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Measurement of oxygen consumption and heat production in plasma from uremic patients on chronic dialysis treatment ☆

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Abstract

The heat production and oxygen consumption of plasma obtained from patients with total renal failure prior to hemodialysis (HD) treatment displayed a positive correlation and showed a significantly ($p < 0.05$) higher rate of both parameters compared with values for plasma from patients on continuous ambulatory peritoneal dialysis (CAPD) treatment. After HD treatment the heat production was significantly ($p < 0.01$) increased and the oxygen consumption significantly ($p < 0.005$) decreased. The thermogenic effect of heparin, after i.v. administration to the uremic patients in order to perform HD treatment and 15 min after a bolus injection, showed a two-fold increase in plasma heat production which could be explained by release of enzymes into the circulation leading to activation of chemical reactions in the blood. Thus, the increased heat production after HD is presumably due to the effect of heparin administration.

Keywords: Calorimetry; Oxygen consumption; Plasma; Uremia

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1. Introduction

The reason for studying the heat production of plasma is that this extracellular liquid is the physiological milieu for the circulating cells and changes in its composition will affect the cells. The uremic plasma, which is characterized by high concentrations of numerous substances not present or detectable in trace amounts in normal plasma [1], has been shown to disturb functions of phagocytic cells [2–5]. In a previous study we have demonstrated that plasma from untreated uremic patients shows a significantly higher heat production compared to normal plasma and that the oxidative heat-producing processes occurring in uremic plasma are correlated to the degree of uremia [6].

These findings prompted us to investigate plasma from patients with end-state chronic renal failure on continuous ambulatory peritoneal dialysis (CAPD) and conventional hemodialysis (HD) treatment with low permeable filters.

The aim of the present study is to investigate by measurement of heat production and oxygen consumption the metabolic changes of plasma from patients with chronic renal failure on dialysis treatment including the effect of heparinization.

2. Materials and methods

Venous blood was collected into vacutainer tubes containing heparin 13 IU cm^{-3} from two groups of uremic patients with end-state chronic renal failure: (a) on CAPD treatment and (b) on regular HD treatment with low permeable dialysis filters. From the latter group blood samples were taken before and after dialysis treatment and before and after heparin infusion. The blood was centrifuged for 10 min at 2500 rpm and the plasma recovered was thereafter recentrifuged at 8000 rpm and 8°C for 20 min in order to obtain cell-free plasma.

2.1. Microcalorimetry

A microcalorimeter of the thermopile heat conduction type 2277 TAM (Thermometrics AB, Sweden) was used. The heat production $P/(\mu W\ cm^{-3})$ of the plasma samples (1 cm^3) was determined under static conditions at 37°C in stainless steel ampoules (1.3 cm^3) for at least 1 h and the peak maximum was read off.

2.2. Oxygen consumption

The kinetics of oxygen consumption was measured polarographically at 37°C by a Clark-type electrode in a Hansatech DW1 oxygen electrode unit (Hansatech, UK). Samples with high oxygen consumption (pre-dialysis) were diluted 1:1 with physiological saline. The oxygen consumption was calculated in mol $O_2\ s^{-1}\ cm^{-3}$, designated VO_2.

2.3. pH measurements

pH measurements were performed on the cell-free plasma samples with a micro electrode unit E 5021 and a PHM 64 pH-meter (Radiometer, Denmark).

2.4. Biochemical analysis

Urea and creatinine were assayed by routine clinical chemistry procedures using a Kodak Ektachem 700 XRC slide analyser.

2.5. Statistics

Numerical data are presented as mean ± standard deviation and group differences were tested by the Student's t-test.

3. Results and discussion

An enhanced thermogenesis of plasma was observed for patients on CAPD as well as on HD, see Table 1. The values of heat production and oxygen consumption from patients on CAPD treatment were found to be similar to earlier presented data from untreated uremics [6]. No correlation was noticed between plasma heat production/oxygen consumption and plasma concentration of urea and creatinine. The difference in plasma heat producton observed between these groups of patients could be explained by the difference in treatment regimes. HD is performed intermittently three times weekly while CAPD is a continuous treatment. Between HD treatments accumulation of metabolic degradation products of higher molecular weight occurred. This could account for the higher plasma heat production compared with that of CAPD patients.

Oxygen consumption and heat production of uremic plasma were significantly correlated ($r = 0.9$). The calorimetric–respirometric ratio, heat production/oxygen consumption, obtained from the experimental measurements is -439 kJ (mol O_2)$^{-1}$ which is in agreement with the thermochemically derived oxycaloric equivalents for some common substrates [7]. Patients on HD show a further increase in plasma heat production and in oxygen consumption as a result of heparinization, Fig. 1. Heparin is used as an anticoagulant to inhibit blood clotting during

Table 1
Heat production, oxygen consumption and pH measurements of uremic plasma are presented as mean ± SD. Group differences are illustrated by $p < 0.05$ *, $p < 0.005$ ** and $p < 0.001$ ***

	pH	P/(μW cm^{-3})	VO_2/(mol O_2 s^{-1} cm^{-3})
CAPD ($n = 8$)	7.6 ± 0.03	2.8 ± 1.5	5.8 ± 3.5
Pre HD ($n = 11$)	7.6 ± 0.04	5.7 ± 2.7 *	9.8 ± 4.2 *
Post HD ($n = 11$)	7.7 ± 0.1	9.0 ± 3.7 **	7.1 ± 2.2 ***

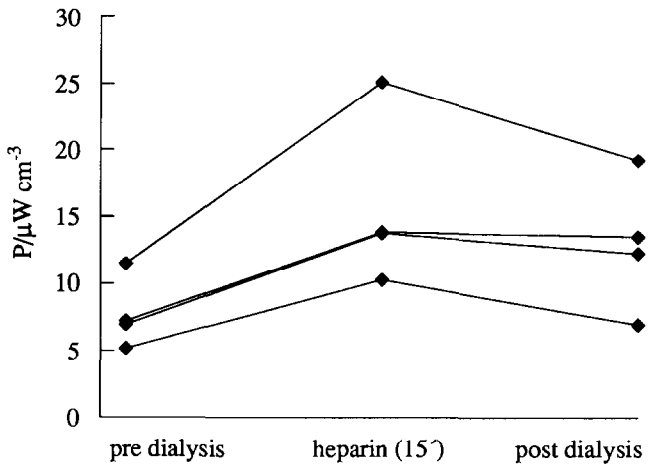

Fig. 1. The effect on the rate of heat production on plasma induced by i.v. administration of heparin followed by HD treatment.

extracorporeal circulation of blood in the artificial kidney. Heparin is known to release enzymes such as lipases and diamino oxidases into the circulation [8]. Thereby exothermic chemical reactions are expected to be induced in the plasma. Increased protein concentration and alkaline pH-shift are other factors which increase plasma heat production after HD.

However, the oxygen consumption is decreased after treatment indicating that HD affects the plasma composition by removing substances which consume oxygen. The different plasma composition between patients on CAPD and HD is partly explained by the intermittent treatments in HD and also by the difference in permeability between the peritoneum and the membrane used in the artificial kidney.

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