were

healthy. The CRI did not have any other kind of associated pathology, nor were they under a relapsing respiratory phase, or had required the use of medication 15 days prior to the blood sampling, which could alter the renal function or interfere with the biochemical measurements. All of the studied sujects consumed a normal caloric content sodium diet.

Arterial blood samples were obtained by radial punture under a rigorous anaerobic condition; the urine sample was the total 24 h discharged, corresponding to the diuresis of the previous day, until the moment of the blood extraction. The patients were under medical care while the tests were performed.

Arterial gasometry and pH were measured in a Kombi-Analyzator MT-A 100 apparatus (Eschweiler & Co. Kiel), sodium and potassium by flame photometry (Corning EEL 450) and chloride ion by direct potentiometry with silver electrodes (Corning EEL 920). All the remaining parameters were estimated by centrifuge autoanalyser (Gemeni), arranged to the cited techniques (9, 11, 12, 18, 28, 31). All the analyses were done twice. Known samples were included in all series for the quality control, and each one was submitted to the same assay as each problem. Renal clearance values for ions and crystalloids were measured by the Van Slyke's (19) media depuration formula: $Cx = Ux \cdot V/Px$, Cx being the clearance of the x substance, Ux and Px urinary and seric concentrations of the said substance, and V the diuresis in ml/min.

The Mean and SD, Student's «t» test, and Pearson's «r» lineal correlation were .the statistical methods applied to the patients' data.

Results and Discussion

The parameters considered as characteristic for the two studied groups were age, male and female percentage, body surface, and body mass index (BMI). A statistical comparison between these two groups showed no differences, and for this reason they were judged physically alike (table I) and adequate enough, so that the results obtained in the different tests could in turn be subjected to a statistical comparison.

In accordance with CAMPBELL's and SYKES' criteria, those patients with arterial pO_2 lower than 8 KPa at rest, were considered suffering from CRI. There was not a single case of an anomalous cardiovascular shunt in any of the patients (5, 27). The healthy group were patients with normal values of pO_2, pCO_2 and $[H^+]$. Highly significant differences were found between the latter parameters and for those who were CRI affected.

The hypoxemic group had lower renal clearance values for ions and metabolites than the normoxemic group did, with significant differences for sodium, potassium, chloride, calcium and urea (table II). The results obtained in the water, sodium, potassium and calcium excretion were similar to those found by other authors (1, 2, 6, 15, 16, 20, 25, 30), and altohugh the reported bibliographic abnormality for the creatinine clearance (6) was not found, the magnitude of the standard deviations for the creatinine is considered to justify the absence of a sta-

Table I. *Classifications criteria in healthy and pathologic groups.*
Mean of age, body surface and body mass index (B.M.I.) and sex percentage of both groups.

Parameter	Healthy	C.R.I.
pO_2 KPa	> 9.8	> 7.7
Sat. HbO_2 %	> 94	> 90
Age	54.5	65.5
Male %	73.4	77.7
Female %	26.6	33.3
Body surface	1.76	1.72
B.M.I.	24.5	25.1

Table II. *Acid-basic parameters and renal clearances (C) of ions and metabolites (ml/min) in normoxemic and hypoxemic groups.*
Values are the mean ± S.D. Statistical signification between groups of Student's «t» test. N.S.: no significant.

	Normoxemic		Hypoxemic		p <
pO_2 KPa	10.58	0.72	6.64	1.05	0.001
pCO_2 KPa	5.69	0.53	6.79	1.05	0.001
(H^+) nmol/l	39.3	2.10	41.32	3.23	0.01
C_{Na}	0.886	0.148	0.658	0.247	0.001
C_K	12.59	3.20	7.91	2.54	0.001
C_{Cl}	1.251	0.280	0.873	0.350	0.001
C_{Ca}	2.317	1.097	0.914	0.551	0.001
C_{Mg}	4.855	1.654	4.457	2.595	N.S.
C_{Pi}	19.801	7.472	16.093	9.512	N.S.
C_{urea}	42.010	14.86	30.112	12.33	0.01
$C_{creatinine}$	139.98	92.64	101.01	49.77	N.S.

tistical significance when comparing clearances between the hypoxemic and normoxemic groups. In coincidence with some authors, a diminished urea was found (6, 24, 29), but as hyperzotemia was not found, the renal functions seemed to have been preserved in this case. This fact could be interpreted as a secondary one after a decreased endogenous urea production, perhaps due to a lower protein catabolism following the restricted physical activity entailed in the respiratory disease.

Table III. *Lineal correlation Pearson's «r» coefficient values, between acid-basic parameters and renal clearances of ions and metabolites in the total subjects, both normoxenic and hypoxemic (N = 51).*

«r» Pearson	pO_2	pCO_2	$[H^+]$
C_{Na}	0.42	–0.37	–0.25
C_K	0.52	–0.10	–0.25
C_{Cl}	0.43	–0.29	–0.13
C_{Ca}	0.58	–0.31	–0.23
C_{Mg}	0.08	0.07	–0.02
C_{Pi}	0.23	–0.12	–0.34
C_{urea}	0.45	–0.12	–0.05
$C_{creatinine}$	0.26	–0.14	–0.28

Correlation coefficients below r = = 0,37 were found between renal clearances and arterial pCO_2 and $[H^+]$ levels, while those clearances which decreased in the pathologic group showing statistical differences with the control group, had correlation coefficients between 0.42 and 0.58 with the blood pO_2 rate (table III).

From the latter considerations, we may conclude by saying that in the chronic respiratory insufficiency there is a kidney depuration restriction to some ions and metabolites that keep a causal relationship with the oxemia levels and not with the pCO_2 and $[H^+]$ ones.

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Resumen

Se analiza la función renal del insuficiente respiratorio crónico, así como la participación de la hipoxemia arterial en su génesis. Los aclaramientos renales de los iones Na, K, Cl, Ca, Mg y Pi, y de urea y creatinina, son inferiores en 36 pacientes con hipoxemia crónica frente a 15 controles normoxémicos, con diferencias estadísticas muy significativas para el Na, K, Cl, Ca y urea. Las correlaciones entre los aclaramientos de estas substancias y los niveles de pO_2 arterial, son de mayor significación estadística que las obtenidas al correlacionarlos con pCO_2 y $[H^+]$. Se infiere una dependencia causal, en estos pacientes, entre disfunción renal e hipoxemia.

References

1. Anderson, R. J., Pluss, R. G., Berns, A. S., Jackson, J. T., Arnold, P. E., Schrier, R. W. and Donald, K. M.: *J. Clin. Invest.*, **62**, 769-777, 1978.
2. Bermudo, F., Piñero, J., Moreno, J., Jiménez-Castellano, R., Cobo, R. and López-Campos, J. L.: *Rev. Clin. Esp.*, **167**, 219-223, 1982.
3. Bruns, F. J.: *Proc. Soc. Exp. Biol. Med.*, **159**, 468-472, 1978.
4. Campbell, E. J. M.: *Am. Rev. Resp. Dis.*, **96**, 626-639, 1967.
5. Campbell, E. J. M., Claverley, P. M. and Lamb, D.: *Thorax*, **37**, 607-611, 1982.
6. Cruz-Hernández, J., Delpino, J., Sánchez, A., Sánchez, M. and Martínez, J.: *Rev. Clin. Esp.*, **162**, 201-205, 1981.
7. Farber, M. O., Robert, L. R., Weinberger, M. H., Robertson, G. L., Finenberg, M. S. and Manfredi, F.: *Arch. Inter. Med.*, **142**, 1326-1330, 1982.
8. Freeman, H. R., Davis, J. O., Spielman, W. S. and Lohemeier, T. E.: *Am. J. Physiol.*, **229**, 474-478, 1975.
9. Gindler, E. M. and Peth, D. A.: *Clin. Chem.*, **17**, 662, 1971.
10. Granberg, P. O.: *Scand. J. Clin. Invest.*, **14**, 1-62, 1962.
11. Helger, R., Rindfrey, H. and Hilgenfeldt, J.: *J. Clin. Chem. Clin. Biochem.*, **12**, 344, 1974.
12. Henry, J. H.: In «Clinical diagnosis» (Davidsohn and Henry, J. H., eds.), W. B. Saunders, Philadelphia, 1974.
13. Heyes, M. P., Farber, M. O., Manfredi, F., Robertson, G. L., Weinberger, M. H., Finenberg, M. S. and Robertson, G.: *Am. J. Physiol.*, **243**, 265-270, 1982.
14. Kilburn, K. H. and Dowell, A. R.: *Arch. Inter. Med.*, **127**, 754-762, 1971.
15. Kleeman, C. R., Bohannan, J., Bernstein, D., Ling, S. and Maxwel, M. H.: *Proc. Soc. Exptl. Biol. Med.*, **115**, 29-32, 1964.
16. Kleeman, C. R., Ling, S., Bernstein, D., Maxwel, M. H. and Chapman, J.: *J. Clin. Invest.*, **45**, 1032-1037, 1966.
17. Liang, C. S. and Gauras, H.: *Clin. Invest.*, **62**, 961-970, 1978.
18. Maclin, E.: *Clin. Chem.*, **21**, 1004, 1975.
19. Moller, E., Mc Intosh, J. F. and Van Slyke, D. D.: *J. Clin. Invest.*, **6**, 427, 1929.
20. Ortega, M. A., Alvarez, C., Cabezudo, M. A. and Ferreiro, M. G.: *Patol. Ap. Resp.*, **24**, 23-27, 1984.
21. Polak, A., Haynie, G. D., Hays, P. M. and Schwartz, W. B.: *J. Clin. Invest.*, **40**, 1223-1237, 1961.
22. Schwartz, W. B., Brackett, N. C. and Cohen, J. J.: *J. Clin. Invest.*, **44**, 291-301, 1965.
23. Schwartz, W. B. and Cohen, J. J.: *Am. J. Med.*, **7**, 203-213, 1978.
24. Serizady, B.: *Vie Med.*, **15**, 36-49, 1972.
25. Siripaisarnpipat, S., Johnson, J. A. and Kurz, K. D.: *Am. J. Physiol.*, **240**, H2-H8, 1981.
26. Sjostrom, K. and Crapo, J. D.: *Lab. Invest.*, **48**, 68-79, 1983.
27. Sykes, M. K., McNicol, M. W. and Campbell, E. J. M.: Blacwell Scientific Publication, Oxford, 1976.
28. Tiffany, T. O.: *Clin. Chem.*, **18**, 829, 1972.
29. Ullman, E.: *J. Physiol.*, **155**, 417-437, 1961.
30. Walser, M.: *Am. J. Physiol.*, **200**, 1099-1104, 1961.
31. Young, D. S.: *Clin. Chem.*, **21**, 1014, 1975.