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Influence of continuous haemofiltration on haemodynamics and central blood volume in experimental endotoxic shock

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Abstract. In order to asses the influence of continuous haemofiltration (HF) on haemodynamics and central blood volume in endotoxic shock, endotoxinaemia was invoked in 20 swine (28–32 kg). 15 min after doubling the mean pulmonary pressure, the animals were randomly assigned to receive either a zero-balanced veno-venous HF with an ultrafiltration and replacement rate of 600 ml/h (HF group, $n = 10$) or to observe the spontaneous course (E group, $n = 10$) under a constant infusion of endotoxin for 4 h. A trend to a higher survival rate in the HF group (6/10 vs. 3/10; E group) during the observation period was evident, but not statistically significant. Early initiation of HF during endotoxic shock modifies the haemodynamic response, lowering the pulmonary artery pressure (PAP), PCWP, pulmonary (PVR) and systemic vascular resistance (SVR), compared to the spontaneous course, whereas the decrement of central blood volume was comparable in both groups. These changes cannot be explained by effects of the HF on the volume status, but supports and additional effect by the filtration of small and medium-sized molecules.

Key words: Septic shock – Haemofiltration – Haemodynamics – Pulmonary circulation

Continuous haemofiltration (HF) for treatment of acute renal failure is a well accepted method in intensive care medicine [1–4], especially in cases of sepsis and septic shock [1, 2, 5], maintaining haemodynamic stability by smooth, precise regulation of volume status [1–4]. In addition, appropriate pharmacological therapy and parenteral nutrition without the necessity of fluid restriction are of major importance. The early initiation of this invasive therapy may improve haemodynamic data and the overall survival rate, as reported in anecdotal clinical [2, 5] and experimental studies [6]. This suggests that HF represents, in this situation, not only an adequate renal replacement therapy but is a therapeutic approach in its own right with beneficial influence on haemodynamics due to its capacity to filtrate small and medium-sized molecules [5, 6].

The porcine endotoxic shock model mimics several important aspects of human sepsis [6–12]. Using a zero-balancing technique with a simultaneous high ultrafiltration – and replacement rate, we considered it suitable for investigating whether HF in endotoxic shock has any effect on central blood volume, on pulmonary and systemic haemodynamics and on the survival rate, compared to the spontaneous course.

Materials and methods

The experimental protocol described here was approved by the Administrative Government in Tübingen, FRG (reg. no. 339).

Anasthesia procedures and preparation

Twenty domestic pigs (28–32 kg body weight, 16 weeks old) were premedicated with azaperone (3 mg/kg IM) and atropine (0.08 mg/kg IM). The trachea was intubated after sedation with metomidate (5 mg/kg IV) and buprenorphine (0.6 mg IV) and continuous positive pressure ventilation commenced (FiO_2: 0.4, PEEP 3 cmH_2O, breaths/min: 24–28, minute volume: 9–10 l/min). The respiration mixture consisted of N_2O and O_2 during preparation, and of air and O_2 during the observation period. Anaesthesia was maintained during the preparatory period by continuous administration of metomidate (2.5–5 mg/kg/h IV), and during the observation period by a reduced dose of metomidate (0.2–0.7 mg/kg/h IV), controlled by EEG monitoring (Neurotrac, Interspec Inc., Cronskohocken, USA).

A 7F catheter and a thermistor probe for monitoring cardiac output (CO) were inserted into the aortic arch, and a 5F fiberoptic probe (PV 2024 FO-TD, Cold System, Pulsion, Munich, FRG) advanced to the level of the diaphragm (45 cm proximal to the femoral artery). A 5F flow-directed, thermistor-equipped catheter was situated in the pulmonary artery, and another 7F catheter placed into the right atrium. A silicon tube (ID 4.5 mm) served as an HF catheter for drawing blood from the right femoral vein; the blood was returned via a silicon catheter (ID 3.45 mm) to the external jugular vein. A suprapubic catheter was inserted to drain urine. ECG and rectal temperature were monitored contiuously in all animals.

CO was determined by thermodilution (Cardiac Output Computer HMV 7905, Hoyer, Bremen, FRG) using the thermistor in the pulmo-

nary artery, simultaneously with the assay of central blood volume (CBV) by the thermodye technique using Indigozyanin green (Cardiogreen®, 0.25% in 10 ml Water at 1–1.5 °C).

CBV as the distribution volume of the injected dye (Indigozyanin green) between the right atrium (site of injection) and tip of the fiberoptic probe in the aorta at diaphragm level (signal perception), using a hemoreflectometer (IVH® 4, Schwarzer, FRG; computer: Cold System with software Z 02®, Pulsion, Munich, FRG), was calculated by the formula [13]: $CBV = CO \times MTT_{dye}$.

Experimental protocol

After baseline data had been obtained, all animals ($n = 20$) were given E. coli endotoxin (0.111 : B4, Difco Lab., Detroit, USA) by continuous central venous infusion. Starting with 2 µg/kg/h, dosage was augmented at 10-min-intervals by 2 µg/kg/h until the haemodynamic endpoint of doubling the mean pulmonary artery pressure was achieved (designated time $1/PAP_{max}$). Thereafter the prevailing infusion rate was reduced by half, and this dosage maintained for another 4 h until the end of the experiment. 15 min after the pulmonary artery pressure levelled off the animals were randomly assigned to two groups either to observe the spontaneous course (defined as E group, $n = 10$) or to undergo a continuous veno-venous haemofiltration (HF) until the end of the experiment (defined as HF group, $n = 10$).

"Zero-balanced" HF was performed by ultrafiltration of 600 ml/h and concurrent replacement of a Ringer's lactate solution (600 ml/h, SH 01, Schiwa, Glandorf, FRG) via two infusion pumps, as described recently [14] and using a HF pump (NFG 05 SN, Dialysetechnik, Karlsruhe, FRG) and a polysulfone haemofilter (AV 400, Fresenius, Oberursel, FRG, inulin sieving coefficient: 0.99) at a blood flow rate of 50 ml/min. Monitoring of haemodynamic variables and sampling of arterial and mixed venous blood for analysis of blood gases, O_2 saturation and haemoglobin (IL 1302, IL 282, Instrumentation Laboratories, Lexington, USA) and metabolic variables (plasma lactatic acid level; Lactatanalyser 640, Roche, Schweiz; plasma glucose; GOD-perid-method) were done first to obtain baseline data, at time $1/PAP_{max}$, and thereafter at hourly intervals (designated time 2 to 5) until the end of the experiment. The total amount of blood withdrawn averaged 120 ml in each animal. All animals were given 7 ml/kg/h LV of Ringer's lactate solution for the duration of the experiment without further application of colloid solutions. Severe hypoglycaemia (< 3.0 mMol/l) occurred in 2 animals (1 E group, 1 HF group) and was treated with additional administration of glucose 40% solution (10–15 ml/h).

Calculations and statistics

Oxygen delivery (DO_2) and arterio-venous oxygen difference (a-v DO_2) were calculated from standard equations and systemic and pulmonary vascular resistance from: $SVR = MAP\text{-}RAP/CO \times 79.9$ and $PVR = PAP\text{-}PCWP/CO \times 79.9$. The SAS program (SAS® System, Carey, USA) was used for statistical analysis, performing analysis of variance with repeated measurements (ANOVA procedure), the *t*-test for independent paired data from both groups and Mann–Whitney's *U*-test for nonnormally distributed data. $p < 0.05$ was regarded as significant. Means and standard deviation are given. Because of the small number of surviving animals in the E group at the end of the experiment (time 5, $n = 3$), only the descriptive statistics are given.

Results

Table 1 shows the endotoxin dosage and the period in which pulmonary artery pressure doubled (designated time $1/PAP_{max}$), defined as the haemodynamic endpoint of the endotoxin priming. Cumulative metomidate dosage for the preparatory and observation periods is also presented.

The survival rate in the HF group was higher both at time 4 (8/10 animals in the HF group vs. 5/10 in the E group) and the end of the experiment, defined as time 5 (6/10 HF vs. 3/10 E). Statistical analysis showed no significant difference between both groups, however.

Table 1. Mean ± SD of the endotoxin infusion rate, cumulative endotoxin dose during the priming period and the total observation period, duration of the priming time (period from basal pulmonary artery pressure to PAP_{max}) and cumulative dose of metomidate during preparation and observation period

	E-group	HF-group
Endotoxin infusion rate [µg/kg/h]	3.8 ±0.8	3.5 ±0.5
Endotoxin – total cumulative dose – [µg]	497.7 ±211	503 ±170
Endotoxin – priming cumulative dose – [µg]	90.9 ±56.3	72.9 ±37.6
Priming time [minutes]	36 ±9	34 ±6
Metomidate – cumulative dose preparation – [mg/kg/h]	3.81 ± 1.4	3.46 ± 1.2
Metomidate – cumulative dose experiment – [mg/kg/h]	0.38 ± 0.22	0.4 ±0.33

Systemic haemodynamics

Table 2 summarises the effects of continuous endotoxin infusion on mean arterial pressure (MAP), oxygen delivery (DO_2), arterio-venous oxygen difference (a-v DO_2) and plasma lactic acid level. Two of the three surviving pigs in the E group showed less decrease in MAP, a-v DO_2 and plasma lactic acid level so that this positive selection could explain the amelioration of these parameters from time 4 to the end of the experiment (time 5). Endotoxinaemia was accompanied by an increased haemoglobin concentration (Hb) in all animals at time $1/PAP_{max}$ (Table 2). After initiation of HF, Hb dropped in the HF group towards initial levels, becoming significantly lower at time 4 ($p < 0.05$). Cardiac output (CO), the course of which is shown in Fig. 1, fell more slowly in the HF group, and was significantly higher at time 4 ($p < 0.05$). Stroke volume (SV) showed the same time course and difference at time 4 (Table 2). The course of systemic vascular resistance (SVR) is illustrated in Fig. 2. In the E group it is biphasic, with an initial increment during endotoxin priming (until time $1/PAP_{max}$), followed by a decrease to initial levels, reflecting the marked hypotension at time 2 (1 h after time $1/PAP_{max}$). The large CO decrement compared to that of MAP leads to a progressive increase of SVR after time 2. Following initiation of HF, the HF group showed constant SVR values until the end of the experiment; levels were significantly lower than those in the E group at times 3 and 4 ($p < 0.05$).

Central blood volume and pulmonary haemodynamics

Figure 3 shows a significant decrement of CBV to 62% (E group) and 60% (HF group) at time 2, as compared to the baseline data (22.7 ± 2.5 ml/kg b.w. for the E group,

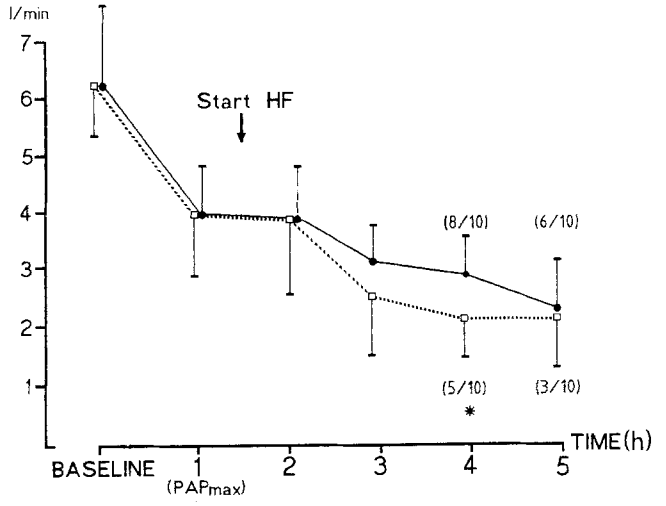

Fig. 1. Cardiac output during the stages of the experiment. Time $1/PAP_{max}$ is approximated as hour 1 of endotoxinaemia (51 ± 12 min). E group ($n = 10$) = endotoxin-treated group (□), HF group ($n = 10$) = haemofiltrated and endotoxin-treated group (●). Statistical significance (E/HF) *: $p < 0.05$

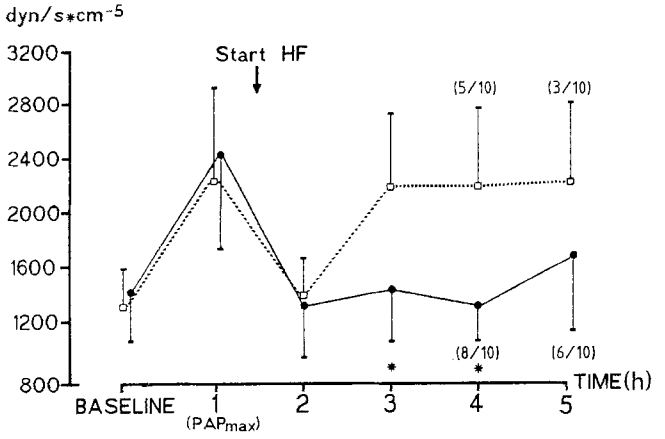

Fig. 2. Systemic vascular resistance (SVR) during the stages of the experiment. E group ($n = 10$) = endotoxin-treated group (□), HF group ($n = 10$) = haemofiltrated and endotoxin-treated group (●). Statistical significane (E/HF) *: $p < 0.05$

21.8 ± 2.5 ml/kg for the HF group). HF did not cause any other changes in CBV.

The course of mean pulmonary artery pressure ($\overline{PAP}$), pulmonary capillary wedge pressure (PCWP), and pulmonary vascular resistance (PVR) are depicted in Figs. 4–6. Once the endpoint for terminating endotoxin priming was reached ($\overline{PAP}$ 47.4 ± 6.9 mmHg for the E group and 46.8 ± 4.2 mmHg for the HF group), $\overline{PAP}$, PCWP and PVR showed a biphasic course with a decrement (time 2) followed by a renewed progressive augmentation until the end of the experiment. After the initiation of zero-balanced HF these variables remained consistently lower in the HF group, significant differences being observed for $\overline{PAP}$ at time 2 and 3 ($p < 0.05$), for PCWP at time 2 and 4 ($p < 0.05$) and PVR at time 3 (HF started 45 min before time 2 in HF group).

In addition, the ANOVA within each group (baseline, time 1–5) showed statistically significant differences in the time course of PAP, PCWP, PVR, CO, stroke volume and SVR between the two groups, corresponding to the described differences per point of measurement.

Discussion

Human septic shock requires the early and simultaneous application of different therapeutic approaches to counteract the dynamics of this life-threatening illness and to improve the still high mortality rate. The benefit of basic therapeutic principles such as fluid resuscitation [2, 8, 11] and the use of catecholamines is well understood and the need for it has been demonstrated in our experiments by the course of CBV, MAP and CO. Since sepsis and septic shock represents the main cause of acute renal failure in intensive care medicine [1, 2, 4, 15], procedures each as

Table 2. Mean ± SD of mean arterial pressure (MAP), stroke volume (SV), oxygen delivery (DO_2), arterio-venous oxygen difference (av DO_2), plasma lactic acid level (Lactate) and hemoglobin (Hb) during the stages of the experiment

Time	Group	MAP [mmHg]	SV [ml]	DO_2 [ml/Min]	av DO_2 [ml/dl]	Lactate [mMol/L]	Hb [g/dl]
Baseline before Endotoxin	E	103.8 ± 15.8	43.4 ± 8.0	780 ± 153	3.7 ± 0.9	4.0 ± 2.3	9.3 ± 0.9
	HF	107.2 ± 13.3	46.6 ± 7.1	800 ± 155	4.0 ± 0.6	3.5 ± 2.5	9.6 ± 0.9
$1/PAP_{max}$ before HF	E	109.0 ± 19.6	28.9 ± 8.8	590 ± 143	6.8 ± 2.7	3.8 ± 1.7	11.3 ± 1.0
	HF	116.4 ± 10.0	30.3 ± 5.3	599 ± 95	6.8 ± 1.4	3.4 ± 2.0	11.4 ± 1.0
2 (30′ HF)	E	65.7 ± 15.6	21.5 ± 4.6	558 ± 141	6.2 ± 2.5	5.3 ± 1.2	11.1 ± 1.2
	HF	61.9 ± 12.2	21.4 ± 7.6	539 ± 134	6.1 ± 0.9	5.3 ± 1.5	10.5 ± 0.8
3 (90′ HF)	E	63.6 ± 15.9	11.6 ± 4.6	364 ± 154	8.6 ± 2.5	8.2 ± 3.7	11.5 ± 1.2
	HF	55.1 ± 10.2	15.6 ± 3.6*	431 ± 77	7.7 ± 2.0	8.4 ± 2.2	10.6 ± 0.8
4 (150′ HF)	E (n = 5)	58.8 ± 15.8	12.3 ± 2.3	363 ± 63	9.3 ± 2.3	8.9 ± 3.4	11.7 ± 1.1
	HF (n = 8)	48.1 ± 11.1	15.5 ± 6.9	389 ± 83	8.5 ± 2.3	9.9 ± 2.3	10.4 ± 1.0*
5** (210′ HF)	E (n = 3)	64.6 ± 14	13.6 ± 5.9	337 ± 145	7.5 ± 2.4	5.5 ± 4.3	10.7 ± 1.3
	HF (n = 6)	43.3 ± 11.7	10.0 ± 4.7	303 ± 58	9.3 ± 1.9	11.6 ± 3.2	10.5 ± 1.2

E group: endotoxinaemia, spontaneous course; HF group: endotoxinaemia, treated with HF. Statistical significance between the two groups
* $p < 0.05$
** No statistical calculations were performed because of the low number of surviving pigs in the E group

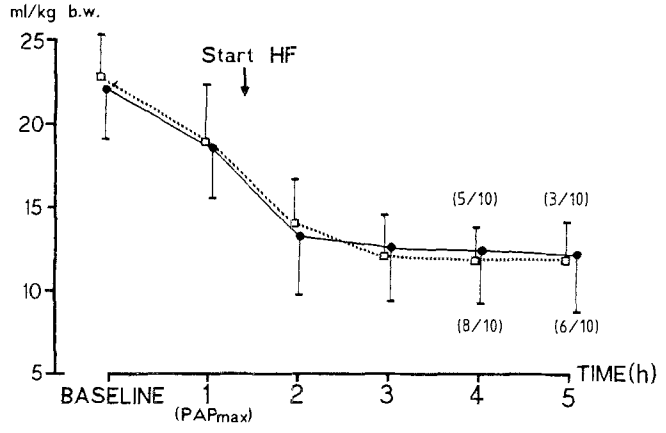

Fig. 3. Central blood volume (CBV) during the stages of the experiment. E group ($n = 10$) = endotoxin-treated group (□), HF group ($n = 10$) = haemofiltrated and endotoxin-treated group (●)

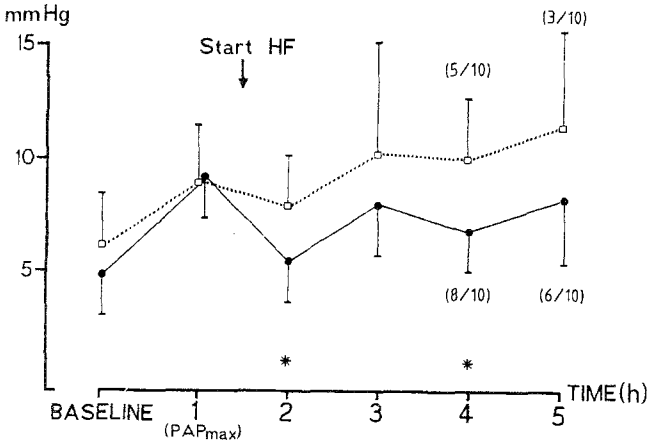

Fig. 5. Pulmonary capillary wedge pressure (PCWP) during the stages of the experiment. E group ($n = 10$) = endotoxin-treated group (□), HF group ($n = 10$) = haemofiltrated and endotoxin-treated group (●). Statistical significance (E/HF) *: $p < 0.05$

continuous haemofiltration are essential to replace partially excretory renal function [1–4] and to "clear the way" for curative therapy. Its interference with the dynamics of the haemodynamic status in sepsis is an important problem in intensive care medicine [1, 2], but hardly investigated until now. The question of whether it has an influence on haemodynamics in endotoxic shock on its own required two methodical considerations in our model. Firstly, prior to initiation of HF a definable haemodynamic change due to endotoxin had to be present. For this purpose we selected pulmonary hypertension as an appropriate target [7, 8, 10, 11]. Doubling of the mean pulmonary pressure produces a profound haemodynamic and pulmonary endotoxic effect, as Lava demonstrated [9]. The necessary titration of endotoxin infusion rate to achieve this haemodynamic point produced small inter-individual differences in the dosage of endotoxin and the duration of the priming period without any difference between the two groups (Table 1). Secondly, no changes in volume status, which fluctuates rapidly in sepsis [8, 11, 16] should be caused by the HF itself. This requirement was met by the "zero-balanced" technique with simultaneous and identical rates of ultrafiltration and replacement, controlling the prescribed ultrafiltration rate by a new balancing device [14]. This experimental approach was necessary to avoid the interference of two different therapeutic principles, ultrafiltration and fluid resuscitation, with the implication that a hypodynamic state of endotoxic shock was produced in which diminished CBV and cardiac filling contributed to the decrement of cardiac output. In consequence, our model is in contrast to the hyperdynamic shock with lowered SVR and high CO seen in septic patients [16–18] or in other endotoxic shock models [8]. The latter reflects the therapeutic goal to improve as soon as possible cardiac filling by massive fluid resuscitation [8, 16].

Use of metomidate drip anaesthesia in endotoxic shock poses some problems. Modig [10] reported detrimental effects on haemodynamic and metabolic variables and on the survival rate, probably by impairing adrenal

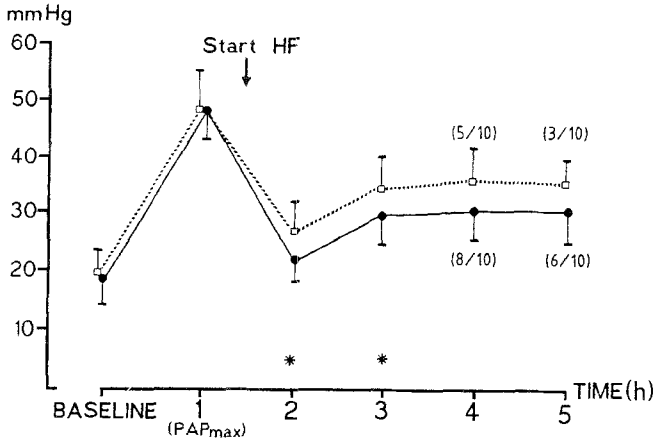

Fig. 4. Mean pulmonary artery pressure (PAP) during the stages of the experiment. E group ($n = 10$) = endotoxin-treated group (□), HF group ($n = 10$) = haemofiltrated and endotoxin-treated group (●). Statistical significance (E/HF) *: $p < 0.05$

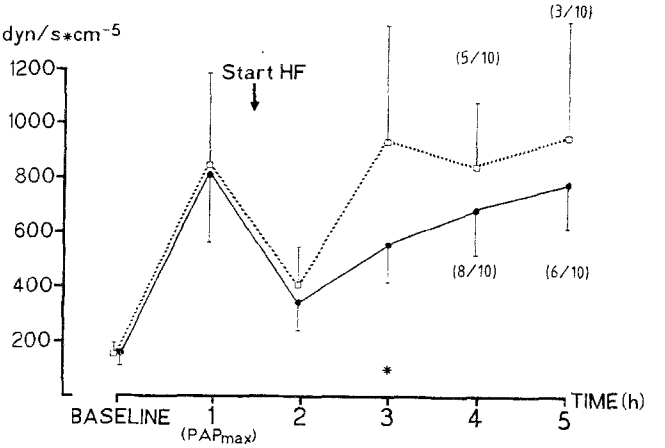

Fig. 6. Pulmonary vascular resistance (PVR) during the stages of the experiment. E group ($n = 10$) = endotoxin-treated group (□), HF group ($n = 10$) = haemofiltrated and endotoxin-treated group (●). Statistical significance (E/HF) *: $p < 0.05$

function. After reducing the overall dosage to 3–4% of that described by Modig, we believe its influence on haemodynamics and mortality to be negligible in our model. This reduction was not merely justified, but necessary, as indicated by the EEG derived in all animals (unpublished data, Pfenninger et Stein).

The most substantial result of this study was that the process of ultrafiltration in HF in endotoxic shock is not haemodynamically inert, but leads to a lowering of PAP, PCWP, PVR and SVR, as we were able to show. Although there is no overall benefit of "zero-balanced" HF in terms of survival rate, describing only a trend to a higher survival rate of the animals undergoing HF (6/10 vs. 3/10 in the spontaneous course), and of oxygen delivery and metabolic parameters, the demonstrated modification of haemodynamic parameters may be of interest.

In contrast to previous experiments [6, 19] and clinical studies [5], describing a favourable influence of HF on haemodynamics and outcome of sepsis, the design of the study and the identical decrement of CBV in the two groups exclude an additional effect of "zero-balanced" HF on the intravascular volume in this endotoxin shock model. The lowering of SVR, PAP and PCWP in the haemofiltrated animals is in contrast to the observations in healthy [20] or uraemic persons [20, 21] with a rise in SVR after initiation of HF and not comparable to the decrement of PAP and PCWP caused by HF in other disorders such as uraemia [20, 21], cardiogenic shock [22] or septic ARDS [5], attributed to negative balancing.

These data support the hypothesis that ultrafiltration per se may induce an alteration of haemodynamic response by the convective elimination of mediators formed in endotoxic shock via the ultrafiltrate [5, 6, 22]. Following initiation of HF in a porcine endotoxic shock model, Staubach [6] found the ultrafiltrate to contain thromboxane A_2 and PG I_2, whereas plasma levels of these arachidonic acid metabolites decreased. In a non-controlled study involving observations of several septic patients on whom HF was performed, Gotloib [5] observed favorable responses of MAP, CO, PAP and an improved outcome; he related this to the presence of thromboxane A_2, PG I_2, bradykinin and beta-endorphine [5] in the ultrafiltrate. Although proof is still awaited, the size of the molecules make it likely that additional mediators of importance in human sepsis or in endotoxic shock models, e.g. leucotrienes [12], platelet aggregating factor [23], interleukin 1 or α-TNF [24] and myocardial depressive substances [22, 25] are eliminated by convective transport.

In particular, the investigation of Kühl [26], demonstrating that thromboxane A_2 is essentially involved in the early pulmonary response to endotoxin, suggests that the described lowering of PAP, PCWP and PVR by HF represent a diminished pulmonary vascular damage. These alterations may affect the development of permeability edema [9], lymphatic drainange from the lungs [26], afterload of the right ventricle [27], compliance of the left ventricle [27] and interfere with changes in lung mechanics during endotoxinaemia [26]. The decrement of SVR as an altered relation between CO and MAP could be the expression of a better myocardial performance, indicated by the higher values for CO and stroke volume in the HF group. The continuous increment of PCWP in the spontaneous course mitigated by HF and the identical decline of CBV in both groups underline these interpretations, but no conclusive answer can be given by our data.

In conclusion, regarding the limited application of animal experimental findings in this model of hypodynamic endotoxic shock to human patients and the cautious interpretation of our data due to the small number of animals studied, clinical relevance could be seen in three aspects: (1) There is evidence of haemodynamic effects of HF in endotoxic shock which are independent of an influence on the intravascular volume status and may be attributed to the ultrafiltration of small and medium sized molecules, (2) The modification of haemodynamic parameters such as PAP, PCWP and SVR by the process of ultrafiltration, representing essential parameters for the regulation of the therapy with fluids and catecholamines, should be regarded in their clinical interpretation during HF and sepsis and (3) Our data ensure that early initiation of a "zero-balanced" HF with a high ultrafiltration rate aggravates neither the hypodynamic status of an endotoxic shock nor the metabolic response, compared to the spontaneous course, favouring the early installation of this therapy before established renal failure. The question whether this procedure improves outcome and the changes described in SVR and pulmonary haemodynamics are related to the higher survival rate cannot be explained conclusively, showing only a trend for a better outcome of the haemofiltrated animals.

The modification of haemodynamic measurement data by this model of a "zero-balanced" haemofiltration as a new experimental approach may represent a link betwen the evidence of endotoxin generated mediator substances in the ultrafiltrate [5, 6] and their lowering by the haemofiltration procedure [6] and the improvement of haemodynamics and outcome in some clinical studies [1, 2, 5]. The described modification of SVR and pulmonary haemodynamics by the ultrafiltration process should stimulate further investigation, concerning the impact of the early initiation of this important procedure in intensive care medicine on clinical course and outcome of sepsis and septic shock in man.

References

1. Mauritz W, Sporn P, Schindler I, Zadrobilek E, Roth E, Appel W (1986) Akutes Nierenversagen bei abdomineller Sepsis – Vergleich von Hämodialyse und kontinuierlicher arteriovenöser Hämofiltration. Anästh Intensivther Notfallmed 21:212–217
2. Simpson K, Allison M (1988) Acute renal failure – continuous ultrafiltration and bicarbonate haemodialysis (CUPID). Intensive Care World 5:83–84
3. Schetz M, Lauwers PM, Ferdinande P (1989) Extracorporeal treatment of acute renal failure in the intensive care unit: a critical view. Intensive Care Med 15:349–357
4. Wendon J, Smithies M, Sheppard M, Bullen K, Tinker J, Bihari D (1989) Continuous high volume venous-venous haemofiltration in acute renal failure. Intensive Care Med 15:358–363

5. Gotloib L, Barzilay E, Shustak A, Wais Z, Jaichenko J, Lev A (1986) Hemofiltration in septic ARDS. The artifical kidney as an artificial endocrine lung. Resuscitation 13:123–132
6. Staubach KH, Rau HG, Kooistra A, Schardey HM, Hohlbach G, Schildberg FW (1988) Can Hemofiltration increase survival time in acute endotoxinemia – a porcine shock model. Abstract: 2nd Vienna Shock, Forum, May 11–14, 1988, Vienna, Austria, p 69
7. Borg T, Alvfors A, Gerdin B, Modig J (1985) A porcine model of early adult respiratory distress syndrome induced by endotoxinaemia. Acta Anaesthesiol Scand 29:814–830
8. Kreimeier U, Gerspach S, Veitinger K, Neuhof H, Meßmer K (1988) Hyperdyname Endotoxinämie – Mikrozirkulationsstörung und Eicosanoide. In: Schriefers KH (ed) Chirurgisches Forum 88 für experimentelle und klinische Forschung. Springer, Berlin Heidelberg New York, pp 291–295
9. Lava JS, Rice CL, Levine HA, Moss GS (1982) Extravascular lung water as a function of the magnitude of pulmonary artery pressure in the septic pig. J Surg Res 32:440–447
10. Modig J (1987) Positive effects of Ketamine versus Metomidate anesthesia on cardiovascular function, oxygen delivery and survival. Acta Chir Scand 153:7–13
11. Modig J (1988) Comparison of effects of dextran-70 and Ringers acetate on pulmonary function, hemodynamics and survival in experimental septic shock. Crit Care Med 16:266–271
12. Ball HA, Cook JA, Wise WC, Halushka PV (1986) Role of thromboxane, prostaglandins and leukotrienes in endotoxic and septic shock. Intensive Care Med 12:116–126
13. Pfeiffer UJ (1987) Das intrathorakale Blutvolumen als Leitparameter zur Blutvolumenregulation in der Intensivmedizin. Habilitationsschrift, Technische Universität München, 1987
14. Stein B, Maucher H, Wiedeck H, Born B, Ahnefeld FW (1989) Die Steuerung der Ultrafiltrationsrate als Hauptkomponente eines neuen Bilanzierungssystems während kontinuierlicher Hämofiltration. Anaesthesist 38:536–538
15. Wardle N (1982) Acute Renal Failure in the 1980's: the Importance of Septic Shock and of Endotoxinaemia. Nephron 30:193–200
16. Houtchens BA, Westenkow DR (1984) Oxygen consumption in septic shock. Circ Shock 13:361–384
17. Groeneveld ABJ, Nauta JJP, Thijs LG (1988) Peripheral vascular resistance in septic shock: its relation to outcome. Intensive Care Med 14:141
18. Bond RF (1985) Peripheral circulatory responses to endotoxin. In: Proctor RA (ed) Handbook of endotoxin, vol 2. Pathophysiology of endotoxin. Elsevier, Amsterdam New York, pp 36–75
19. Magilligan DJ (1985) Effects of ultrafiltration on lung water. In: Sieberth HG, Mann H (eds) Continuous arteriovenous hemofiltration (CAVH). Karger, Basel München, pp 80–95
20. Baldamus CA (1986) Hemodynamics in hemofiltration. In: Henderson LW, Quellhorst EA, Baldamus CA, Lysaght MJ (eds) Hemofiltration. Springer, Berlin Heidelberg New York, pp 155–200
21. Vagge R, Cavatora F, Queirelo C, Rosselli P, Gentile A, Bertulla A (1988) Hemodynamic changes during acetate dialysis, bicarbonate dialysis and hemofiltration. Blood Purif 6:43–50
22. Coraim F, Pauser G, Stellwag F, Werner T, Ziegler W (1985) Positive Beeinflussung der Hämodynamik bei postkardiochirurgischen Patienten durch die Hämofiltration. Anaesthesist 34:236
23. McManus LM, Hanahan DJ, Demopoulos CA, Pinckard RN (1980) Pathobiology of the intravenous infusion of acetyl glyceryl ether phosphorylcholine (AGEPC), a synthetic platelet-activating factor (PAF), in the rabbit. J Immunol 124:2919–2921
24. Beutler B, Cerami A (1987) Cachectin: more than a tumor necrosis factor. N Engl J Med 316:379–385
25. Parillo JE, Burch C, Shelhamer JH, Parker MM, Natanson C, Schuette W (1985) A circulating myocardial depressant substance in humans with septic shock. J Clin Invest 76:1539–1553
26. Kühl PG, Bolds JM, Loyd J, Snapper JR, Fitzgerald GA (1988) Thromboxane receptor-mediated bronchial and haemodynamic responses in ovine endotoxinemia. Am J Physiol 254:R310–319
27. Parillo JE (1985) Cardiovascular dysfunction in septic shock: new insights into a deadly disease. Int J Cardiol 7:314–316

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