# Extended hemodialysis in acute kidney injury

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Submitted on: 01/31/2012.
Approved on: 03/18/2013.

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DOI: 10.5935/0101-2800.20130023

## 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.[1]

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%.[2] RRT modes in this population may be intermittent (conventional hemodialysis and peritoneal dialysis) or continuous (continuous hemodialysis, hemofiltration or hemodiafiltration).[3] The choice of the optimal method depends on the patient's clinical status, the medical knowledge and the availability in each center.[4] Although there are studies comparing these treatment modalities, differences on mortality and renal function recovery have not been investigated.[5-8] 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).[9,10] Intradialytic hypotension reduces the dialysis dose and maintains the ischemic lesion, thus delaying AKI recovery.[11]

When compared with intermittent treatment, continuous methods provide for better hemodynamic stability, being preferable in hemodynamically unstable patients.[12] However, the need for continuing anticoagulation, skilled nursing and its high cost makes them unavailable in many centers.[13]

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.[14,15] 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.[16]

## Extended hemodyalisis (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.[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.[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)[19] and in some situations there is also the possibility for continuous mode operation.[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).[21,22]

**Table 1** Extended hemodialysis prescription model

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

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[23] or saline solution flush.[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,[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.[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.[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*.,[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), Berbece *et al*.[24] found higher dialysis doses when compared to continuous hemofiltration.

Kumar *et al*.[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*.[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*.[28] also observed no differences in relation to hemodynamic instability between EH and continuous therapies.

The HANNOVER[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.*[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.*[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.*[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.*[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.[34]

Abe *et al.*[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.[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.[37]

In cases of exogenous poisoning (salicylate and lithium), EH also proved effective, with effects comparable to those achieved with continuous therapies.[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.[40-42]

## Conclusion

In Europe and the United States, EH still accounts for only 25% of ICU dialyses.[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.[45,46]

## References


1. Ricci Z, Ronco C. Dose and efficiency of renal replacement therapy: continuous renal replacement therapy versus intermittent hemodialysis versus slow extended daily dialysis. Crit Care Med 2008;36:S229-37. http://dx.doi.org/10.1097/CCM.0b013e318168e467 PMid:18382199
2. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, et al.; Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA 2005;294:813-8. http://dx.doi.org/10.1001/jama.294.7.813 PMid:16106006
3. Ricci Z, Ronco C, D'Amico G, De Felice R, Rossi S, Bolgan I, et al. Practice patterns in the management of acute renal failure in the critically ill patient: an international survey. Nephrol Dial Transplant 2006;21:690-6. http://dx.doi.org/10.1093/ndt/gfi296 PMid:16326743
4. Davenport A. Renal replacement therapy in acute kidney injury: which method to use in the intensive care unit? Saudi J Kidney Dis Transpl 2008;19:529-36. PMid:18580008
5. Gabriel DP, Caramori JT, Martin LC, Barretti P, Balbi AL. Continuous peritoneal dialysis compared with daily hemodialysis in patients with acute kidney injury. Perit Dial Int 2009;29 Suppl 2:S62-71. PMid:19270234

6. Vanholder R, Van Biesen W, Lameire N. What is the renal replacement method of first choice for intensive care patients? J Am Soc Nephrol 2001;12 Suppl 17:S40-3. PMid:11251030
7. Uehlinger DE, Jakob SM, Ferrari P, Eichelberger M, Huynh-Do U, Marti HP, et al. Comparison of continuous and intermittent renal replacement therapy for acute renal failure. Nephrol Dial Transplant 2005;20:1630-7. http://dx.doi.org/10.1093/ndt/gfh880 PMid:15886217
8. Vinsonneau C, Camus C, Combes A, Costa de Beauregard MA, Klouche K, Boulain T, et al. Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. Lancet 2006;368:379-85. http://dx.doi.org/10.1016/S0140-6736(06)69111-3
9. Doshi M, Murray PT. Approach to intradialytic hypotension in intensive care unit patients with acute renal failure. Artif Organs 2003;27:772-80. http://dx.doi.org/10.1046/j.1525-1594.2003.07291.x PMid:12940898
10. Murray P, Hall J. Renal replacement therapy for acute renal failure. Am J Respir Crit Care Med 2000;162:777-81. http://dx.doi.org/10.1164/ajrccm.162.3.ncc400 PMid:10988080
11. Garg N, Fissell WH. Intradialytic hypotension: a case for going slow and looking carefully. Nephrol Dial Transplant 2013;28:247-9. http://dx.doi.org/10.1093/ndt/gfs316 PMid:22848109
12. Uchino S, Ronco C. Continous Renal Replacement Theraphy. In: Jorres A, Ronco C, Kellum JA, editors. Management of Acute Kidney Problems. 1st ed. New York: Springer; 2010. p.525-35. http://dx.doi.org/10.1007/978-3-540-69441-0_52
13. Kumar VA, Craig M, Depner TA, Yeun JY. Extended daily dialysis: A new approach to renal replacement for acute renal failure in the intensive care unit. Am J Kidney Dis 2000;36:294-300. http://dx.doi.org/10.1053/ajkd.2000.8973 PMid:10922307
14. Kihara M, Ikeda Y, Shibata K, Masumori S, Fujita H, Ebira H, et al. Slow hemodialysis performed during the day in managing renal failure in critically ill patients. Nephron 1994;67:36-41. http://dx.doi.org/10.1159/000187885 PMid:8052365
15. Marshall MR, Golper TA, Shaver MJ, Alam MG, Chatoth DK. Urea kinetics during sustained low-efficiency dialysis in critically ill patients requiring renal replacement therapy. Am J Kidney Dis 2002;39:556-70. http://dx.doi.org/10.1053/ajkd.2002.31406 PMid:11877575
16. Fliser D, Kielstein JT. Technology Insight: treatment of renal failure in the intensive care unit with extended dialysis. Nat Clin Pract Nephrol 2006;2:32-9. http://dx.doi.org/10.1038/ncpneph0060 PMid:16932387
17. Marshall MR, Golper TA. Low-efficiency acute renal replacement therapy: role in acute kidney injury. Semin Dial 2011;24:142-8. http://dx.doi.org/10.1111/j.1525-139X.2011.00829.x PMid:21517979
18. Marshall M, Shaver M, Alam M, Chatoth D. Prescribed versus delivered dose of sustained low-efficiency dialysis (SLED) [Abstract]. J Am Soc Nephrol 2000;11:324A.
19. Lima EQ, Burdmann EA, Yu L. Adequação de diálise em insuficiência renal aguda. J Bras Nefrol 2003;25:149-54.
20. Salahudeen AK, Kumar V, Madan N, Xiao L, Lahoti A, Samuels J, et al. Sustained low efficiency dialysis in the continuous mode (C-SLED): dialysis efficacy, clinical outcomes, and survival predictors in critically ill cancer patients. Clin J Am Soc Nephrol 2009;4:1338-46. http://dx.doi.org/10.2215/CJN.02130309 PMid:19628685 PMCid:2723965
21. Paganini EP, Sandy D, Moreno L, Kozlowski L, Sakai K. The effect of sodium and ultrafiltration modelling on plasma volume changes and haemodynamic stability in intensive care patients receiving haemodialysis for acute renal failure: a prospective, stratified, randomized, cross-over study. Nephrol Dial Transplant 1996;11 Suppl 8:32-7. http://dx.doi.org/10.1093/ndt/11.supp8.32 PMid:9044338
22. Lima EQ, Silva RG, Donadi EL, Fernandes AB, Zanon JR, Pinto KR, et al. Prevention of intradialytic hypotension in patients with acute kidney injury submitted to sustained low-efficiency dialysis. Ren Fail 2012;34:1238-43. http://dx.doi.org/10.3109/0886022X.2012.723581 PMid:23006063
23. Clark JA, Schulman G, Golper TA. Safety and efficacy of regional citrate anticoagulation during 8-hour sustained low-efficiency dialysis. Clin J Am Soc Nephrol 2008;3:736-42. http://dx.doi.org/10.2215/CJN.03460807 PMid:18272829 PMCid:2386695
24. Berbece AN, Richardson RM. Sustained low-efficiency dialysis in the ICU: cost, anticoagulation, and solute removal. Kidney Int 2006;70:963-8. http://dx.doi.org/10.1038/sj.ki.5001700 PMid:16850023
25. Costa MC, Curvello Neto AL, Yu L. Métodos hemodiáliticos contínuos para tratamento da Insuficiência Renal Aguda. In Riella MC. Princípios de Nefrologia e Distúrbios Hidroeletrolíticos. 5ª ed. Rio de Janeiro: Guanabara-Koogan; 2010. p.1020-31.
26. Marshall MR, Golper TA, Shaver MJ, Alam MG, Chatoth DK. Sustained low-efficiency dialysis for critically ill patients requiring renal replacement therapy. Kidney Int 2001;60:777-85. http://dx.doi.org/10.1046/j.1523-1755.2001.060002777.x PMid:11473662
27. Kielstein JT, Kretschmer U, Ernst T, Hafer C, Bahr MJ, Haller H, et al. Efficacy and cardiovascular tolerability of extended dialysis in critically ill patients: a randomized controlled study. Am J Kidney Dis 2004;43:342-9. http://dx.doi.org/10.1053/j.ajkd.2003.10.021 PMid:14750100
28. Fieghen HE, Friedrich JO, Burns KE, Nisenbaum R, Adhikari NK, Hladunewich MA, et al.; University of Toronto Acute Kidney Injury Research Group. The hemodynamic tolerability and feasibility of sustained low efficiency dialysis in the management of critically ill patients with acute kidney injury. BMC Nephrol 2010;25;11-32.
29. Faulhaber-Walter R, Hafer C, Jahr N, Vahlbruch J, Hoy L, Haller H, et al. The Hannover Dialysis Outcome study: comparison of standard versus intensified extended dialysis for treatment of patients with acute kidney injury in the intensive care unit. Nephrol Dial Transplant 2009;24:2179-86. http://dx.doi.org/10.1093/ndt/gfp035 PMid:19218540
30. VA/NIH Acute Renal Failure Trial Network, Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, et al. Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med 2008;359:7-20. http://dx.doi.org/10.1056/NEJMoa0802639 PMid:18492867 PMCid:2574780
31. Marshall MR, Creamer JM, Foster M, Ma TM, Mann SL, Fiaccadori E, et al. Mortality rate comparison after switching from continuous to prolonged intermittent renal replacement for acute kidney injury in three intensive care units from different countries. Nephrol Dial Transplant 2011;26:2169-75. http://dx.doi.org/10.1093/ndt/gfq694 PMid:21075821
32. Schwenger V, Weigand MA, Hoffmann O, Dikow R, Kihm LP, Seckinger J, et al. Sustained low efficiency dialysis using a single-pass batch system in acute kidney injury - a randomized interventional trial: the REnal Replacement Therapy Study in Intensive Care Unit PatiEnts. Crit Care 2012;16:R140. http://dx.doi.org/10.1186/cc11815 http://dx.doi.org/10.1186/cc11445 PMid:22839577 PMCid:3580725
33. Marshall MR, Ma T, Galler D, Rankin AP, Williams AB. Sustained low-efficiency daily diafiltration (SLEDD-f) for critically ill patients requiring renal replacement therapy: towards an adequate therapy. Nephrol Dial Transplant 2004;19:877-84. http://dx.doi.org/10.1093/ndt/gfg625 PMid:15031344
34. Holt BG, White JJ, Kuthiala A, Fall P, Szerlip HM. Sustained low-efficiency daily dialysis with hemofiltration for acute kidney injury in the presence of sepsis. Clin Nephrol 2008;69:40-6. PMid:18218315

35. Abe M, Okada K, Suzuki M, Nagura C, Ishihara Y, Fujii Y, et al. Comparison of sustained hemodiafiltration with continuous venovenous hemodiafiltration for the treatment of critically ill patients with acute kidney injury. Artif Organs 2010;34:331-8. http://dx.doi.org/10.1111/j.1525-1594.2009.00861.x PMid:20420616
36. Violi F, Nacca RG, Iengo G, Iorio L, et al. Long-term sustained low efficiency dialysis in eight patients with class IV NYHA heart failure resistant to high-dose diuretic treatment. G Ital Nefrol 2009;26 Suppl 46:50-2. PMid:19644818
37. Bandyopadhyay S, Jakobson D, Chhabra KD, Baker A . Improvement of cerebral blood flow patterns in hepatorenal syndrome using sustained low-efficiency dialysis. Br J Anaesth 2010;105:547-8. http://dx.doi.org/10.1093/bja/aeq253 PMid:20837726
38. Fiaccadori E, Maggiore U, Parenti E, Greco P, Cabassi A. Sustained low-efficiency dialysis (SLED) for acute litium intoxication. Clin Kidney J 2008;1:329-32.
39. Lund B, Seifert SA, Mayersohn M. Efficacy of sustained low-efficiency dialysis in the treatment of salicylate toxicity. Nephrol Dial Transplant 2005;20:1483-4. http://dx.doi.org/10.1093/ndt/gfh796 PMid:15797887
40. Bogard KN, Peterson NT, Plumb TJ, Erwin MW, Fuller PD, Olsen KM. Antibiotic dosing during sustained low-efficiency dialysis: special considerations in adult critically ill patients. Crit Care Med 2011;39:560-70. http://dx.doi.org/10.1097/CCM.0b013e318206c3b2 PMid:21221000
41. Mushatt DM, Mihm LB, Dreisbach AW, Simon EE. Antibiotic dosing in slow extended daily dialysis. Clin Infect Dis 2009;49:433-7. http://dx.doi.org/10.1086/600390 PMid:19580416
42. Lorenzen JM, Broll M, Kaever V, Burhenne H, Hafer C, Clajus C, et al. Pharmacokinetics of ampicillin/sulbactam in critically ill patients with acute kidney injury undergoing extended dialysis. Clin J Am Soc Nephrol 2012;7:385-90. http://dx.doi.org/10.2215/CJN.05690611 PMid:22223613 PMCid:3302675
43. Ricci Z, Ronco C, D'Amico G, De Felice R, Rossi S, Bolgan I, et al. Practice patterns in the management of acute renal failure in the critically ill patient: an international survey. Nephrol Dial Transplant 2006;21:690-6. http://dx.doi.org/10.1093/ndt/gfi296 PMid:16326743
44. Overberger P, Pesacreta M, Palevsky PM.; VA/NIH Acute Renal Failure Trial Network. Management of renal replacement therapy in acute kidney injury: a survey of practitioner prescribing practices. Clin J Am Soc Nephrol 2007;2:623-30. http://dx.doi.org/10.2215/CJN.00780207 PMid:17699474 PMCid:2325917
45. Vanholder R, Van Biesen W, Hoste E, Lameire N. Pro/con debate: continuous versus intermittent dialysis for acute kidney injury: a never-ending story yet approaching the finish? Crit Care 2011;15:204. http://dx.doi.org/10.1186/cc9345 PMid:21345275 PMCid:3222013
46. Kielstein JT, Schiffer M, Hafer C. Back to the future: extended dialysis for treatment of acute kidney injury in the intensive care unit. J Nephrol 2010;23:494-501. PMid:20853250