SLIDE FORUM 27

HEMOFILTRATION/APHERESIS

Acute Renal Failure in Critical Illness

Conventional Dialysis *Versus* Acute Continuous Hemodiafiltration

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The dialytic therapy of choice in critically ill patients with acute renal failure (ARF) is a matter of controversy. The clinical outcome of such patients managed with either conventional dialytic therapy (CDT) or acute continuous hemodiafiltration (ACHD) was compared through retrospective review of medical records from the intensive care unit of a tertiary institution. Records from 167 critically ill patients with ARF consecutively treated in the same intensive care unit were reviewed. Eighty-four patients with ARF treated by CDT were compared to 83 treated with ACHD. The etiology of ARF and the degree of illness severity were similar in both groups (failing organs: CDT 3.9 *vs.* ACHD 4.1; mean APACHE II score: CDT 25.8 *vs.* ACHD 28.1). Overall survival was 29.8% for the CDT patients and 41% for the ACHD group (NS). In those with two to four failing organs, survival was greater in the ACHD group (53.8% vs. 31.1%; $p < 0.025$). This was also true for patients with an intermediate APACHE II score (24–29) who demonstrated better survival when treated by ACHD (46.4% *vs.* 12.5%; $p < 0.025$). Acute continuous hemodiafiltration was associated with better control of azotemia and hyperphosphatemia and increased nutritional intake. This retrospective study suggests that ACHD may offer clinically significant advantages over CDT, particularly in patients with an intermediate degree of critical illness severity. *ASAIO Journal* 1992; 38: M654–M657.

The conventional approach to the management of the azotemia of acute renal failure has, in the past, included peritoneal dialysis or intermittent hemodialysis with or without periods of slow continuous ultrafiltration.[1] These techniques, however, have limitations when applied to critically ill patients with hemodynamic instability.

Newer techniques that combine dialysis and filtration on a continuous basis now offer excellent control of azotemia, solute and water removal, and hemodynamic stability.[2-13] It is unknown, however, whether their use leads to diminished morbidity and mortality in critically ill patients with acute renal failure. We sought to address this issue by retrospectively reviewing the clinical outcome of such patients treated with either modality.

Methods

The medical records of 167 consecutive patients with acute renal failure and critical illness were reviewed. All patients were treated in the same intensive care unit by a team of physicians led by the same core group of specialists over the study period. The institution to which the intensive care unit belongs is a university teaching hospital that acts as a tertiary referral center for a large suburban and country cachment area. The referral pattern and case mix has been constant over the study period. Patients admitted between July 1, 1982 and July 1, 1991 were the subject of the study.

The following information was obtained from the records: name, age and sex, date of admission, etiology of acute renal failure and critical illness, biochemistry on admission and on first testing after >24 hr of dialytic or hemodiafiltration therapy. Hematologic variables on admission also were obtained. The date of either death or hospital discharge was noted, as was the duration of stay in the ICU.

To establish whether the two groups were truly comparable, disease severity was assessed by means of an APACHE II score[7] for the first 24 hr after ICU admission and by an assessment of the number of failing organs in the 48 hr following the introduction of renal replacement therapy. The definition of organ failure was based on criteria taken from the pertinent literature.[6,8]

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Population means and confidence intervals were calculated. Differences between means were calculated using the two sample independent groups t-test and confidence intervals for the difference between means.[10] The chi-square test, with Yates' correction where appropriate, was used to assess nominal differences between the two groups. The Wilcoxon rank-sum test was used for data sets without normal distribution of values.

Modes of Therapy

The group of patients treated by conventional dialytic therapy (CDT) received either intermittent hemodialysis (usually 4 hr every second day) or peritoneal dialysis. A number of patients were sequentially treated with both modalities. Some also received slow continuous ultrafiltration in addition, usually for periods lasting <24 hr. This was a supplement to CDT, applied intermittently for water and solute removal.

Acute Continuous Hemodiafiltration

Acute continuous hemodiafiltration (ACHD) was performed either as continuous arteriovenous hemodiafiltration (CAVHD), or as continuous venovenous hemodiafiltration (CVVHD). In all patients, 0.43 m^2 polyacrylonitrile flat-plate hemofilters (Hospal AN69S: Hospal, Paris, France) were used. The ACHD circuit was as previously described[3] for CAVHD. For CVVHD, a peristaltic pump (AK 10, Gambro, Lund, Sweden) directed blood flow at a rate of 150 ml/min. Conventional peritoneal dialysate was pumped countercurrent to blood at a rate of 1 L/hr.

Results

Of the 167 patients studied, 84 received CDT and 83 ACHD. All patients treated before July 1988 received CDT. From July 1988 to July 1991 all patients were treated with ACHD. The two populations were clinically, biochemically, and hematologically similar **(Table 1)**.

Table 1. Comparison of Clinical, Hematologic, and Biochemical Data from Conventionally Treated and Hemodiafiltration Treated Patients

	CDT	ACHD	*p* Value
Mean age (yr)	55.5 (15–76)	59.6 (21–80)	NS
Gender	60M/24F	57M/26F	NS
Sepsis/infect	62/84	64/83	NS
APACHE II score	25.8 (24.4–27.2)	28.1 (26.9–29.3)	<0.01
Bacteremia/fungemia	35/84	33/83	NS
No. of failing organs	3.9 (3.6–4.2)	4.1 (3.8–4.4)	NS
Mean WCC	15.3 (13.2–17.4)	21.6 (10–33.2)	NS
Presence of DIC	30/84	37/83	NS
Predialysis biochemistry			
Creatinine (μmol/L)	675 (606–744)	594 (519–669)	NS
Urea (mmol/L)	40 (36.3–43.7)	31.3 (28.3–34.3)	<0.001
HCO_3 (mmol/L)	18.6 (17.4–19.8)	18.7 (17.4–20)	NS
K^+ (mmol/L)	4.9 (4.6–5.2)	4.7 (4.5–4.9)	NS

Values in parentheses are 95% confidence intervals.

Table 2. Changes in Biochemical Variables After 24 Hours of Dialytic Therapy

	CDT	ACHD	*p* Value
Urea (mmol/L)			
0 hr	40 (36.3–43.7)	31.3 (28.3–34.3)	<0.001
24 hr	31.7 (28.2–35.2)	20.4 (18.9–21.9)	<0.001
Creatinine (μmol/L)			
0 hr	675 (606–744)	594 (519–669)	NS
24 hr	560 (507–613)	400 (360–440)	<0.001
Glucose (mmol/L)			
0 hr	10.6 (9.5–11.7)	10.6 (9.4–11.8)	NS
24 hr	9.8 (8.8–10.8)	13.7 (12.1–15.3)	<0.001
Phosphate (mmol/L)			
0 hr	2.1 (1.9–2.3)	2.02 (1.82–2.22)	NS
24 hr	2.0 (1.8–2.2)	1.38 (1.22–1.54)	<0.001

Values in parentheses are 95% confidence intervals.

Analysis of the patterns of biochemical change in the first 24 hr (which were representative of subsequent biochemical control) demonstrated that ACHD offered superior control of serum phosphate, although patients receiving ACHD demonstrated greater hyperglycemia **(Table 2)**.

The serum creatinine and plasma urea at the initiation of treatment were lower for patients receiving ACHD.

Different complications occurred in the two groups **(Table 3)** that particularly highlight the known hemodynamic consequences of each therapy. The use of ACHD was associated with a trend toward a shorter hospital stay. Patients requiring total parenteral nutrition were more likely to have received planned therapy if on ACHD **(Table 4)**.

When overall mortality was compared, there was a trend toward diminished mortality in ACHD treated patients. A significant survival advantage for ACHD was seen when patients with two to four failing organs were compared. No significant differences were found for patients with in excess of four failing organs **(Table 4)**. Such patients tended to be older in the ACHD group (mean age: 56.8 years *vs.* 52.4 years for CDT) and to have a higher mean APACHE II score (30.8 *vs.* 28.6 for CDT); these differences were not statistically significant. The same pattern was maintained when patients were stratified into illness severity categories according to their APACHE II scores: those with a score between 24 and 29 showed a significant fall in mortality when treated by ACHD. No differences in mortality were demonstrated with less severe or extreme illness severity categories **(Table 4)**.

Discussion

This study seeks to address the major issue pertaining to the use of the newer hemodiafiltration based techniques: that is, whether they have a clinically significant positive impact on critically ill patients with acute renal failure.

It reveals a number of important data. First, ACHD is associated with an overall trend toward increased survival. A significant survival advantage was demonstrated in those patients with an intermediate degree of illness severity (APACHE II score of 24 to 29, or number of failing organs <4). Despite the limitations of retrospective studies, this is an important finding. It may be that patients with a critical illness of moderate severity have more potential for ultimate salvage; the techniques of renal replacement may thus potentially have their major impact on outcome in these patients. Equally, in patients with a dramatic degree of illness severity (APACHE II score >30) and a high number of failing organs (>4), it may be more difficult to demonstrate a benefit from intervention techniques, such as ACHD, by virtue of their inherently unfavorable prognosis.

A number of clinical advantages occur with the use of ACHD, including the opportunity to provide adequate nutritional support with better control of azotemia and improved hemodynamic stability. These findings alone may encourage clinicians to use ACHD in preference to CDT.

A number of criticisms can be directed at the current study. It is retrospective. Patients treated by CDT may have failed to benefit from nondialytic advances in the management of critically ill patients. All patients studied, however, received inotropic and vasopressor drugs as clinically indicated, all received antibiotic therapy according to microbiologic isolates or empirical prediction of the likely bacterial flora responsible for infection, and the ventilatory strategies employed were comparable in both groups. In addition, no major changes in mortality associated with acute renal failure management in critically ill patients have been reported in the period covered by the study.[9-11] Another potential criticism is that differences in patient populations may have biased outcome in favor of ACHD. Most data would indicate that the contrary may be true.

It may be thought that observed mortality in the CDT group (70.2%) was excessive. The literature would not support this contention.[10] Furthermore, there are no reports of populations with a mean APACHE II score >28 or a mean number of failing organs >4 achieving an in-hospital survival of >40%.

Our findings are consistent with growing evidence that hemodiafiltration may provide a degree of blood purification that goes beyond the simple control of uremia,[14] and that this effect may actually contribute to a more favorable outcome.[15]

Table 3. Complications of Different Forms of Dialytic Therapy

	CDT	ACHD
Peritoneal leak	3	0
Hemodynamic instability	4	0
Shunt thrombosis	4	3
Peritonitis	4	0
Infected shunt site	1	1
Within minutes of starting hemodialysis		
Rapid SVT	1	0
Cardiac arrest and death	2	0
Ventricular fibrillation	1	0
Bleeding from shunt site	0	1
Bleeding from femoral artery	—	4
Femoral hematoma	—	3
Infected femoral lines	—	1
False aneurysm femoral artery	—	1
Thrombosis femoral cannula	—	1
A-V fistula femoral vessels	—	1
Bleeding from venous cannula	—	1

Table 4. Comparison of Clinical Consequences and Outcome Related to Conventional Dialysis and Acute Continuous Hemodiafiltration

	CDT	ACHD	*p* Value
Overall survival	25 (29.8%)	34 (41%)	NS
Survival in patients with			
<2 failing organs	6 of 12	14 of 16	NS
2–4 failing organs	17 of 58	26 of 50	<0.025
>4 failing organs	6 of 23	6 of 31	NS
Apache II score <24	17 of 35	14 of 26	NS
Apache II score 24 of 29	3 of 24	13 of 28	<0.025
Apache II score >29	5 of 25	7 of 29	NS
Total parenteral nutrition			
Full dose	28 of 52	42 of 47	<0.025
Duration of hospital stay			
(days)	45	29	NS
(median, range)	(7–176)	(14–123)	

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