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CLINICAL STUDY

Continuous Renal Replacement Therapy (CRRT) or Intermittent Hemodialysis (IHD)—What Is the Procedure of Choice in Critically Ill Patients?

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ABSTRACT

Although at present there is no prospective randomized study which could show significantly better survival of patients on continuous procedures, the majority of intensivists advocate this technique of renal function replacement due to generally accepted opinion that it has less effect on circulation of already hemodynamically unstable patients. In our prospective randomized study with 104 patients, we also did not observe any difference in 28 days survival, in total survival, as well as in circulatory instability between two treatment modalities. Even in subgroup of 80 patients with sepsis and septic shock there were no difference in survival. Sepsis was the underlying disorder in 52 and septic shock in 28 patients out of 104 patients analyzed in this study

Our prospective randomized study did not show a statistically significant difference between the two methods of renal replacement therapy. Survival rates were not affected and neither was the occurrence of hemodynamic instability.

We believe that both methods are complementary; IHD for faster elimination of electrolytes and waste products elimination, CRRT for regulation of higher calories requirements and for hemodynamically unstable patients. The expectations that one method is superior to the other in the term of better survival have

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not been corroborated by the current data available in the literature. The choice of the method should be individualized. ARF, which is an integral part of MOF, is a problem frequently encountered in critically ill patient treated in the ICU, but outcome of these patients depends closely on the control of basic event. Evaluation of each of the supportive procedures is therefore hindered by the fact that the underlying disease has the crucial effect on survival and the type of supportive procedure less so.

Key Words: Continuous renal replacement therapy (CRRT); Intermittent hemodialysis (IHD); Acute renal failure (ARF).

INTRODUCTION

Acute renal failure as a rule is only a part of the problem in patients with multiple organ failure. All supportive procedures are in the function of maintenance of impaired organ function, and they mostly aid in overcoming acute disorders in critically ill. The most important condition for a favorable outcome is control of the underlying disease, mainly sepsis.[1,2] In the light of this knowledge the place of intermittent hemodialysis procedures should be viewed, compared to continuous hemofiltration procedures and their effect on the survival of critically ill.

PATIENTS AND METHODS

Eighteen months ago we started a prospective randomized study on patients with acute renal failure, always in conjunction with multiple organ failure with the aim to evaluate the place, role, and problems inherent in the mentioned extracorporeal procedures. The study included 104 patients hospitalized in general surgical, cardiac surgical, and medical intensive care units. Table l presents different etiology of ARF/MOF in our study. Tables 2–5 present other results of this study.

Table 1. Etiology of multiple organ failure and extracorporeal procedure (ECP).

Dg	IHD	CRRT	Totals
Sepsis	23	29	52
Septic shock	14	14	28
Sy. renopulmonale	4	1	5
Febris hemorrhagica	4	3	7
Rhabdomyolysis	3	2	5
Cardiomyopathia ishemica	4	3	7
All groups	52	52	104

Most of our patients with multiple organ failure (MOF) had sepsis and septic shock as a etiologic event.

Table 2. Severity scores in patients with mof on ihd/crrt (mean ± SD).

ECP	APACHE II_0	$MARSHAL_0$	$SOFA_0$	APACHE II_1	$MARSHAL_1$	$SOFA_1$	APACHE II_2	$MARSHAL_2$	$SOFA_2$
$IHD_{(N)}$	20.3 ± 8.4 (52)	8.8 ± 4.0 (52)	9.8 ± 4.7 (52)	16.6 ± 6.6 (48)	7.7 ± 5.1 (48)	8.4 ± 4.7 (48)	16.3 ± 7.3 (44)	7.3 ± 3.8 (44)	7.8 ± 4.2 (44)
$CRRT_{(N)}$	21.9 ± 8.8 (52)	10.1 ± 3.7 (52)	11.0 ± 3.9 (52)	19.1 ± 7.9 (46)	9.1 ± 3.6 (46)	9.9 ± 3.8 (46)	18.6 ± 8.0 (43)	8.8 ± 3.9 (43)	9.7 ± 4.1 (43)
P	NS	NS	NS	NS	NS	NS	NS	NS	NS
ECP	APACHE II_3	$MARSHAL_3$	$SOFA_3$	APACHE II_7	$MARSHAL_7$	$SOFA_7$	APACHE II_{14}	$MARSHAL_{14}$	$SOFA_{14}$
$IHD_{(N)}$	16.4 ± 7.5 (44)	7.1 ± 3.8 (44)	7.7 ± 4.6 (44)	15.5 ± 8.2 (35)	6.1 ± 3.9 (35)	6.6 ± 4.3 (35)	13.9 ± 7.7 (24)	5.4 ± 3.7 (24)	5.9 ± 4.1 (24)
$CRRT_{(N)}$	18.3 ± 8.2 (39)	8.1 ± 3.7 (39)	9.3 ± 7.2 (39)	18.2 ± 8.5 (31)	7.3 ± 4.1 (31)	8.5 ± 4.6 (31)	14.7 ± 6.9 (19)	6.0 ± 4.1 (19)	7.3 ± 4.7 (19)
P	NS	NS	NS	NS	NS	NS	NS	NS	NS
ECP	APACHE II_{21}	$MARSHAL_{21}$	$SOFA_{21}$						
$IHD_{(N)}$	13.0 ± 6.4 (17)	5.1 ± 3.2 (17)	5.4 ± 3.2 (17)						
$CRRT_{(N)}$	12.7 ± 8.7 (15)	5.2 ± 4.4 (15)	6.4 ± 5.1 (15)						
P	NS	NS	NS						

In our randomized prospective study there were no differences in scoring (APACHE II, MARSHAL, SOFA) between two groups on extracorporeal procedure (ECP).

Table 3. Survival depends on extracorporeal procedure.

ECP	Survivors	Dead	Total
IHD	21	31	52
CRRT	15	37	52
	36	68	104

P = NS.
There was no difference in total survival rate between two groups.

Table 4. Blood pressure instability (> 10 mmHg) depends on procedure.

ECP	*N*	Rank sum	*p*
HD	52	2505.0	
HF	52	2955.0	
Total	104		NS

There was no difference in total number of blood pressure drops between two groups.

Table 5. Survival of hemofiltration patients depends on exchanged volume.

ECP	Survivors	Dead	Total
HF low	9	22	31
HF high	6	15	21
	15	37	52
p			NS

There was no difference in total survival rate between two groups.

Acute renal failure is defined as a clinical syndrome characterized by a threefold increase in creatinine, hyperkalemia with serum potassium over 5.5 mmol/L, base deficit BE > -6, or at least two of these parameters. Multiple organ failure is a clinical syndrome of organ systems failure requiring appropriate replacement of the function (artificial ventilation in respiratory failure, vasoactive therapy in hypotension). Intermittent hemodialysis (IHD) was defined as a procedure lasting 3–4 h with blood flow rate 200–250 mL/min and dialysate flow rate 500 mL/min, using biocompatible polysulfone membrane with surface area 1.4–1.6 m^2. Hemodialysis was performed every day, most frequently without heparin utilization.

By means of continuous renal replacement therapy—continuous venovenous hemofiltration (CVVH) 18 mL/kg/h were replaced in the first 33 patients (low volume hemofiltration), and subsequently 35 mL/kg/h (high volume hemofiltration). The membrane employed for CVVH was of polysulfone. Systemic heparin was used in case of problems with premature clotting in the extracorporeal procedure.

Standard biochemical and hematologic parameters were followed daily.

Severity of an organ function failure was defined with three different scoring systems: APACHE II, Marshall score, and SOFA score.[3–5] Mean values for patients were marked with the index 0 for the day of admission, 1 for 24 h later, 2 for 48 h later, 3 for 72 h later, 7 for a week later, 14 for two weeks later, and 21 for three weeks later. The tables show the results of the prospective randomized study.

RESULTS

All results are presented in Tables 1–5.

DISCUSSION

Multiple organ failure is a clinical syndrome burdened with a high mortality rate. It is well known that a higher number of failing organs result in an increased death rate. One organ failure results in the death rate of 25–30%, two organs 50–60%, three organs 80% or more, and four organs 100%. As pointed out in the introduction, evaluation of the role of a supportive procedure is hindered by the fact that the principal indicator of the outcome is the underlying disease itself. Since sepsis is the most frequent cause of multiple organ failure in surgical as well as medical intensive care, only control over sepsis allows evaluation of the procedure of extracorporeal circulation. In current literature there is no prospective randomized study, which showed better patient survival on continuous in relation to intermittent procedures. Although at present there is no prospective randomized study which could show significantly better survival of patients on continuous procedures, the majority of intensivists advocate this technique of renal function replacement due to generally accepted opinion that it has less effect on circulation of already hemodynamically unstable patients.[6–8] In oral communications it is not infrequent to hear that this procedure is ''probably better.'' In order to answer the question what is the procedure of choice in critically ill patients, one must eliminate certain forms of intermittent hemodialysis, which by themselves carry frequent problems during extracorporeal circulation. Since the machines with controlled ultrafiltration and bicarbonate dialysate imply smaller incidence of complications, only these devices can be considered comparable with continuous hemofiltration. Meta-analysis of a number of studies, which compared biocompatible to bioincompatible membranes gave advantage to biocompatible membrane, we used machines with controlled ultrafiltration, bicarbonate dialysate solution, and biocompatible polysulfone membrane in our study. It is indisputable that hemodialysis can affect hyperkalemia and volume excess faster, and it solves more rapidly the acute threat of electrolyte and water derangements. Weekly dose of hemodialysis in chronic renal failure is defined, mainly by the quotient $Kt/V > 1.2$. The required dose of extracorporeal elimination in acute renal failure is not defined well enough, however it does not essentially differ from the said quotient. The length of intermittent procedure is also not well defined. It mostly lasts 3–4 h, but some used prolonged intermittent dialysis lasting 9 h and did not obtain different survival

compared to continuous procedures. It has been well established that cytokines affect the severity of the septic process. According to some recent publications CRRT might play a significant role in the elimination of pro-inflammatory cytokines, in addition to clearing nitrogen products as well as other medium and large sized molecules. The possible removal of proinflammatory mediators may permit a blockade of systemic inflammation, a modulation of the altered immune response in these patients, and it may lead to a partial or total restoration of the lost homeostasis.[9–13] A statistically significant reduction in heart rate, increase in systemic vascular resistance an systolic blood pressure were documented in the group of patients who underwent CRRT.[14–16] On the other side, according meta analysis in published and unpublished trials in any language, CRRT in comparison to IHD does not improve survival or renal recovery in unselected critically ill patients with ARF.[17] On the other hand, continuous procedure of hemofiltration has less effect on the stability of circulation. Comparison of value of intermittent hemodialysis with continuous procedures of hemofiltration should therefore be considered in the light of the mentioned fact. In our prospective randomized study with 104 patients, we also did not observe any difference in 28 days survival, in total survival, as well as in circulatory instability between two treatment modalities. Even in subgroup of 80 patients with sepsis and septic shock there were no difference in survival. Sepsis was the underlying disorder in 52 and septic shock in 28 patients out of 104 patients analyzed in this study. The statistical evaluation of the obtained data revealed no significant difference in patient outcome between the two observed methods of renal replacement therapy. This data is corroborated by the available data in the literature. The number of hypotensive attacks defined by blood pressure fall over 10 mmHg in our group of patients on continuous procedures was not significantly smaller. However, there is a randomized prospective study, which showed better survival with high volume hemofiltration 35 mL/kg/h compared to low volume ultrafiltration in which 25 L of volume are replaced in 24 h.[18] We were not able to validate this difference. When choosing the method of extracorporeal circulation, despite the fact that prospective randomized studies did not prove better survival using one of them, intensivists are advised to use the method with less side effects, and of greater benefit in a given case. Our prospective randomized study did not show a statistically significant difference between the two methods of renal replacement therapy. Survival rates and the occurrence of hemodynamic instability were not affected. We therefore believe that the management of the underlying condition outweighs the choice of the procedure of renal replacement. Currently, the use of these methods in the world varies. Almost all intensive care units in England utilize continuous methods. In the USA intermittent procedures are used more commonly than continuous ones, which is similar to the situation presently found in Croatia. We believe that both methods are complementary; IHD for faster elimination of electrolytes and waste products elimination, CRRT for regulation of higher calories requirements and for hemodynamically unstable patients. The expectation that one method is superior to the other in terms of better survival have not been corroborated by the current data available in the literature. The choice of the method should be individualized because both methods have advantages and disadvantages. ARF, which is an integral part of MOF, is a problem frequently encountered in critically ill patient treated in the ICU, but outcome of

these patients depends closely on the control of basic event. Evaluation of each of the supportive procedures is therefore hindered by the fact that the underlying disease has the crucial effect on survival and the type of supportive procedure less so. It is our opinion that these patients will more likely be treated by continuous methods by appropriately trained ICU personnel.

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