Section 5.2. DIALYSIS INTERVENTIONS FOR THE TREATMENT OF ACUTE KIDNEY INJURY

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GUIDELINES

1. Dose and delivery of dialysis
   We recommend the following dose of dialysis should be prescribed / delivered in AKI patients:
   a. An effluent volume of 20-25 ml/kg/hr when using CRRT. (1A)
   b. A Kt/V of 3.9 per week when using intermittent HD. (1A)
   c. A target plasma urea of < 25 mmol/l when using intermittent HD or SLED. (1B)

2. CRRT vs. IRRT
   a. We suggest using CRRT and IRRT as complementary therapies in AKI patients and in the context of local resources available (2C) however, we suggest that CRRT be used in preference to IRRT in AKI patients:
      ● Who are haemodynamically unstable (2B); or
      ● Who have acute brain injury or generalised brain oedema. (2B)

UNGRADED SUGGESTIONS FOR CLINICAL CARE

● In AKI, peritoneal dialysis may be prescribed in order to achieve the goals of fluid, electrolyte and acid-base balance, depending on local resources that are available. (Ungraded)

BACKGROUND

Acute kidney injury is a common problem in critically ill patients which may be associated with substantial morbidity and mortality. Renal replacement therapy (RRT) is often required in such patients in order to maintain fluid, electrolyte and acid-base balance. Whilst continuous RRT (CRRT) and intermittent haemodialysis (HD) are the most commonly used modalities, controversy remains as to what is the optimal dose and method of delivery of RRT. There is emerging use of alternative modalities, such as sustained low-efficiency dialysis (SLED) and peritoneal dialysis (PD), particularly in the
context of locally available resources, however mortality rates of acute kidney injury (AKI) remain largely unchanged.

SEARCH STRATEGY

The search strategy was an update of that used by KDIGO (refer to Table 21 in the Appendix of the KDIGO guideline) (Kidney International Supplements 2 (2012); 2: 102-113). Additional key papers have been identified by the authors that were published after the KHA-CARI update search.

Databases searched: Medline, Central, Cochrane database of systematic reviews.
Date of searches: June 2012

ADEQUACY OF KDIGO SEARCH STRATEGY

The search strategy and evidence provided was comprehensive and included some important randomised controlled trials (RCTs). A number of systematic reviews and RCTs have subsequently been identified in the updated search by KHA-CARI and included in this update.

APPLICABILITY OF KDIGO RECOMMENDATIONS AND SUGGESTIONS

Many of the KDIGO guidelines for the dose and delivery of dialysis in AKI are in keeping with local practice in Australia and New Zealand. Use of PD in AKI is generally quite limited in the region as HD resources are widely available.

OVERVIEW OF THE EVIDENCE

The following search provides an overview of the evidence as identified in the KDIGO guidelines and the updated searches conducted by KHA-CARI as part of the adaptation process.

Intensity of dialysis

Earlier studies suggested benefit of more intense over less intense dose of RRT in AKI. Although there is some variability in the definition of intensive versus less intensive RRT, there is no evidence to suggest superiority of intensive RRT. Several systematic reviews have been published in the last 2 years. Casey et al [1] examined 7 RCTs with 3545 participants (mean age 64 yrs.) in which differing dosing regimens of CRRT were compared. The mean study duration was 60 days for mortality and 71 days for RRT dependence. There was no difference in mortality (RR 0.88 [0.75-1.03]), RRT dependence
(RR 1.02 [0.86-1.46]) or length of hospital/ICU stay with a higher prescribed dose (35-65 vs. 20-35 ml/kg/h) or delivered (29-62 vs. 17-32 ml/kg/h) dose of CRRT.

Jun et al [2] examined 7 RCTs and 1 quasi-RCT with 3841 participants comparing intensive versus less intensive RRT with either CRRT (prescribed dose 35-48 vs. 20-25 ml/kg/h) or intermittent HD (target weekly Kt/V 8.4 vs. 4.2, target urea < 90 (i.e. 15 mmol/l) vs. 120-150 mg/dl, or delivered dose 36.2 vs. 21.5 ml/kg/h). Whilst there was no difference in mortality (RR 0.89 [0.76-1.04]) or RRT dependence (RR 1.12 [0.86-1.46]), significant heterogeneity was identified with both publication year and Jadad score.

Van Wert et al [3] included 12 studies (n=3999) examining CRRT, intermittent HD and SLED. There was considerable variability between studies in study duration for both mortality and RRT dependence (varying from 28 days – 6 months post randomisation, time of hospital discharge and 14-15d following cessation of RRT). Intensive versus less intensive RRT was variably defined according to modality used. Regardless, there was no difference in pooled mortality (RR 0.89 [0.77-1.03]), RRT dependence (RR 1.15 [0.92-1.44]) or subgroup analysis thereof (sepsis, risk of bias or modality used).

A systematic review by Zhongheng et al [4] examined 6 studies of CRRT in 3490 participants. Mean age of patients and their baseline renal function was not stated. Again, there was no difference in pooled mortality (RR 0.91 [0.77-1.08]), RRT recovery (RR 0.95 [0.89-1.00] or ICU length of stay.

Finally, Negash et al [5] examined 5 RCTs with 2402 participants (mean age 51-68yrs). The mean study duration was 28 days for pooled mortality and 71 days for RRT dependence. No difference in mortality (RR 0.88 [0.70-1.11]) was identified for patients receiving more intense (prescribed dose 35-45 vs. 20-34 ml/kg/h, delivered dose 29-48.2 ml/kg/h vs. 17-22 ml/kg/h).

There is very little published literature examining PD in AKI. Ponce et al [6] conducted an RCT of 51 patients examining more versus less intense PD therapy (prescribed Kt/V 0.8 vs. 0.5/session treated for 5.7-6.1d). There was no difference in the primary outcome of 30 day mortality, renal recovery or metabolic control.

Two recent observational studies, one a retrospective review of patients with sepsis-induced AKI requiring continuous veno-venous hemofiltration (CVVH) (n=97) [7], the other a prospective multicentre study of 553 patients treated with CRRT or intermittent RRT (IRRT) (n=553) [8], suggested outcomes that differed somewhat to those of other studies. In patients with sepsis-induced AKI, a lower delivered dose (< 19.7 ml/kg/h) was associated with increased mortality, independent of disease, substitution fluid and azotaemic control. In the other study, whilst there was no difference in ICU mortality, more intensive RRT was associated with a favourable effect on ICU length of stay (CRRT: 15 vs. 19.5 days, P=0.063; IRRT: 8 vs. 18 days, P=0.008) and duration of
mechanical ventilation among survivors (CRRT: 7 vs. 14 days, P=0.031; IRRT 2.5 vs. 12 days, P=0.026).

Continuous versus intermittent RRT

The theoretical advantages and disadvantages of CRRT, SLED and PD are well known. These relate primarily to issues of haemodynamic stability, fluid control, solute removal, anticoagulation and cost. Despite this and as identified in the KDIGO guidelines, neither the recent systematic review by Rabindranath et al [9] (15 RCTs, n=1550) nor a subsequently published RCT [10] (SHARF trial, n=316) identified any clear benefit of CRRT over intermittent HD in terms of hospital or ICU mortality, length of hospitalisation or renal recovery.

Abe et al [11] conducted a small RCT (n=60), examining a novel approach using sustained haemodiafiltration (S-HDF) in comparison to continuous venovenous haemodiafiltration (CVVHDF). Whilst there was no difference in the primary outcome of survival at ICU discharge of 30 days, S-HDF was associated with better hospital survival (83 vs. 63%, P<0.05) and more patients with renal recovery.

Again, there is a paucity of literature relating to PD versus HD in AKI. George et al [12] conducted an RCT of 50 patients treated with either CVVHDF or continuous PD. There was no difference in the primary outcome of composite correction of uraemia, acidosis, fluid overload and hyperkalaemia (48 vs. 56%) or mortality (84 vs. 72%); however CVVHDF was associated with increased cost whilst continuous PD was associated with better correction of acidosis. A RCT examining continuous PD compared to daily HD [13] (n=120) similarly found no survival benefit but duration of therapy was longer with daily HD (7.5 vs. 5.5 days, P=0.02). Finally, a small retrospective, observational study of 145 patients [14] found no difference between those treated with intermittent PD vs. HD.

Acute brain injury (ABI) and other causes of increased intracranial pressure

Patients with various types of ABI may be at increased risk of neurological deterioration in the face of intermittent RRT. This is likely to be related to rapid changes in serum osmolality and blood pH coupled with a reduction in mean arterial pressure which collectively may lead to concomitant increases in intracranial and cerebral perfusion pressure. Whilst there is no literature comparing outcomes in patients treated with continuous versus intermittent RRT, it would seem reasonable to suggest that CRRT should be used in patients with ABI and other conditions associated with increased intracranial pressure.
Cost of dialysis

Cost is relevant when considering the modality of RRT in AKI, particularly given the lack of evidence to indicate superiority of either continuous or intermittent RRT. Srisawat N et al [15] conducted a post hoc analysis of the BEST study (a prospective epidemiologic study of 53 centres from 23 countries) to determine the range and variation of costs between CRRT and IRRT. The median difference in cost was $289.60 per day (that is, greater with CRRT) with a wide range varying from $3629.80/day more for CRRT to $378.60/day more for IRRT. Cost domains examined included nursing, replacement fluid, anticoagulation and extracorporeal circuit, and the study indicated that cost could be substantially reduced (by $67.20/day) by limiting effluent flow rate to 25 ml/min (~ 25 ml/kg/h).

SUMMARY OF EVIDENCE

RCTs and systematic reviews demonstrate no evidence for a survival benefit with either CRRT or IRRT. Considerations when deciding upon modality should therefore include clinical circumstances (such as haemodynamic stability and conditions such as ABI), locally available resources and cost. More compelling evidence exists to indicate that there is no benefit in more intensive over less intensive dialysis regimens, whether the modality used is CRRT, intermittent HD or, to a lesser extent, PD.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcome Quality Initiative (2013):
No recommendations

UK Renal Association (2011): [16]
Guideline 6.1 – AKI: Choice of renal replacement modality
We recommend that the choice of renal replacement therapy modality should be guided by the individual patient’s clinical status, medical and nursing expertise, and availability of modality. (1B)
Guideline 10.1 – AKI: Renal Replacement Therapy prescription
We recommend that the delivered dose of RRT should be assessed to ensure the adequacy of the prescription. (1A)
Guideline 10.2 – AKI: Renal Replacement Therapy prescription
We recommend that the prescribed dose should be assessed at each session (for intermittent haemodialysis) and daily (for continuous techniques) to account for any measured shortfalls in delivered dose. (1A)
Guideline 10.3 – AKI: Renal Replacement Therapy prescription
We recommend that patients with AKI and multi-organ failure treated by continuous renal replacement therapy (CRRT) should receive treatment doses equivalent to post dilution ultrafiltration rates ≥ 25 ml/kg/hr. A proportionate upward adjustment to the prescribed ultrafiltration rate should be made in pre-dilution continuous haemofiltration. (1A)

Guideline 10.4 – AKI: Renal Replacement Therapy prescription

We recommend that patients with AKI and multi-organ failure treated by intermittent haemodialysis should receive either alternate day haemodialysis with at least the minimum dose considered appropriate for end-stage renal disease (ESRD), urea reduction ratio (URR) >65% or eKt/V>1.2 or daily haemodialysis. (1B)

Guideline 10.5 – AKI: Renal Replacement Therapy prescription

We suggest that renal replacement therapy dosing methods that require an assessment of patient weight should use a measured weight rather than an extrapolated weight from pre-morbid readings. (2B)

Canadian Society of Nephrology (2013):
No recommendations.

European Renal Best Practice Guidelines (2012):
No Recommendations.

SUGGESTIONS FOR FUTURE RESEARCH

RCTs should be conducted to examine the utility of therapies other than CRRT, including SLED and PD. Parameters examined should include optimal dose and cost utility analyses.

CONFLICT OF INTEREST

REFERENCES


