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Biocompatible membranes in acute renal failure (ARF), hope or illusion?

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SUMMARY

We have retrospectively analyzed all group of 47 patients with acute renal failure. They have been divided into two subgroups. Each group underwent hemodialysis on a different membrane. We have furthermore studied the number of hemodialysis sessions required for the recovery of the renal function in surviving patients. We have documented a difference in the outcome as well as in the number of hemodialysis sessions required for renal function restitution between the two groups. The groups were comparable with respect to their APACHE II score. Patients who underwent hemodialysis on the polysulfone membrane had statistically significant better survival rates when compared to those whose hemodialysis protocol included modified cellulose sulfate. This data stresses the importance of the selection of the membrane in patients with ARF.

Key words: ***Biocompatible membranes. Acute renal failure. Outcome.***

MEMBRANAS BIOCOMPATIBLES EN EL FRACASO RENAL AGUDO. ¿ESPERANZAO ILUSION?

RESUMEN

Analizamos retrospectivamente un grupo de 47 pacientes con fracaso renal agudo. Dividimos los pacientes en dos subgrupos. Cada grupo se dializó con una membrana diferente. Estudiamos a continuación el número de sesiones necesarias para la recuperación de la función renal en los pacientes que sobrevivieron. Observamos diferencias entre los dos grupos tanto por lo que se refiere a los resultados como al número de sesiones de hemodiálisis necesarias para la recuperación de la función renal. Los grupos se compararon en cuanto al nivel de difi -

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cultad APACHE II score. Los pacientes dializados con polisulfona tenían una mayor supervivencia que los dializados con acetato de celulosa. Este dato resalta la im - portancia que tiene la selección de la membrana en pacientes con fracaso renal agudo.

Palabras clave: ***Membranas biocompatibles. Fracaso renal agudo. Pronóstico.***

INTRODUCTION

The technological progress in medicine, as in other categories of science, brings new discoveries, but sometimes disappointments, as well. There is a constant need for objective evaluation of new techniques. One must always question new ideas in terms of their true benefit. Acute renal failure remains associated with high mortality rates. Different attempts to increase survival have not been successful[1-3]. The use of biocompatible polyacrylonitrile membrane gave promising, but controversial results[4-7]. This paper compares the outcome of patients with ARF treated with different hemodialysis protocols: modified cellulose acetate membrane (BIC) versus (polysulfone (BC).

PATIENTS AND METHODS

During a past period (one year) we have analyzed all dialyzed patients with ARF. Group 1 was dialyzed on the modified cellulose acetate membrane (BIC), and Group 2 on the polysulfone membrane (BC). The aim of our retrospective study was to evaluate the benefits of biocompatible membranes in the treatment of patients with ARF. ARF is defined by serum creatinine values exceeding 400 µmol/L, with or without hiperkalemia, and diuresis levels of less than 400 mL/24 hours. In both groups there was no nonoliguric patients. The choice of the membrane was accidental, but we have not followed a uniform randomization plan. The protocol was predefined, and invariant of the underlying condition of the patient. All patients admitted to the medical and the surgical ICU we analyzed in the same way and by the same team of medical doctors. ARF was not observed at the time of admission. In both the surgical and the medical group ARF had developed at a later stage, once the management of the underlying condition was well under way (following cardiac surgery, sepsis, etc.) Out of a group of 49 patients with ARF (both surgical and medical patients, 34 males and 15 females, average age 61.73 ± 12.99 years) scheduled for hemodialysis, cellulose acetate membrane was used in 23 patients (group 1), polysulfone membrane in 24 patients (group 2). The exclusion of two patients (Number 4 and Number 25) from the study was based on insufficient data and the fact that the membrane used was neither of the above mentioned two. On inclusion into the study, there were no significant differences in the severity of the underlying disease between the observed groups. Regardless of the type of membrane used all observed patients were dialysed without heparin. Anticoagulation therapy was avoided in both the surgical and medical group of patients, because the risk of bleeding was considered too high. For the comparison of the two groups we have used the APACHE II Score.

The APACHE II score is generated in 3 parts.

I. Acute Physiology Score (APS). This consists of 12 measurements obtained within the first 24 hours of admission to the ICU. The most abnormal measurement for each variable is selected and the total APS score is the sum of the scores from the individual measurements.
II. Age Adjustment. A point total of zero to 6 points is alloted for the age of the patient.
III. Chronic Health Adjustment. Up to 5 additional points are alloted for chronic illnesses involving the major organ systems.

The score is based upon acute physiological parameters such as body temperature, blood pressure, PaO_2, arterial pH, serum concentrations of Na^+, K^+, creatinine, hematocrit, WBC count (I), and is also modified for the age (II) and by the presence of chronic conditions (III). The final APACHE II score is the sum of the above 3 score[8]. APACHE II scores were registered at the introduction into the study (APACHE II_0) and 1, 2, 3, 7, 14 and 21 days after the commencement of hemodialysis (APACHE $II_{1,2,3,7,14,21}$). The APACHE II Score was statistically

comparable between the two groups at the beginning of the study, as well as at all later measurements.

Hemodialysis was performed on the modified cellulose acetate membrane (Group 1), or on the polysulfone membrane (Group 2). The area of the modified cellulose acetate (Plivadial MCA 130) equaled 1,3 m^2. The blood flow was 150-200 mL/min. The area of the polisulfone membrane (Fresenius F60) equaled 1,3 m^2. The blood flow was 150 mL/min.

The dialysate flow was 500 mL/min invariant of the type of membrane used. Our statistical analysis included the t-test for independent samples for the APACHE II Scores, as well as the χ^2 test and the Fisher exact test for the outcome with respect to the type of membrane used. Pearson Chi square test, as well as Kruskal Walis test were also used.

RESULTS

The clinical characteristics are presented in table I.

APACHE II Scores upon inclusion into the study are shown in table II and III.

The outcome of patients with ARF was independent of patient sex (Pearson Chi square, NS). The outcome of the patients with ARF was not influenced by patients age (Kruskal Walis test, NS). There was no difference in the choice of membrane with respect to patient age and to patient sex (Kruskal Walis test, NS).

The variances in the outcome with respect to different hemodialysis membranes in whole group, as well as in the septic patients are presented in table IV and V.

The mean number of hemodialysis treatments required for recovery of renal function in surviving patients with ARF is shown in table VI.

Table I. Clinical characteristics & outcome of patients with ARF on hemodialysis.

Groups	Sex	Age	Diagnosis	APACHE II_0	APACHE II_1	APACHE II_3	APACHE II_7	Outcome
Modified celulose acetate[1]	14M + 9F	63.8 +/ 10.1	**1**(14), **2**(3), **3**(3), **4**(2), **7**(1)	34.65 ± 11.22	32.77 ± 11.86	29.83 ± 12.13	27.23 ± 10.70	5/23
Polisulfone[2]	17M + 7F	57,9 +/ 13.1	**1**(16), **2**(4), **3**(1), **4**(1), **5**(1), **6**(1)	31.04 ± 9.50	29.54 ± 9.76	28.65 ± 12.67	29.12 ± 11.92	13/24

Diagnosis:
1 = sepsis following open herat surgery.
2 = sepsis following abdominal surgery.
3 = vasculitis.
4 = sepsis in the medical ICU.
5 = leptospirosis.
7 = severe heart failure.

APACHE II
APACHE II_0 = APACHE II upon inclusion into the study.
APACHE II_1 = APACHE II 24 horus following inclusion into the study.
APACHE II_3 = APACHE II at 72 horus.
APACHE II_7 = APACHE II 7 days following inclusion in the study.

Table II. APACHE II score at inclusion into the study, and 24, 48 and 72 hours therafter (mean values ± SD).

	0	24	48	72	7 days
Group 1	34.65 ± 11.22 (23)	32.77 ± 11.86 (22)	30.55 ± 12.19 (20)	29.83 ± 12.13 (18)	27.23 ± 10.70 (13)
Group 2	31.04 ± 9.50 (24)	29.54 ± 9.76 (22)	29.25 ± 10.96 (20)	28.65 ± 12.67 (20)	29.12 ± 11.92 (16)
p	NS	NS	NS	NS	NS

Table III. APACHE II score of patients with ARF secondary to sepsis at inclusion into the study, and 24, 48 and 72 hours therafter (mean values ± SD).

	0	24	48	72	7 days
Group 1	37.21 ± 10.08 (19)	35.61 ± 10.61 (19)	32.70 ± 11.25 (17)	32.26 ± 10.86 (15)	29.50 ± 10.30 (10)
Group 2	31.19 ± 8.74 (21)	29.26 ± 10.10 (19)	30.27 ± 10.75 (18)	29.88 ± 12.69 (18)	30.21 ± 12.41 (14)
p	NS	NS	NS	NS	NS

Table IV. The differences in the outcome of patients with ARF with respect to the type of membrane used

	Survived	Died	Total number of pts
Group 1	5	18	23
Group 2	13	11	24
Total			47
p =	0.0223 Chi square test 0.0355 Fisher exact two-tailed test		

Table V. The differences in the outcome of patients with ARF secondary to sepsis with respect to the type of membrane used

	Survived	Died	Total number of pts
Group 1	2	17	19
Group 2	11	10	21
Total	13	27	40
p =	0.0048 Chi square test 0.0069 Fisher exact two-tailed test		

Table VI. Mean number of haemodialysis session required for recovery of renal function in surviving patients with ARF

	Survived	Mean number of HD ± SD until recovery of renal function
Group 1	5	21.2 ± 10.42
Group 2	13	9.85 ± 8.92
p =	0.048316 Chi square 0.019788 Mann Whitney test	

Group 1 = Modified cellulose acetate membrane.
Group 2 = Polysulfone membrane.

DISCUSSION

The past attempts of ARF management with dopamine, dobutamine, diuretics of the ascending loop of Henle have proven disappointing. Many efforts have been made in the prevention of ARF, but few have proven to be useful. On the other hand, the more aggressive types of treatment often employed by modern medicine result in an increased frequency of ARF occurrence. The high mortality rates of patients with ARF in both the surgical and medical group of patients demand an evaluation of new approaches to the treatment[9,10]. Inclusion of the elderly population into the more aggressive medical management, conditions surrounding wars, as well as the more progressive approaches in cardiac and abdominal surgery, maintain the mortality rates of patients with ARF between 60% and 70%[11,12]. According to certain studies the incidence of ARF in the patients admitted to the hospital is approximately 5%. Our goal was to determine the variance in the outcome of patients with ARF when different types of hemodialysis membranes were used. The severity of the underlying condition upon inclusion into the study was comparable between the two groups observed. Their condition was objectively represented by the APACHE II score (table II, ref 8). Recognising the fact that the APACHE II_0 score was somewhat higher in the group 2 (the difference was not statistically significant) we have separately analysed patients with ARF following sepsis, in an effort to evaluate the accuracy of the results. The severity of the disease was comparable in both groups, as we have shown in table III. We have seen that greather portion of patients with ARF were males, as is consistent with the observations of other authors. On the other side there was no statistically significant difference in the representation on either membrane for both sexes. There was no difference in number of hypotensive atacs between two groups, all patients demand some kind of vasoactive therapy (dopamin, dobutamin someone noradrenalin). It is important to note that the survival rates of the patients with ARF were higher in the group of patients who were subjected to hemodialysis on the biocompatible polysulfone membranes, when compared to the patients dialysed on the purified cellulose acetate membrane (p = 0.0223 Chi square test). Patients developing ARF secondary to sepsis following open heart and abdominal surgery, as well as those suffering from ARF caused by medical sepsis, were studied apart from the patients developing ARF as a result of a non-sepsis etiologic factor. We have documented a significantly better outcome in patients dialysed on biocompatible membranes when compared to those dialysed on the modified cellulose acetate membrane (p = 0.0048 Chi square test). The group of patients with ARF secondary to sepsis dialysed on biocompatible membranes showed a speedier recovery with a significantly lower number of hemodialysis sessions required for the renal function recovery (p = 0.019788), Mann Whitney test, p = 0.048316, Chi square test (table VI).

The number of hospital days required for the renal function restitution was significantly higher in patients who underwent hemodialysis on the modified celullose acetate membrane. None of the patients had previous compromitation of the renal function. A complete recovery of the renal function was observed in all surviving patients.

This points the significance of the biocompatible membranes in the treatment of the patients with ARF. The explanation for this may be in the decreased activation of complement and its fractions, as well as in the less pronounced influence of the biocompatible membranes on the patient's granulocyte[13]. The effect of high flux procedure compared to low flux should be investigated to. Various authors agree that further confirmation of results in this fields is warranted[15]. One must stress that ARF is usually a component of multiple organ failure[14]. Therefore, the management of ARF is only a segment of the treatment. The control over the basic etiologic factor remains of paramount importance. The mortality rate of ARF remains high. Patients die due to the clinical syndrome of MOF, despite the utilization of artificial ventilation, vasoactive therapy and hemodialysis. The high mortality rates of patients dialyzed on both the biocompatible and the bioincompatible membrane is secondary to protracted sepsis, caused by resistant microorganisms (staphylococci, pseudomonas, acinetobacter), which usually progresses to death[16].

In the domain of ARF management a number of issues remain unresolved; i.e. the role of intermittent procedures in comparison to continuous ones, hemodialysis versus peritoneal dialysis, etc. Our work points to the significance of biocompatible membranes in the treatment of ARF. The restitution of the kidney function does not guarantee patient recovery, as we have observed in some of our patients. Today we find that a patient may die with ARF, but should not die from it. We believe that the institution of biocompatible membranes into the treatment of patients with ARF has improved their chances for a favourable outcome. The use of biocompatible polysulfone membrane in acute renal failure, along with other measures, represents advancement in patient management.

BIBLIOGRAFIA

1. Brady HR, Singe GG. Acute renal failure: *The Lancet* 346: 1533-1540, 1995.
2. Mehtra RL: Therapeutic alternatives to renal replacement for critically ill patients in acute renal failure. *Sem Nephrol* 14:64-82, 1994.
3. Bonomini V, Coli V, Scolari MP, Stefoni S: Structure of Dialysis Membranes and Long-Term Clinical Outcome. *Am JNeph - rol* 15: 455-462, 1995.
4. Schifl H, Sitter, Lang S: Hemodialysis in acute Renal Failure: Which Type of Dialysis Membrane? Years book of Intensive Care Medicine, Brusseles, 758-763, 1995.
5. Schiffl H, Lang SM, Koenig A, Strasser T, Haider MC, Held E: Biocompatible membranes in acute renal failure: prospective case-controlled study. *Lancet* 344: 570-572, 1994.
6. Turney JH: Acute renal failure-some progress? *N E J M* 331: 1372-1374, 1994.
7. Kurtal HD, von Herrath, Schaefer K: Is the Choice of Membrane Important for Patients with Acute Renal Failure Requiring Hemodialysis. *Art Org* 19: 391-394, 1995.
8. Knaus WA: APACHE II: A severity of disease classification system. *Crit Care Med* 13: 818-829, 1985.
9. Kaplan A, Paganini P, Bosch P: Effect of the dialysis membrane in acute renal failure. *N E J M* 332: 961-962, 1995.
10. Corwin HL, Bonventre JV: Acute renal failure in the intensive care unit. Part 2. *Intensive Care Med* 14: 86-96, 1988.
11. Husedžinović I, Sutlić ž, Bio čina I, Rudež I: Inotropic Agents in the Treatment of Postoperative Low Cardiac Output Syndrome. *Acta Med Croat* 49: 201-205, 1995.
12. Gašparović V, Radonić R, Gjurašin M, Ivanović D, Kvarantan M, Husar J: Acute renal failure in the war in Croatia. *Nephrol Dialys Transpl* 10: 1261, 1995.
13. International Co-operative Biocompatibility Study (ICBS). *Nephrol Dial Transplant* 8(S2), 1-42, 1993.
14. Merkler M, Gjurašin M, Ivanović D, Gašparović V, Radonić R: Acute renal failure within multiple organ deficiency syndrome duo to sepsis in patients treated at intensive care unit. *Neurol Croat* 45 (S) 1: 99-102, 1996.
15. Jacobs C: Membrane biocompatibility in the treatment of acute renal failure: what is the evidence in 1996? *Nephrol Dialys Transpl* 12: 38-42, 1997.
16. Gašparović V, Radonić R, Gjurašin M, Gasparović H, Ivanović D, Merkler M, Jelić I: Aetiology and outcome of acute renal failure secondary to war related trauma and infectious disease in Croatia. *Nephrology* 3: 155-158, 1997.