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Pulmonary gas exchange during hemodialysis

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Pulmonary gas exchange during hemodialysis. Pulmonary gas exchange was continuously measured in 13 mechanically ventilated patients during 24 hemodialyses for acute renal failure. Minute-ventilation was maintained constant by controlled ventilation and gas exchange was continuously measured by a mass-spectrometer system. Three groups were compared: 1) a cuprophan membrane with an acetate dialysate; 2) a polyacrilonitrile membrane (PAN) with an acetate dialysate; and 3) PAN with a bicarbonate dialysate. Arterial PO_2 and the O_2 alveolar–arterial gradient were the same regardless of the membrane used. $[H^+]$ mildly decreased with all dialysates used. Arterial PCO_2 decreased only with the acetate dialysate. O_2 consumption increased, up to 20 ± 5% of the initial values during hemodialysis, and remained increased during the two hours following the hemodialysis. Respiratory exchange ratio was lower after than before the hemodialysis. In conclusion: 1) the maintenance of a constant minute ventilation prevented hemodialysis induced hypoxemia. 2) $\dot{V}O_2$ increased during hemodialysis.

Hemodialysis (HD) with an acetate dialysate can be responsible for hypoxemia in chronic renal failure. Craddock and co-workers [1] pointed out the role of the dialysis membrane with poor biocompatibility (cuprophan). They suggested ventilation to perfusion ($\dot{V}A/\dot{Q}$) inequalities as the main cause of arterial hypoxemia. Subsequent experimental [2] and clinical [3] studies using inert gas analysis showed that there was no worsening in $\dot{V}A/\dot{Q}$ relationships during HD. Alveolar hypoventilation due to carbon dioxide (CO_2) loss into the acetate dialysate appears, therefore, to be the main factor of arterial oxygenation impairment. When the acetate dialysate is replaced by a bicarbonate one, hypoxemia has also been described [4–6] and attributed to an alveolar hypoventilation secondary to a metabolic alkalosis. However, hypoxemia has also been reported in patients in which alveolar hypoventilation was prevented by mechanical ventilation [7, 8].

Moreover, changes in oxygen consumption ($\dot{V}O_2$) during HD remain a matter of controversy. $\dot{V}O_2$ was found to be decreased [9, 10], unchanged [3, 7, 11–13] or increased [14–16] during HD with an acetate as well as a bicarbonate dialysate. The discrepancies between these findings could have been the result of differences in study design, particularly the choice of patients, the measurement methods, and the time course of data collection.

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The objective of this study was to determine the effect of HD on arterial oxygenation and $\dot{V}O_2$ in mechanically ventilated patients with acute renal failure. Two types of dialysis membrane [cuprophan (cupro) and polyacrilonitrile (PAN)] and two types of dialysate [acetate (Ac), bicarbonate (Bic)] were used. Pulmonary gas exchange was measured continuously by a mass spectrometer system.

Methods

Patients

Thirteen patients (mean age: 60 ± 14 years, range: 28 to 76) treated for acute renal failure and requiring mechanical ventilation were studied. They were hospitalized in our intensive care unit for a neurological disease and/or a severe sepsis (Table 1). At the time of the study, they were mechanically ventilated from six to 11 days and had stable hemodynamic state and core temperature. PaO_2 was above 8 kPa with an FIO_2 under 0.4 in all patients. Patients were given intravenous sedation as necessary to tolerate mechanical ventilation. Siemens' Servo ventilators were used in the control mode for all patients, thus keeping the minute ventilation constant (13 ± 0.8 liter · min^{-1}) and the $PaCO_2$ within the normal range. All patients had central venous and peripheral arterial catheters. During the study, glucose infusion was constant and no lipid solutions were infused.

This protocol was approved by the ethical committee of our institution, and informed consent was obtained from the nearest relatives.

Protocol

Group 1 (Ac Cupro). For patient 1 to patient 8, HD was performed with an acetate dialysate (35 mmoles · $liter^{-1}$) and a cuprophan membrane (parallel flow, 1.4 m^2, Bellco). Two hours before the beginning of HD, the mass spectrometer system was set up for an eight hour period. Hemodynamic parameters were monitored throughout the study and the core temperature was measured three times. Blood samples were taken according to Table 2. Each session of HD, made without loss of weight, lasted four hours. A single pass system (Monitral Hospal or BL714 Bellco) was used. Access to blood was provided by a single venous catheter. Sessions were performed with a double blood pump and with the usual heparinization. The dialysate flow was 500 ml · min^{-1}.

Group 2 (Ac PAN). For the same eight patients, HD was performed with the acetate dialysate and a polyacrilonitrile

Table 1. Patient's clinical characteristics

Patient	Sex	Age	Diagnosis
1	M	76	Head and chest trauma
2	M	76	Hemopathy–sepsis
3	M	47	Head trauma–sepsis
4	M	66	Hemopathy–sepsis
5[a]	F	73	Thoracic surgery–sepsis
6[a]	M	72	Gas gangrene
7[a]	M	56	Quadriplegia–septicemia
8[a]	M	57	Polyneuropathy–septicemia
9	M	60	Choledochal stenosis–septicemia
10[a]	F	64	Colic surgery–septicemia
11	M	43	Septicemia–pneumopathy
12[a]	F	65	Colic surgery–septicemia
13	F	28	Pregnancy–sepsis

[a] Survived.

membrane (parallel flow, 1 m^2, Hospal). All the manipulations were the same as in group 1.

Group 3 (Bic PAN). For patient 6 to patient 13, HD was performed with a bicarbonate dialysate (30 mmoles · $liter^{-1}$) and the polyacrilonitrile membrane. This protocol was the same as for group 1 but no blood cell counts were done.

Measurements and calculations

Blood analysis. The samples for blood gas analysis were collected anaerobically in heparinized plastic syringes and immediately iced. Blood pH, PO_2, and PCO_2 were measured with a Corning 175 (Corning Inc., Midfield, Massachusetts, USA), and hemoglobin concentration and oxygen saturation with a hemoxymeter OSM2 Radiometer. Leukocyte counts and platelet counts were made with a Coulter Counter S plus.

Pulmonary gas exchange studies

$\dot{V}O_2$ and pulmonary CO_2 elimination ($\dot{V}CO_2$) were continuously recorded by a mass spectrometer system (Perkin Elmer MGA 1100, Perkin Elmer Co., Norwalk, Connecticut, USA). Details of this procedure and thorough validation have been given in a previous report [17]. The system can be briefly described as follows. Gas samples were drawn from the Y piece of the patient's breathing circuit to a mass spectrometer and analyzed for inspired O_2 concentration (FIO_2) and CO_2 wave–form recognition. The latter analysis allowed rejection of artifacted cycles, such as coughing. Then, expired gas was sampled from the outlet of a mixing chamber for the measurements of the mixed expired O_2 and CO_2 concentrations. The duration of the whole analysis sequence was about three minutes. Expired flow was measured by a pneumotachometer (Gould Statham Instruments, Hato Rey, Puerto Rico). All the signals were collected by a microcomputer (Kontron) which was programmed to reject artifacted respiratory sequences and to compute $\dot{V}O_2$, $\dot{V}CO_2$, expired minute volume, and end–tidal CO_2 partial pressure ($PETCO_2$).

Calculations

The following formulae were used:

$RE = \dot{V}CO_2/\dot{V}O_2$ RE = respiratory exchange ratio

$(A - a)\,O_2 = PAO_2 - PaO_2$

$(A - a)\,O_2$ = alveolar–arterial gradient in O_2

$$PAO_2 = [PBAR - 6.3]\,FIO_2 - PETCO_2\left[FIO_2 + \frac{1 - FIO_2}{RE}\right]$$

Blood CO_2 contents were calculated using PCO_2 before and after the dialyzer according to Kelman's procedure [18].

The amount of CO_2 extracted by the dialyzer ($\dot{V}CO_2$ dial) was calculated as the product of the blood flow through the dialyzer and the difference between blood CO_2 contents before and after the dialyzer.

$$RQ = \frac{\dot{V}CO_2 + \dot{V}CO_2\ \text{dial}}{\dot{V}O_2} \qquad RQ = \text{Respiratory quotient}$$

Volumes were expressed in BTPS conditions and metabolic parameters ($\dot{V}O_2$, $\dot{V}CO_2$) in STPD conditions.

The results were presented as the means ± SEM and further statistical analysis used one–way analysis of variance and two–way analysis of variance when necessary. Duncan's multiple range test was used for multiple comparisons of means whenever analysis of variance showed significance.

Results

The patients remained hemodynamically stable throughout the study period. No patient was hypotensive. Temperature did not change more than one degree Celsius in any patient. Minute ventilation was constant for each patient.

Group 1. Platelet count did not change. The leukocyte count significantly decreased at the beginning of HD (Fig. 1). PaO_2, $(A - a)O_2$ and $[H^+]$ did not change, and $PaCO_2$ decreased (Fig. 2). As shown in Figure 3, $\dot{V}O_2$ increased during HD whereas $\dot{V}CO_2$ and RE decreased. $\dot{V}O_2$ remained increased after HD. By comparison with the pre-dialysis values, $\dot{V}CO_2$ was unchanged after HD. So, RE decreased after HD. The mean decrease of $\dot{V}CO_2$ during HD was 24 ± 7 ml · min^{-1}. The mean $\dot{V}CO_2$ dial was 63 ± 6 ml · min^{-1}. Therefore, total CO_2 elimination increased by 39 ml · min^{-1}; RQ was 1.06 during HD.

Group 2. Platelet and leukocyte counts did not change (Fig. 1), nor did PaO_2, $(A - a)O_2$ or $[H^+]$ (Fig. 2). Changes in $\dot{V}O_2$, $\dot{V}CO_2$ and RE were parallel to those of group 1 (Fig. 3). The mean decrease of $\dot{V}CO_2$ was 31 ± 7 ml · min^{-1}. The mean $\dot{V}CO_2$ dial was 59 ± 6 ml · min^{-1}. Therefore, total CO_2 elimination increased by 28 ml · min^{-1}; RQ was 1.06 during HD.

Group 3. PaO_2, $PaCO_2$, $(A - a)O_2$ and $[H^+]$ did not change (Fig. 2). $\dot{V}O_2$ increased during and after HD. $\dot{V}CO_2$ remained stable, RE decreased after HD (Fig. 3). There was a small increase of CO_2 in the blood across the dialyzer (5.9 ± 1.9 ml · min^{-1}).

Discussion

During HD for acute renal failure, the maintenance of a constant ventilation prevented hypoxemia no matter which membrane or dialysate was used. The oxygen alveolar–arterial gradient did not increase. These results confirm that the mechanism of hypoxemia during HD in a patient spontaneously breathing must be an alveolar hypoventilation.

As experimentally demonstrated by Phillipson, Duffin and Cooper [19], extra pulmonary excretion of CO_2 by an extra corporeal circuit leads to hypoventilation. This adaptative mechanism, the objective of which is to maintain the $PaCO_2$ level unchanged, is prevented by mechanical ventilation. In our patients, the loss of CO_2 into the acetate dialysate was associ-

Table 2. Timetable of blood samples

	−120	−60	To	+10	+30	+60	+120	+240	+300	+360
Blood gas analysis:										
Arterial		■				■	■	■	■	
Pre-dialyzer						■	■	■		
Post-dialyzer						■	■	■		
Leukocyte count and platelet count		■		■	■	■		■		
Time, *min*			↑ Hemodialysis					↑		
	↑ Mass spectrometer system analysis									↑

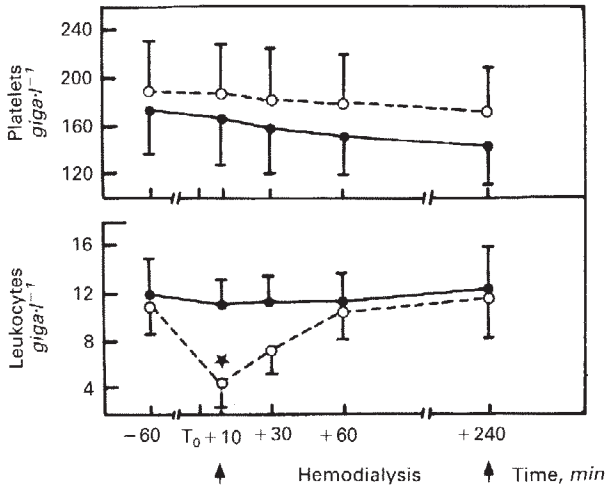

Fig. 1. *Leukocyte count and platelet count during hemodialysis for acute renal failure in mechanically ventilated patients: (○---○) Group 1, Ac Cupro; (●—●) Group 2, Ac PAN.* Values are expressed as the means ± SEM. * significant difference from first value, $P < 0.05$.

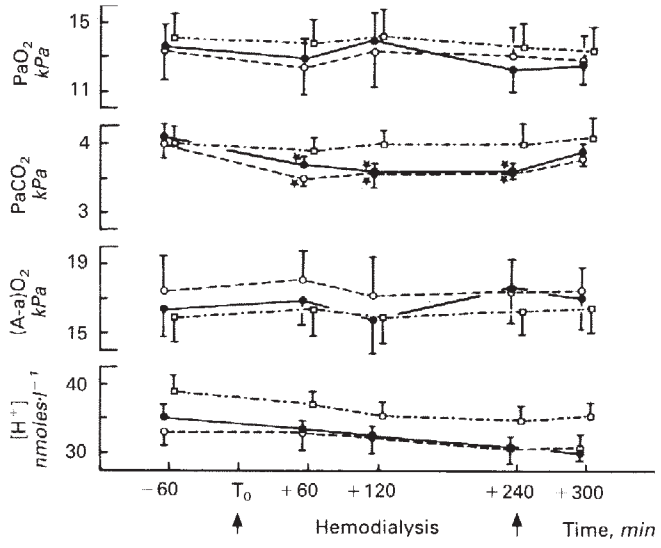

Fig. 2. *Respiratory parameters during hemodialysis for acute renal failure in mechanically ventilated patients: (○---○) Group 1, Ac Cupro; (●—●) Group 2, Ac PAN; (□-·-□) Group 3, Bic PAN.* Values are expressed as the means ± SEM. * significant difference from first value, $P < 0.05$.

ated with hypocapnia, whereas $PaCO_2$ was unchanged during HD with a bicarbonate dialysate.

The lack of hypoxemia during HD was found with both the cuprophan and the polyacrilonitrile membrane. Therefore, leukopenia, which has been observed at the beginning of HD with a cuprophan membrane, was not associated with pulmonary dysfunction. Several studies are in agreement with this result. In mechanically ventilated dogs, Ralph et al did not find hypoxemia using a cuprophan membrane [2]. In human studies, Jacob et al showed that hypoxemia was dependent neither on the membrane, the presence or absence of leukopenia, nor on complement activation [20]. In a study on rabbits, Webster et al demonstrated that complement activation leading to acute leukopenia was an insufficient insult to produce significant lung injury [21]. On the other hand, Carlon et al, in five mechanically-ventilated patients, found hypoxemia and leukopenia [7]. Their patients had a moderate to severe pulmonary impairment (venous pulmonary admixture: 20.9 ± 5.1%) and a complement activation during HD could, in this case, worsen the pulmonary function. Finally, our study permits the conclusion that in acute renal failure patients without major pulmonary injury a difference in membrane biocompatibility has no deleterious consequences on pulmonary function, at least after the first hour of HD.

The increase in $\dot{V}O_2$ was constant for the acetate and bicarbonate dialysates for both membranes. This increase lasted for two hours post-dialysis. The total CO_2 elimination was increased with the acetate dialysate and remained constant with the bicarbonate one. The pH increased mildly with both acetate and bicarbonate dialysates. The increase in $\dot{V}O_2$ and total $\dot{V}CO_2$ with acetate could be due to the oxidation of acetate, which consumes O_2 and produces CO_2 with a RQ of one [22]. During HD, the acetate load approaches the maximal metabolic capacity of acetate (300 mmoles · hr^{-1}) [23] and oxidation of acetate represents up to 40% of the energetic expenditure [22]. But, the metabolism of acetate can not account for all of the increase in $\dot{V}O_2$ since $\dot{V}O_2$ increased also with the bicarbonate dialysate. Alkalosis could be an additional explanation. Indeed, alkalosis has been found to increase $\dot{V}O_2$ [24] and $\dot{V}CO_2$ with a stable RE [25]. Moreover, the increase in

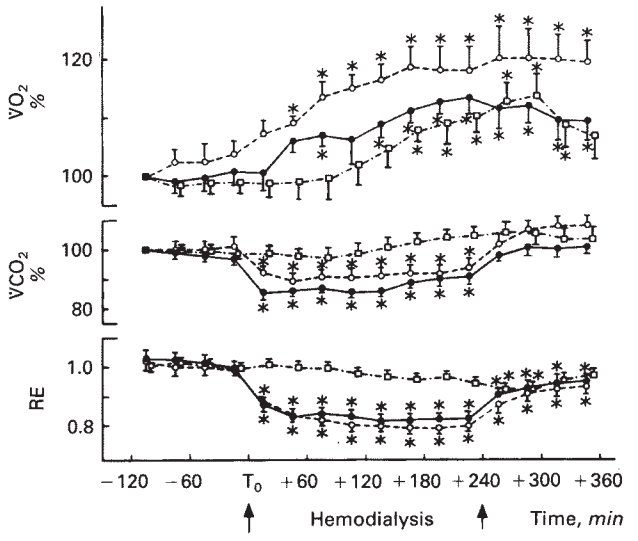

Fig. 3. *Evolution of $\dot{V}O_2$, $\dot{V}CO_2$ and respiratory exchange ratio (RE) during hemodialysis for acute renal failure in mechanically ventilated patients.* Symbols are the same as Fig. 2. Each point of $\dot{V}O_2$ and $\dot{V}CO_2$ is the mean of measurements during thirty min for each patient. Values of $\dot{V}O_2$ and $\dot{V}CO_2$ are expressed as percent of the initial values (means ± SEM). Initial values (ml · min^{-1}) are for Group 1: $\dot{V}O_2$ = 212 ± 8, $\dot{V}CO_2$ = 217 ± 6; for Group 2: $\dot{V}O_2$ = 230 ± 10, $\dot{V}CO_2$ = 235 ± 7; for Group 3: $\dot{V}O_2$ = 226 ± 21, $\dot{V}CO_2$ = 228 ± 21. * significantly different from pre-dialysis values, $P < 0.05$.

$\dot{V}O_2$ is proportional to the degree of alkalosis [26]. Despite these data, the rise in pH, which we found in our patients, was not significant and, thus, could not explain the entire increase in $\dot{V}O_2$. Finally, it is of interest to observe that RE was decreased in the post-dialysis period. This would suggest a dialysis induced change in the quality of metabolized substrates, leading to a lipolysis, and thus to an enhanced $\dot{V}O_2$.

In conclusion, this study showed that: 1) the maintenance of a constant ventilation avoided hypoxemia during HD; and 2) $\dot{V}O_2$ increased during HD.

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References

1. Craddock PR, Fehr J, Brigham KL, Kronenberg RS, Jacob HS: Complement and leukocyte-mediated pulmonary dysfunction in hemodialysis. *N Engl J Med* 296:769–774, 1977
2. Ralph DD, Ott SM, Sherrard DJ, Hlastala MP: Inert gas analysis of ventilation–perfusion matching during hemodialysis. *J Clin Invest* 73:1385–1391, 1984
3. Romaldini H, Rodriguez-Roisin R, Lopez FA, Ziegler TW, Bencowitz HZ, Wagner PD: The mechanisms of arterial hypoxemia during hemodialysis. *Am Rev Respir Dis* 129:780–784, 1984
4. De Backer WA, Verpooten GA, Borgonjon DJ, Vermeire PA, Lins RR, De Broe ME: Hypoxemia during hemodialysis: Effects of different membranes and dialysate composition. *Kidney Int* 23:738–743, 1983
5. Hunt JM, Chappell TR, Henrich WL, Rubin LJ: Gas exchange during dialysis. *Am J Med* 77:255–260, 1984
6. Raja RM, Kramer MS, Rosenbaum JL, Bolisay CG, Krug MJ: Hemodialysis associated hypoxemia. Role of acetate and pH in etiology. *Trans Am Soc Artif Int Organs* 27:180–183, 1981
7. Carlon GC, Campfield PB, Goldiner PL, Turnbull AD: Hypoxemia during hemodialysis. *Crit Care Med* 7:497–499, 1979
8. Jones RH, Broadfield JB, Parsons V: Arterial hypoxemia during hemodialysis for acute renal failure in mechanically ventilated patients: Observations and mechanisms. *Clin Nephrol* 14:18–22, 1980
9. Dolan MJ, Whipp BJ, Davidson WD, Weitzman RE, Wasserman K: Hypopnea associated with acetate hemodialysis: Carbon dioxide–flow–dependent ventilation. *N Engl J Med* 305:72–75, 1981
10. Faro S, Stabile C, Dos Santos ML, Romaldini H, Ratto OR: Central venous blood composition and the pulmonary ventilation during hemodialysis. *Nephron* 41:45–49, 1985
11. Henrich WL, Woodard TD, Meyer BD, Chappell TR, Rubin LJ: High sodium bicarbonate and acetate hemodialysis: Double-blind cross over comparison of hemodynamic and ventilatory effects. *Kidney Int* 24:240–245, 1983
12. Blanchet F, Kanfer A, Cramer E, Benyahia A, Georges R, Mery JP, Amiel C: Relative contribution of intrinsic lung dysfunction and hypoventilation to hypoxemia during hemodialysis. *Kidney Int* 26:430–435, 1984
13. Patterson RW, Nissenson AR, Miller J, Smith RT, Narins RG, Sullivan SF: Hypoxemia and pulmonary gas exchange during hemodialysis. *J Appl Physiol* 50:259–264, 1981
14. Eiser AR, Jayamanne D, Kokseng C, Che H, Slifkin RF, Neff MS: Contrasting alterations in pulmonary gas exchange during acetate and bicarbonate hemodialysis. *Am J Nephrol* 2:123–127, 1982
15. Sherlock J, Ledwith J, Letteri J: Determinants of oxygenation during hemodialysis and related procedures. *Am J Nephrol* 4:158–168, 1984
16. Vaziri NO, Wilson A, Nukai D, Darwish R, Rutz A, Hyatt J, Moreno C: Dialysis hypoxemia: Role of dialyzer membrane and dialysate delivery system. *Am J Med* 77:828–833, 1984
17. Bertrand O, Viale JP, Annat G, Sebes F, Delafosse B, Percival C, Bui Xuan B, Motin J: A mass spectrometer system for long term continuous measurements of $\dot{V}O_2$ and $\dot{V}CO_2$ during artificial ventilation. *Med Biol Eng Comput* 24:174–181, 1986
18. Kelman GR: Digital computer procedure for the conversion of PCO_2 into blood CO_2 content. *Respir Physiol* 3:111–115, 1967
19. Phillipson EA, Duffin J, Cooper JD: Critical dependence of respiratory rhythmycity on metabolic CO_2 load. *J Appl Physiol* 50:45–54, 1981
20. Jacob AJ, Gavellas G, Zarco R, Perez G, Bourgoignie JJ: Leukopenia, hypoxia and complement function with different hemodialysis membranes. *Kidney Int* 18:505–509, 1980
21. Webster RO, Larsen GL, Mitchell BC, Goins AJ, Henson PM: Absence of inflammatory lung injury in rabbits challenged intravascularly with complement-derived chemotactic factors. *Am Rev Respir Dis* 125:335–340, 1982
22. Skutches CL, Sigler MH, Teehan DP, Cooper JH, Reichard GA: Contribution of dialysate acetate to energy metabolism: Metabolic implications. *Kidney Int* 23:57–63, 1983
23. Gonzalez FM, Pearson JE, Garbus SB, Holbert RD: On the effects of acetate during hemodialysis. *Trans Am Soc Artif Int Organs* 20:169–174, 1974
24. Cain SM: Increased oxygen uptake with passive hyperventilation of dogs. *J Appl Physiol* 28:4–7, 1970
25. Khambatta HJ, Sullivan SF: Carbon dioxide production and washout during passive hyperventilation alkalosis. *J Appl Physiol* 37:665–669, 1974
26. Karetzky MS, Cain SM: Effect of carbon dioxide on oxygen uptake during hyperventilation in normal men. *J Appl Physiol* 28:8–12, 1970