
Neuroanesthesia and Intensive Care

Best evidence in critical care medicine

Treatment: Daily hemodialysis reduces mortality in patients with acute renal failure

Article appraised

Schiffl H, Lang SM, Fischer R. Daily hemodialysis and the outcome of acute renal failure. *N Engl J Med* 2002 Jan 31; 346(5): 305–10.

Structured abstract

Question: Does daily intermittent hemodialysis improve survival as compared with conventional (alternate day) intermittent dialysis in patient with acute renal failure?

Design: Prospective, nonrandomized (alternating allocation), controlled trial. Patients, physicians and nursing staff were unaware of treatment assignment before the first dialysis but blinding was impossible thereafter.

Setting: Medical and surgical intensive care units in a single teaching hospital in Germany from January 1993 to September 1998.

Patients: One hundred and sixty adult patients with acute renal failure (ARF) from acute tubular necrosis were alternatively assigned to one of two treatment regimens. ARF was defined as a serum creatinine increase of at least $88 \text{ mmol}\cdot\text{L}^{-1}\cdot\text{day}^{-1}$ or a value $> 353 \text{ mmol}\cdot\text{L}^{-1}$. Exclusion criteria were chronic renal failure (serum creatinine $> 265 \text{ mmol}\cdot\text{L}^{-1}$); other causes for acute renal failure (obstructive, interstitial nephritis, glomerulonephritis); previous renal transplantation; prior dialysis treatment; or treatment with continuous renal replacement therapy (CRRT).

Intervention: Eighty patients were allocated to each treatment arm. Fourteen patients were withdrawn during the course of the study. Seventy-four patients received daily dialysis (six days/week) and 72 patients received dialysis every other day (three days/week). The dose of hemodialysis was adjusted based on the basis of the urea kinetic formula (Kt/V) and pre-treatment body weight. Hemodialysis was stopped at partial recovery of renal function defined as a return of diuresis, absence of uremia and improved metabolic

homeostasis as judged by the nephrologists, without specified values.

Main outcomes: Mortality from any cause 14 days after the last dialysis was the primary outcome. Frequency of treatment-related complication and the duration of renal failure were secondary outcomes.

Main results: Analysis was by "intention-to-treat". Baseline characteristics were similar in both groups including the etiology of renal failure, APACHE III score, serum creatinine, blood urea nitrogen and the percentage of patients with oliguria at entry. The daily dialysis group had 28% mortality compared to 46% in the conventional group with an absolute risk reduction of 18% and number-needed-to-treat of 6. There were fewer complications in the daily dialysis group and a shorter time to recovery from renal failure. The sample size was powered to detect a 20% difference in mortality.

Conclusion: Daily dialysis reduces all-cause mortality in patients with acute renal failure.

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Commentary by F. Bernard, C.L. Verdant, T. Gorman, M. Leblanc, and P. Dagenais

The study by Schiffl *et al.* addresses an important question considering that treatment of ARF in intensive care is resource-consuming and the associated mortality high. This study brings new insight to the matter but cannot definitively settle the debate.

We question internal validity aspects of this study as we identified problems in design, patient selection as well as the way the intervention was carried out. The study is neither randomized nor blinded. Criteria of initiation and discontinuation of renal replacement therapy (RRT) are not specified. Usually accepted indications for RRT are stated without specifying levels of biochemical disturbances required to take action. Timing of RRT was thus left to the discretion

of the nephrologist. This could potentially introduce a bias in treatment aggressiveness or duration. Although no consensus exists to define the best timing for RRT initiation, earlier treatment in the daily dialysis group might have influenced the outcome.

We suspect that an important selection bias was introduced in the study since patients requiring CRRT were excluded. They usually represent sicker patients with a high mortality rate. Mortality in the control group is lower than any rate reported in the literature for aggressively treated ARF patients.¹ This suggests that the population evaluated represents a subgroup of ARF patients with a better prognosis. A table of concomitant interventions such as vasopressors or nutrition would have been useful to better characterize the groups. Was treatment in the control group standard of care in North-America?² The low efficiency of alternate day dialysis ($Kt/V < 1$) resulted in high levels of urea and creatinine ($37.1 \text{ mmol}\cdot\text{L}^{-1}$ and creatinine $839.8 \text{ mol}\cdot\text{L}^{-1}$). This level of Kt/V efficiency has been shown to be inadequate in chronic renal insufficiency. The mortality difference shown in the study could thus represent the detrimental effect of under-treatment rather than the benefit of daily dialysis. For all these reasons, although a statistically significant difference in mortality favoured daily dialysis, we wonder if the results can be generalized to all intensive care unit patients.

It is biologically plausible that a higher Kt/V could result in improved homeostasis in these patients. The fact that daily dialysis (higher Kt/V) resulted in less oliguria, respiratory failure, SIRS, altered mental status and gastrointestinal bleeding supports this assumption. Ronco *et al.* have shown reduced mortality in patients with higher doses of CRRT.³

It is our opinion that this study showed better outcome not because of daily dialysis but because of a higher delivered dose of RRT. We cannot conclude, as the authors suggest, that daily dialysis should be the standard of care but, rather, that a sufficient Kt/V has to be achieved. Alternate-day-dialysis with a high blood flow or a longer duration could probably achieve similar results.⁴ It seems clear that patients fare better with more dialysis but the debate will go on as to how (daily, alternate day or continuous), when (timing of initiation) and how much (minimal Kt/V) dialysis should be delivered.

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- 3 Ronco C, Bellomo R, Homel P, *et al.* Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. *Lancet* 2000; 356: 26–30.
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