Extended hemodialysis in acute kidney injury

ABSTRACT

About 10% of patients in the intensive care unit which develop acute renal failure will depend on renal replacement therapy. Although there are no data showing reduction in mortality when compared with intermittent therapy, continuous therapies provide higher cumulative doses of dialysis and greater hemodynamic stability. However, have high costs and are not available in many centers. In this context the Extended Hemodialysis gaining ground in clinical practice because it combines the hemodynamic tolerability, slow and sustained solute control and effective doses of continuous dialysis therapies associated with reduced costs and logistics facilities of intermittent therapy.

Keywords: acute kidney injury; dialysis; Intensive Care Units.

INTRODUCTION

Acute Kidney Injury (AKI) is a common complication in critically ill patients, affecting up to 30% of those admitted to the Intensive Care Unit (ICU). Unfortunately, despite major advances in the treatment of these patients, AKI mortality remains high. About 5%-10% of ICU patients develop acute kidney failure requiring renal replacement treatment (RRT), while in more severe forms of AKI, RRT-dependence exceeds 60%. RRT modes in this population may be intermittent (conventional hemodialysis and peritoneal dialysis) or continuous (continuous hemodialysis, hemofiltration or hemodiafiltration). The choice of the optimal method depends on the patient’s clinical status, the medical knowledge and the availability in each center. Although there are studies comparing these treatment modalities, differences on mortality and renal function recovery have not been investigated. The main limiting factor of intermittent treatment in critically ill patients is hemodynamic instability. Intradialytic hypotension is associated with dialysis-related factors (ultrafiltration rate and volume, plasma osmolality reduction) and patient-related factors (hypovolemia, cardiac dysfunction, vasodilation). Intradialytic hypotension reduces the dialysis dose and maintains the ischemic lesion, thus delaying AKI recovery.

When compared with intermittent treatment, continuous methods provide for better hemodynamic stability, being preferable in hemodynamically unstable patients. However, the need for continuous anticoagulation, skilled nursing and its high cost makes them unavailable in many centers.

In this context, since the 1990’s there have been descriptions of adaptations of conventional hemodialysis machines for “semicontinuous” use, seeking thereby to create a treatment mode that could join the advantages of the intermittent and the continuous methods. It all resulted in the extended hemodialysis (also called prolonged hemodialysis or SLED - Sustained Low Efficiency Dialysis), a “hybrid” type of treatment that combines cardiovascular stability and the effective clearance of continuous treatment modes with the operational ease and reduced costs of...
intermittent therapies. This modality is now increasingly being used by nephrologists.\textsuperscript{16}

**Extended hemodialysis (EH) - Physiological and technical aspects**

The physiological basis of EH is a longer duration procedure (with a decreased ultrafiltration/hour rate), with reduced dialysate and blood flow, thus minimizing osmotic imbalance, but without decreasing solute clearance.\textsuperscript{17} The hemodynamic stability is comparable to that of continuous procedures, as well as the dialysis dose supplied, which is equivalent or even higher than continuous and intermittent treatment modalities.\textsuperscript{18}

EH uses the same machines as conventional hemodialysis, usually adapted to provide reduced blood (100-200 ml/min) and dialysate (100-300 ml/min) flow. The session duration is increased to 6 to 18 hours (mean of 8 hours)\textsuperscript{19} and in some situations there is also the possibility for continuous mode operation.\textsuperscript{20}

The session duration, as well as the goals of ultrafiltration, vary according to the degree of hemodynamic instability. Furthermore, the use of low-temperature dialysate (35 degrees), higher levels of calcium in the dialysate (3.5 mEq/l) and sodium and ultrafiltration profiles are often associated to minimize the risk of hypotension (Table 1).\textsuperscript{21,22}

**Table 1. Extended hemodialysis prescription model**

<table>
<thead>
<tr>
<th>Duration</th>
<th>6-8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow</td>
<td>100-200 (ml/min)</td>
</tr>
<tr>
<td>Dialysate flow</td>
<td>200-300 (ml/min)</td>
</tr>
<tr>
<td>Ultrafiltration</td>
<td>Variable (maximum around 250 ml/h) + profile</td>
</tr>
<tr>
<td>Sodium</td>
<td>Fixed 145-150 mEq/L or profile</td>
</tr>
<tr>
<td>Dialysate temperature</td>
<td>35°C</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>Unfractionated heparin 500-1000 UI/hour</td>
</tr>
</tbody>
</table>

There is no difference regarding dialyzers (high or low flow) and the dialysate. Anticoagulation can be done with unfractionated heparin (doses being 50\% to 75\% lower than in continuous treatment), citrate\textsuperscript{23} or saline solution flush.\textsuperscript{24}

The main reason for choosing EH in lieu of conventional intermittent treatment is cardiovascular instability. EH is already preferable in patients dependent on noradrenaline doses greater than 0.2 mcg/kg/min,\textsuperscript{25} as well as in patients with decompensated heart and liver diseases - patients more prone to intradialytic hypotension.

Another EH advantage is the possibility of having evening sessions, not limited to diagnostic procedures during daytime.\textsuperscript{19} Since it uses the same equipment used in conventional intermittent hemodialysis, the costs get to be 6-8 times lower than in continuous treatment.\textsuperscript{24}

**Clinical experience in EH use in critically-ill patients**

Several recently published studies confirm the good hemodynamic tolerability and effective dialysis doses associated with prolonged hemodialysis, even when compared to continuous treatments.

In one of the first publications on this topic, Marshall et al.\textsuperscript{26} analyzed 37 patients submitted to EH sessions (12 hours) and reported excellent solute removal and hemodynamic stability, with less than 8\% of sessions suspended for refractory hypotension. The mortality rate was comparable to that of continuous treatments.

In extended hemodialysis sessions (8 hours, six times per week), Berbeco et al.\textsuperscript{24} found higher dialysis doses when compared to continuous hemofiltration.

Kumar et al.\textsuperscript{13} compared patients under daily treatment with continuous hemodialysis and HE (mean duration of 7.5 hours per session). There was no significant difference in mean arterial pressure during or after the procedure; ultrafiltration goals were similar between the groups (3.000 ml/day versus 3.028 ml/day). In addition, there was significant reduction in the heparin dose used (mean 4.000 IU/day versus 21.000 IU/day).

Kielstein et al.\textsuperscript{27} analyzed patients undergoing extended hemodialysis sessions (12 hour-sessions) and continuous hemofiltration. Again, there was no variation vis-à-vis blood pressure, need for vasoactive drugs and cardiac output during the sessions. The urea reduction rates of both modalities were similar and urea indices normalization was faster with EH. In a similar study (8-hour HE sessions), Fieghen et al.\textsuperscript{28} also observed no differences in relation to hemodynamic instability between EH and continuous therapies.

The HANNOVER\textsuperscript{29} study showed similar survival (14 and 28 days) and renal function recovery after 1 month in patients treated with standard EH (urea target 120-150 mg/dl) or intensive EH (urea lower than...
90 mg/dl). Palevsky et al.\textsuperscript{30} showed that EH - either intensive (mean of 5.4 sessions/week) or conventional (mean of 3 sessions/week) showed no differences in mortality and kidney survival when compared to continuous treatment (similar dialysis dose and ultrafiltration targets).

In a multicentric and randomized study, Marshall et al.\textsuperscript{31} showed that the conversion of continuous hemodialysis into EH (EH either extended or conventional hemodiafiltration) did not affect the mortality of patients while maintaining good hemodynamic tolerability and kidney function recovery.

In a recent publication, Schwenger et al.\textsuperscript{32} compared extended hemodialysis (115 patients, 817 sessions) and continuous hemodialysis (117 patients, 877 sessions) in a prospective randomized study. After 90 days, mortality in both groups was the same. There was no difference in hemodynamic stability. EH patients spent less time on mechanical ventilation and fewer days in the ICU, and had lower demand for nursing care during dialysis, thereby generating lower costs.

**OTHER CLINICAL ASPECTS AND RELEVANT APPLICATIONS**

Continuous approaches enable the association of convective and diffusive clearance (continuous hemofiltration and hemodiafiltration). Similarly, EH may also be broadened to perform extended hemodiafiltration. In this technique, there is an increased elimination of medium-size molecules and inflammatory mediators as well as the dialysis dose supplied. Marshall et al.\textsuperscript{33} analyzed 56 extended hemodiafiltration sessions (8 hours) in 24 patients, and found no complications associated with hypotension (such as the introduction of new inotropic agents). The dialysis dose of was high and costs are lower when compared to continuous hemodiafiltration, due to the online generation of replacement fluids.\textsuperscript{34}

Abe et al.\textsuperscript{35} observed that extended hemodiafiltration (6-8 hours, minimum replacement volume of 14 liters) showed higher doses of dialysis and renal recovery rates when compared to continuous hemodiafiltration, and shorter hospital stay.

In severe cardiac functional class IV patients, with hemodynamic instability, resistant to diuretics and techniques of conventional hemodialysis, clinical improvement was evident with EH.\textsuperscript{36}

In situations where it is extremely important to avoid osmolar imbalance, as in patients with liver disease and encephalopathy, there are reports that EH was effective in maintaining cerebral blood flow, avoiding increases in intracranial pressure.\textsuperscript{37}

In cases of exogenous poisoning (salicylate and lithium), EH also proved effective, with effects comparable to those achieved with continuous therapies.\textsuperscript{38,39}

With the spread of EH in the ICU, recent studies have evaluated the pharmacokinetic changes caused on some antibiotics. Thus, drugs such as vancomycin, carbapenems, linezolid and ampicillin-sulbactam should have their doses increased and supplemented after EH completion.\textsuperscript{40-42}

**CONCLUSION**

In Europe and the United States, EH still accounts for only 25% of ICU dialyses.\textsuperscript{43,44} In Brazil, especially because of the lack of continuous treatment in most centers, EH emerges as an important therapeutic alternative for critically ill patients, and its use should be increasingly encouraged.

Recent published studies have proven its efficiency in terms of supplied dialysis dose, hemodynamic stability, and in mortality and renal function recovery rates, very close to or even higher than those achieved with continuous treatment. Even the addition of convective clearance - which before was an exclusive option of continuous procedures, it is now held in prolonged intermittent treatment with lower costs. For these reasons, EH is becoming the dialysis method increasingly used in hemodynamically unstable patients in the ICU.\textsuperscript{45,46}

**REFERENCES**


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