Renal Association Clinical Practice Guideline on Haemodialysis

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Introduction

The basis for the management of advanced chronic kidney disease is the seamless integration of renal replacement therapy (HD, peritoneal dialysis, and transplantation) with evidence based medical treatment of its complications. The National Service Framework Part 1: Dialysis and Transplantation has stressed the need for a patient-centred approach in the planning and provision of renal replacement therapy with an emphasis on patient education and choice as well as the provision of adequate resources for elective access surgery, dialysis and transplantation [1]. It also identified that a small proportion of patients after counselling may opt for optimal conservative medical therapy without planning to initiate dialysis.

It is estimated that there are more than 1.5 million patients with established renal failure who are treated with HD. Innovations and changes in HD practice have seldom been underpinned by adequately powered randomised trials. Nevertheless, day-to-day clinical decisions on HD are required and standards need to be set on the best available evidence. Consequently clinical practice guidelines for HD have been developed in Australasia, Canada, Europe and the USA [2–5] as well as the UK. These guidelines serve to identify and promote best practice in the delivery of HD and have set clinical standards to allow comparative audit of the key aspects of the HD prescription, laboratory data and patient outcomes. The reports of the UK Renal Registry, Scottish Renal Registry and NHS Quality Improvement Scotland have demonstrated the benefits of performing regular audit to improve clinical standards in HD.

This module provides an update of the 2007 RA clinical practice guidelines in HD and, most importantly, modification of the current guidelines whenever indicated by evidence from new studies. In preparation of this update the authors performed a Medline and Pubmed search of all articles published on HD since the

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last version (2007–2009), searched and reviewed the Cochrane Renal Database in the Cochrane Library 2009, Issue 2 and reviewed the status of all of the HD clinical trials (n = 257) registered at www.clinicaltrials.gov on 29.04.2009. The strength of each of the recommendations and the level of evidence have been documented using the Modified GRADE system, which also has been adopted by all of the other international nephrology guideline development groups including KDIGO [6–8]. The USA (NKF-KDOQI) and European (EBPG) guidelines on HD have also been updated [2, 3] and standardisation with these and other international guidelines on HD has been attempted whenever possible. The sections on vascular access and planning, initiation and withdrawal of renal replacement therapy in the 2007 version have been removed as two separate new modules have been developed to provide guidance on these key areas in the provision of high quality care in HD. Separate sections have been included in this update on anticoagulation, home haemodialysis, frequent and/or extended duration HD and patient safety on HD.

The module format has been designed to permit easy modification on the website to incorporate future changes in practice recommendations based on evidence from new research. This guideline promotes the adoption of a range of standardised audit measures in HD and the proportions of patients who should achieve clinical and laboratory performance indicators have not been specified for most of the clinical practice guidelines. This approach is designed to promote a progressive increase in the achievement of audit measures in parallel with improvements in clinical practice.

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Summary of Clinical Practice Guideline on Haemodialysis

1. Haemodialysis (HD) (Guidelines 1.1–1.6)

Guideline 1.1 – HD: Haemodialysis facilities
We recommend that the specification of new or refurbished HD facilities should adhere to the guidelines that are described in the NHS Estates Health Building Notes 07-01 Satellite Dialysis Unit and 07-02 Main Renal Unit. (1C)

Guideline 1.2 – HD: Haemodialysis facilities
We recommend that the HD facility should have sufficient specialist support staff to fulfil the criteria listed by the Renal Workforce Planning Group 2002. (1C)

Guideline 1.3 – HD: Haemodialysis facilities
We recommend that, except in remote geographical areas the travel time to a HD facility should be less than 30 minutes or a HD facility should be located with 25 miles of the patient's home. In inner city areas travel times over short distances may exceed 30 minutes at peak traffic flow periods during the day. (1B)

Guideline 1.4 – HD: Haemodialysis facilities
We suggest that HD patients who require transport should be collected from home within 30 minutes of the allotted time and be collected to return home within 30 minutes of finishing dialysis. (2C)

Guideline 1.5 – HD: Haemodialysis facilities
We suggest that HD capacity in satellite and main renal units within a geographical area should increase in step with predicted need. The national average number of hospital HD patients per million catchment population reported for the previous year by the UK Renal Registry should be regarded as the minimum capacity for HD in each geographically based renal service. (2C)

Guideline 1.6 – HD: Haemodialysis facilities
We suggest that the required number of HD stations should be based on using each station for 2 patients per day three times per week. This approach allows for patient choice regarding HD schedules, more frequent dialysis schedules, provision of holiday HD and expansion in patient numbers. (2C)

2. Haemodialysis (HD) (Guidelines 2.1–2.3)

Guideline 2.1 – HD: Haemodialysis equipment and disposables
We recommend that all equipment used in the delivery and monitoring of HD should be CE marked and approved to ensure compliance with the relevant safety standards BS EN 60601-1:2006 *General safety standards for electrical equipment in clinical use* (currently under revision with the revised version being available in 2010) and BS EN 60601-2-16:2008 *Particular requirements for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment.* (1C)

Guideline 2.2 – HD: Haemodialysis equipment and disposables
We recommend that all disposable items used in the delivery of HD (such as haemodialysers, associated devices and the extracorporeal circuits used with such devices) should be CE marked to indicate compliance with the relevant standards. (1C)

Guideline 2.3 – HD: Haemodialysis equipment and disposables
We suggest that machines should be replaced after between seven and ten years' service or after completing between 25,000 and 40,000 hours of use for HD, depending upon an assessment of machine condition. (2C)

3. Haemodialysis (HD) (Guidelines 3.1–3.8)

Guideline 3.1 – HD: Concentrates for haemodialysis
We recommend that commercially produced concentrates are classified as medical devices and should be CE marked to demonstrate compliance with BS ISO 13958:2009 *Concentrates for haemodialysis and related therapies* and the water used for diluting the concentrates should comply with BS ISO 13959:2009 *Water for haemodialysis and related therapies* or meet the requirements stated in the European Pharmacopoeia (6th edition, 2007). (1C)

Guideline 3.2 – HD: Specification of water treatment system for haemodialysis
We recommend that the complete water treatment, storage and distribution system should meet the requirements of BS ISO 26722:2009 *Water treatment equipment for haemodialysis applications and related therapies* and be shown to be capable of meeting the requirements of BS

ISO 13959:2009 *Water for haemodialysis and related therapies* at the time of installation. (1C)

Guideline 3.3 – HD: Chemical contaminants in water used for the preparation of dialysis fluid

We recommend that the concentrations of chemical contaminants in water used to prepare dialysis fluid should not exceed the limits stated either in BS ISO 13959:2009 *Water for haemodialysis and related therapies* or in the European Pharmacopoeia (6th edition, 2007). A programme of improvement should begin immediately if routine monitoring demonstrates that concentrations of chemical contaminants exceed the maximum allowable limits. (1B)

Guideline 3.4 – HD: Microbiological contaminants in water used for the preparation of dialysis fluid

We recommend that the concentration of microbiological contaminants in water used for the preparation of the dialysis fluid should not exceed the limits stated in BS ISO 11663:2009 *Quality of dialysis fluid for haemodialysis and related therapies.* (1C)

Guideline 3.5 – HD: Microbiological contaminants in dialysis fluid

We recommend that dialysis fluid is produced by the mixing of treated water, acid and bicarbonate concentrates. The microbiological contaminant levels for acid and bicarbonate concentrates are defined in BS ISO 13958:2009 *Concentrates for haemodialysis and related therapies*. The microbiological quality of the dialysis fluid should not exceed the limits specified in BS ISO 11663:2009 *Quality of dialysis fluid for haemodialysis and related therapies* (100 CFU/ml for bacteria and 0.25 EU/ml for endotoxin). If routine monitoring demonstrates microbiological contaminant levels in excess of 50 CFU/ml and 0.125 EU/ml for bacteria and endotoxin (50% of the maximum permitted levels) a programme of corrective measures should be commenced immediately. (1B)

Guideline 3.6 – HD: Ultrapure dialysis fluid

We recommend that all new water treatment plants should be capable of producing water suitable for the production of 'ultrapure dialysis fluid'. The microbiological contaminant levels of ultrapure dialysis fluid should be <0.1 CFU/mL and <0.03 EU/mL. (1B)

Guideline 3.7 – HD: Monitoring of feed and dialysis water for haemodialysis

We recommend that a routine testing procedure for water for dialysis should form part of the renal unit policy. Each unit should have standard operating procedures in place for sampling, monitoring and recording of feed and product water quality. The operating procedures should include details of the procedures to be followed if the prescribed limits are exceeded. (1C)

Guideline 3.8 – HD: Bicarbonate dialysate for haemodialysis

We recommend that the dialysate should contain bicarbonate as the buffer. (1B)

4. Haemodialysis (HD) (Guidelines 4.1–4.5)

Guideline 4.1 – HD: Biocompatible haemodialysis

We suggest that haemodialysers with synthetic and modified cellulose membranes should be used instead of unmodified cellulose membranes. The proven benefits of low flux synthetic and modified cellulose membranes over unmodified cellulose membranes are limited to advantages arising from different aspects of improved biocompatibility rather than better patient outcomes. (2C)

Guideline 4.2 – HD: High flux HD membranes

We suggest that high flux dialysers should be used instead of low flux dialysers to provide HD. Evidence of improved patient survival with the use of high flux membranes is restricted to incident patients, who have lower serum albumin concentrations (<40 g/L) or have diabetes mellitus, and prevalent patients, who have been on HD for more than 3.7 years. (2B)

Guideline 4.3 – HD: High flux HD and haemodiafiltration

Both modalities are effective extracorporeal techniques for established renal failure but haemodiafiltration can provide higher rates of removal of small and middle molecules and may lower the risk of developing complications due to dialysis related amyloidosis. Haemodiafiltration would be the preferred mode of extracorporeal renal replacement therapy in patients with established renal failure if it was shown in randomised controlled trials to provide better patient outcomes than high flux HD. We suggest that high flux HD using ultrapure water provides non-inferior patient outcomes to haemodiafiltration. (2C)

Guideline 4.4 – HD: Haemodialysis membranes

We recommend that the use of dialysers sterilised with ethylene oxide should be avoided. (1C)

Guideline 4.5 – HD: Haemodialysis membranes

We recommend that ACE inhibitor drugs should not be prescribed in patients who are receiving HD with synthetic membranes which are capable of generating bradykinin. (1B)

5. Haemodialysis (HD) (Guidelines 5.1–5.10)

Guideline 5.1 – HD: Minimum frequency of haemodialysis per week

We recommend that HD should take place at least three times per week in nearly all patients with established renal failure. Reduction of dialysis frequency to twice per week because of insufficient dialysis facilities is unacceptable. (1B)

Guideline 5.2 – HD: Method of measuring haemodialysis dose

We recommend that a standard method of measuring dialysis dose is adopted to permit effective comparative audit within each regional network and national registry. (1B)

Guideline 5.3 – HD: Minimum dose of thrice weekly haemodialysis

We recommend that every patient with end-stage chronic renal failure receiving thrice weekly HD should have consistently:

- either urea reduction ratio (URR) >65%
- or equilibrated Kt/V of >1.2 (or sp Kt/V of >1.3) calculated from pre- and post-dialysis urea values, duration of dialysis and weight loss during dialysis.

To achieve a URR above 65% or eKt/V above 1.2 consistently in the vast majority of the haemodialysis population clinicians should aim for a minimum target URR of 70% or minimum eKt/V of 1.3 in individual patients. Aiming for these target doses also addresses the concerns raised by recent data which suggest that women and patients of low body weight may have improved survival rates if the URR is maintained above 70% or eKt/V is at least 1.3. (1A)

Guideline 5.4 – HD: Minimum duration of thrice weekly haemodialysis

We recommend that the duration of thrice weekly HD in adult patients with minimal residual renal function should not be reduced below 4 hours without careful consideration. (1B)

Guideline 5.5 – HD: Weekly haemodialysis dose

We suggest that adequate HD three times per week should be defined as a combination of the minimum recommended dialysis dose (URR >65% or eKt/V >1.2) and a minimum recommended treatment time per session (240 mins). (2C)

Guideline 5.6 – HD: Increased frequency and/or duration of haemodialysis

We suggest that an increase in treatment and/or frequency of HD should be considered in patients with refractory fluid overload, uncontrolled hypertension, hyperphosphataemia, malnutrition or cardiovascular disease. (2C)

Guideline 5.7 – HD: Frequency of monitoring haemodialysis dose

We suggest that the measurement of the 'dose' or 'adequacy' of HD should be performed monthly in all hospital HD patients and may be performed less frequently in home HD patients. All dialysis units should collect and report this data to their regional network and the UK Renal Registry. (1C)

Guideline 5.8 – HD: Haemodialysis post-dialysis blood sampling

We recommend the use of a standardised method of post-dialysis blood sampling. Post-dialysis blood samples should be collected by the stop-dialysate flow method or, alternatively, the slow-flow or the simplified stop-flow methods may be used. The method used should remain consistent within renal units and should be reported to the Renal Registry. (1B)

Guideline 5.9 – HD: Residual renal function

We suggest that the management of haemodialysis patients should include dialysis strategies that attempt to preserve their residual renal function. As a minimum policies and procedures should be in place to reduce intradialysis hypotension or excessive ultrafiltration and avoid the use of nephrotoxins. (2B)

Guideline 5.10 – HD: Haemodialysis frequency and dose in acute kidney injury

We suggest that patients with acute kidney injury and multi-organ failure, who are treated by intermittent HD, should receive alternate day HD at a dose at least equal to the minimum dose for established renal failure (URR >65% or eKt/V >1.2) or daily HD. Haemodynamically unstable patients with AKI may be treated

by a continuous modality of RRT and the minimum recommended dose of continuous renal replacement therapy is 20 ml/kg/hour. (2C)

6. Haemodialysis (HD) (Guidelines 6.1–6.8)

Guideline 6.1 – HD: Standardisation of the method of pre-dialysis blood sampling

We recommend that blood sampling for biochemical and haematological measurements should be performed before a mid-week HD session using a dry needle or syringe. (1C)

Guideline 6.2 – HD: Frequency of monitoring biochemical and haematological indices

We recommend that monitoring of pre-dialysis biochemical and haematological parameters should be performed monthly in hospital HD patients and at least 3 monthly in home HD patients. (1D)

Guideline 6.3 – HD: Pre-dialysis serum bicarbonate concentrations

We suggest that pre-dialysis serum bicarbonate concentrations measured with minimum delay after venepuncture should be between 18 and 24 mmol/l. (2C)

Guideline 6.4 – HD: Pre-dialysis serum potassium concentrations

We suggest that pre-dialysis serum potassium should be between 4.0 and 6.0 mmol/l in HD patients. (2C)

Guideline 6.5 – HD: Pre-dialysis serum phosphate concentrations

We suggest that pre-dialysis serum phosphate, if elevated, should be lowered towards the normal range, such as between 1.1 and 1.7 mmol/l. (2C)

Guideline 6.6 – HD: Pre-dialysis serum calcium concentrations

We suggest that pre-dialysis serum calcium, adjusted for serum albumin, should be within the normal range. (2C)

Guideline 6.7 – HD: Serum aluminium concentrations

We suggest that serum aluminium concentration should be measured every three months in all patients receiving oral aluminium hydroxide. No patient whose ferritin level is <100 µg/l should have a serum aluminium concentration >60 µg/l (2.2 µmol/l). (2C)

Guideline 6.8 – HD: Pre-dialysis haemoglobin concentrations

We recommend that pre-dialysis haemoglobin concentration should be maintained within the range 10–12 g/dl. (1B)

7. Haemodialysis (HD) (Guidelines 7.1–7.4)

Guideline 7.1 – HD: Anticoagulation without added risk of bleeding

We recommend that patients without increased bleeding risk should be given unfractionated heparin or LMWH during HD to reduce the risk of clotting of the extracorporeal system. (1A)

Guideline 7.2 – HD: Anticoagulation with significant risk of bleeding

We recommend that anticoagulation should be avoided or kept to a minimum in patients with a high risk of bleeding. This can be achieved by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15–30 minutes or regional citrate infusion. (1C)

Guideline 7.3 – HD: Anticoagulation in patients with HIT type 2 or HITTS

We suggest that patients with HIT type 2 or HITTS should not be prescribed unfractionated heparin or low molecular weight heparin (LMWH). (2B)

Guideline 7.4 – HD: Anticoagulation and catheter lock solutions

We suggest that each unit should have policies and procedures for administration of catheter locking solutions to maintain catheter patency and keep systemic leak of the catheter lock solution to a minimum. (2C)

8. Haemodialysis (HD) (Guidelines 8.1–8.4)

Guideline 8.1 – HD: Symptomatic dialysis-related hypotension

We recommend that data on the frequency of dialysis-related hypotension, defined as an acute symptomatic fall in blood pressure during dialysis requiring immediate intervention to prevent syncope, should be collected and audited. (1C)

Guideline 8.2 – HD: Prevention of symptomatic dialysis-related hypotension

We recommend that a stepwise approach is adopted to try and reduce the incidence of intradialysis hypotension:

restrict dietary sodium intake and review 'dry weight' and antihypertensive drugs; increase duration of HD to reduce the hourly ultrafiltration rate; trial use of cool temperature dialysis. (2C)

Guideline 8.3 – HD: Maximum hourly ultrafiltration rate

We suggest that the maximum hourly ultrafiltration rate during haemodialysis should not exceed 10 ml/kg/hour. (2C)

Guideline 8.4 – HD: Prevention and detection of venous fistula needle or venous line disconnection

We suggest that all haemodialysis staff should follow standard operating procedures to minimise the risk of accidental venous needle/line disconnection. In patients who are restless or undergoing haemodialysis at home consideration should be given to the use of commercially available monitoring systems. (2C)

9. Haemodialysis (HD) (Guidelines 9.1–9.3)

Guideline 9.1 – HD: Home haemodialysis and patient choice

We recommend that all patients who may be suitable for home dialysis should receive full information and education about home HD. (1B)

Guideline 9.2 – HD: Home haemodialysis training and technical support

We suggest that patients may need to travel to a sub-regional or regional centre to pursue their choice to train for home HD if home HD training is not available locally. (2C)

Guideline 9.3 – HD: Daily home haemodialysis

We recommend self-treatment at home as the best way to perform daily short or daily nocturnal HD. (1D)

Summary of Audit Measures

1. The distance and travel time between the patient's home and the nearest satellite or main haemodialysis unit
2. The waiting time after arrival before starting dialysis and the waiting time for patient transport after the end of haemodialysis
3. The number of haemodialysis patients in the main renal unit and its satellite units expressed per million catchment population
4. The number of haemodialysis stations in the main renal unit and its satellite units expressed as a ratio of the total number of HD patients
5. The proportion of patients in the main renal unit and its satellite units who are on twice weekly haemodialysis
6. Cumulative frequency curves of urea reduction ratio measured using a standard method of post-dialysis sampling
7. The proportion of patient non-attendances for haemodialysis sessions and the proportion of dialysis sessions shortened at the patient's request
8. The proportion of thrice weekly haemodialysis sessions which have prescribed treatment times less than 4 hours
9. The proportion of hospital (main and satellite unit) and home haemodialysis patients who are prescribed more frequent than thrice weekly haemodialysis
10. Cumulative frequency curves of pre-dialysis serum potassium concentration
11. Cumulative frequency curves of pre-dialysis serum calcium and phosphate concentrations
12. Cumulative frequency curves of pre-dialysis haemoglobin concentration
13. The incidence of symptomatic hypotensive episodes during dialysis sessions
14. The proportion of haemodialysis patients who have ultrafiltration rates in excess of 10 ml/kg/hour
15. The proportion of dialysis patients in the main renal unit and its satellite units who are on home haemodialysis

Full Clinical Practice Guidelines

1. Haemodialysis (HD) (Guidelines 1.1–1.6)

Guideline 1.1 – HD: Haemodialyis facilities

We recommend that the specification of new or refurbished HD facilities should adhere to the guidelines that are described in the NHS Estates Health Building Notes 07-01 Satellite Dialysis Unit and 07-02 Main Renal Unit. (1C)

Rationale

The specification that is required for a modern HD unit has been detailed by NHS Estates and should be followed in all new and refurbished satellite and main renal unit HD facilities [1, 2].

Guideline 1.2 – HD: Haemodialysis facilities

We recommend that the HD facility should have sufficient specialist support staff to fulfil the criteria listed by the Renal Workforce Planning Group 2002. (1C)

Rationale

The number of medical, specialist nursing, technical and allied health professionals that are required to provide high quality HD therapy has been standardised by the Renal Workforce Planning Group [3]. There should be great emphasis on teamwork, quality assurance and audit, health and safety and continuing professional development for all members of the multidisciplinary team [4].

Guideline 1.3 – HD: Haemodialyis facilities

We recommend that, except in remote geographical areas, the travel time to a HD facility should be less than 30 minutes or a HD facility should be located with 25 miles of the patient's home. In inner city areas travel times over short distances may exceed 30 minutes at peak traffic flow periods during the day. (1B)

Rationale

Equity of access to HD is self evident in a patient-centred service. Lack of local HD provision and the inadequacy of patient transport services are the commonest concerns cited by HD patients and Kidney Patient Associations. The acceptance rate for dialysis declines with increasing distance and travel time from the nearest dialysis unit and patients are less likely to be offered dialysis if the travel time from home to the

dialysis unit is more than 37 minutes [5, 6]. The prevalence rate of HD patients was significantly lower in the areas of Wales with travel times greater than a 30 minute drive to the nearest current dialysis unit [7]. To reverse the inverse relationship between acceptance rates for HD and travel time to the nearest HD facility patients should not need to spend more than 30 minutes travelling to and from dialysis unless they live in a remote geographical area. NHS Quality Improvement Scotland has adopted 30 minutes as the maximum routine travel time to and from HD facilities in Scotland except in remote areas [8] but this guideline may be viewed as impractical in some urban areas because of transport delays due to traffic congestion.

Small satellite units should be established also in rural areas or islands to provide more local access to HD and permit travel distances or times that make thrice weekly HD acceptable to patients. Many of the prevalent HD population are elderly, have diabetes and/or overt cardiovascular disease and have suboptimal vascular access in the form of central venous catheters. Some of these patients therefore may not be medically suitable for treatment at a local satellite HD unit and may need to travel further to a main renal unit for dialysis. A comparison of the costs, quality of dialysis, quality of life and frequency of adverse events of HD in satellite and main renal units in England and Wales showed no major differences except the adequacy of HD, as assessed by measurement of the urea reduction ratio, was better in the patients treated in satellite units [9, 10]. The provision of dialysis treatment at the 12 renal satellite units in the study potentially saved the HD patients an additional 19 minutes travel time for each dialysis session [9].

This study has confirmed that HD in a satellite unit is an effective alternative to treatment in a main renal unit and provides support for a national network of HD facilities with adequate capacity to enable all medically suitable patients to receive chronic HD without having routine travel times in excess of 30 minutes. The location of satellite units should provide maximum geographic access to patients within the local catchment population and a centre of population based approach has been used in the planning of small satellite HD units in some regions of the UK [11].

Better local access to HD can only be achieved if there are improvements in patient transport as well as the development of an extensive network of HD facilities. The Cross Party Group on Kidney Disease Report, 2004 reinforces this point since it identified that 49%

of HD patients in Scotland had travel times in excess of 30 minutes even though only 10% patients lived more than a 30 minute drive from the nearest HD facility [12]. The development of patient transport services that avoid the need to collect and drop off other patients at the dialysis centre or at other healthcare facilities would help keep travel times to a minimum.

Audit measure 1

The distance and travel time between the patient's home and the nearest satellite or main haemodialysis unit.

Guideline 1.4 – HD: Haemodialyis facilities

We suggest that HD patients who require transport should be collected from home within 30 minutes of the allotted time and be collected to return home within 30 minutes of finishing dialysis. (2C)

Rationale

Patient travel to and from hospital is the main source of complaint of hospital HD patients [13]. Reduction in the waiting times before travelling to or from the HD unit would significantly shorten the 'dialysis day' for many patients [13]. Provision of designated parking adjacent to the dialysis area would encourage patients to organise their own transport to and from dialysis and so reduce the need for hospital provision of patient transport. Specialised, fully funded transport for dialysis patients is the gold standard and should be developed to facilitate timely transport by car or ambulance to meet these guidelines. The provision of dedicated or individualised HD patient transport services, which can avoid the need to collect and drop off other patients, and the use of staggered starting times for HD would help to reduce patient waiting times before starting and after completing dialysis. Audit of this patient-centred index of quality of HD provision has been reported in the Scottish HD population by Quality Improvement Scotland (QIS) [13].

Audit measure 2

The waiting time after arrival before starting dialysis and the waiting time for patient transport after the end of haemodialysis.

Guideline 1.5 – HD: Haemodialyis facilities

We suggest that HD capacity in satellite and main renal unites within a geographical area should increase in step with predicted need. (2C)

Rationale

HD treatment has evolved rapidly since its introduction and HD is the main mode of dialysis in most developed countries. HD was the established mode of dialysis at 90 days in 67.4% of the UK patient cohort in 2007 compared with 59% in 1998 [14]. About 40% of patients starting renal replacement therapy (RRT) before the millenium were referred as late uraemic emergencies with no time for the planning of, or counselling on, the options for dialysis, and such patients are more likely to remain on HD [15, 16] but late referral had fallen to 21% in 2007 [14]. HD is also the default therapy for all patients with established renal failure.

Despite the success of transplantation and peritoneal dialysis (PD), HD continues to have the highest rate of growth of all treatment modalities. Many patients are maintained by HD after failure of renal transplants or because they have had to abandon PD. After the first 3 years of dialysis 3% of the 1998–2000 cohort of HD patients in the UK had converted to peritoneal dialysis, mostly within the first year, whereas almost 11% of the PD patients had switched to HD each year.

The provision of HD capacity within the UK has tended to lag behind patient demand and this has restricted both patient choice and access to hospital HD [17]. UK Registry data from the end of 2007 showed that there were 314 patients per million population on hospital or satellite HD [14]. 42.1% of the estimated 746 prevalent adult established renal failure patients per million population were receiving hospital HD and only 1.1% were on home HD at the end of 2007 [14]. Regional variation in the level of provision of HD within the UK continues and this needs to be addressed to permit equity of access to HD throughout the country [18].

The national average number of hospital HD patients per million catchment population reported for the previous year by the UK Renal Registry may be regarded as the minimum capacity for HD in each geographically based renal service. This approach should drive the provision of HD upwards in the areas with below average HD capacity. For example provision for an average of 314 hospital HD patients (or 79 stations) per million catchment population at the end of 2007 could be regarded as a minimum HD capacity in all regions in 2009. The required capacity for HD will be greater in areas with a high ethnic or elderly population due to their higher prevalence of established renal failure and these areas will need proportionately greater HD capacity than the national average. HD capacity will need to

expand greatly over the next 10 years as the number of prevalent patients with established renal failure rises progressively and the proportion of the patients who are elderly and/or have co-morbidity also increases [19]. Regional and national audit of HD capacity will highlight if there is inequity of access to HD and provide support for the development of HD facilities in such geographical areas. Meeting the need for HD will be a major challenge and regular audit should be used to raise HD capacity across the UK in step with the projected increase in demand over the next decade.

Audit measure 3
The number of haemodialysis patients in the main renal unit and its satellite units expressed per million catchment population.

Guideline 1.6 – HD: Haemodialyis facilities
We suggest that the required number of HD stations should be based on using each station for 2 patients per day three times per week. (2C)

Rationale
Additional capacity is needed to allow for patient choice of HD schedule, more frequent HD schedules, holiday HD and anticipated expansion in patient numbers. For these reasons the calculated number of dialysis stations that are required in each geographical area should be based on using each machine only for two patients per day three days per week. The degree of flexibility in HD capacity and scheduling then depends on the proportion of HD patients who are on a third shift each day [4].

Audit measure 4
The number of haemodialysis stations expressed as a ratio of the total number of HD patients.

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2. Haemodialysis (HD) (Guidelines 2.1–2.3)

Guideline 2.1 – HD: Haemodialyis equipment and disposables

We recommend that all equipment used in the delivery and monitoring of HD should be CE marked and approved to ensure compliance with the relevant safety standards BS EN 60601-1:2006 *General safety standards for electrical equipment in clinical use* (currently under revision with the revised version being available in 2010) and BS EN 60601-2-16:2008 *Particular requirements for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment.* (1C)

Rationale

The equipment used in renal units represents a substantial asset that must be carefully maintained. The selection of equipment should be in accordance with a policy that conforms to the recommendations of the MHRA (MHRA DB2006 (05): – Managing Medical Devices – Guidance for Healthcare and Social Services Organisations) and National Audit Office (The management of medical equipment in NHS acute trusts in England, National Audit Office, 1999). The BS EN 60601-2-16 standard for electrical equipment for renal replacement therapy was updated in 2008.

Guideline 2.2 – HD: Haemodialysis equipment and disposables

We recommend that all disposable items used in the delivery of HD (such as haemodialysers, associated devices and the extracorporeal circuits used with such devices) should be CE marked to indicate compliance with the relevant standards. (1C)

Rationale

All disposable equipment such as haemodialysers, blood tubing sets and related devices should display the CE mark. The presence of such a mark signifies compliance with the requirements of the statutory Medical Device Directive and also national and international standards where they exist for new products: ISO 8637:2009 *Cardiovascular implants and artificial organs – Haemodialysers, haemodiafilters, haemofilters and haemoconcentrators*, ISO 13960 *Plasmafilters* (the 2003 version is currently in a final committee draft and will be republished in 2010) and ISO 8638:2009 *Cardiovascular implants and artificial organs – Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters.*

Guideline 2.3 – HD: Haemodialyis equipment and disposables

We suggest that machines should be replaced after between seven and ten years' service or after completing between 25,000 and 40,000 hours of use for HD, depending upon an assessment of machine condition. (2C)

Rationale

The routine maintenance of the equipment used for renal replacement therapy is essential and the service history of each machine should be documented fully throughout its use-life by the renal unit technicians. Renal units should endeavour to adopt a programme of phased replacement of older HD machines. Although it is possible to keep a dialysis machine operating safely for many years, practical considerations of obsolescence and maintenance costs require a more structured approach. When a particular model of a machine becomes obsolete, companies generally only undertake to supply replacement parts for seven years. Intensive use of HD machines for three 4 hour shifts per day, 6 days per week would complete 26208 hours of use after 7 years. We accept that there is no firm evidence that replacement, as suggested above, is the most cost-effective strategy.

3. Haemodialysis (HD) (Guidelines 3.1–3.8)

Guideline 3.1 – HD: Concentrates for haemodialysis

We recommend that commercially produced concentrates are classified as medical devices and should be CE marked to demonstrate compliance with BS ISO 13958:2009 *Concentrates for haemodialysis and related therapies* and the water used for diluting the concentrates should comply with BS ISO 13959:2009 *Water for haemodialysis and related therapies* or meet the requirements stated in the European Pharmacopoeia (6th edition, 2007). (1C)

Rationale

The presence of the CE mark signifies compliance with the requirements of the statutory Medical Device Directive and also national and international standards where they exist. BS ISO 13958:2009 specifies the minimum requirements for concentrates used for HD and related therapies [1]. In this context, 'concentrates' are defined as a mixture of chemicals and water or a mixture of chemicals in the form of dry powder or other highly concentrated media delivered to the end user to produce dialysis fluid used in HD and related therapies. In house produced concentrates should also meet the requirements of BS ISO 13958:2009 or the requirements stated in the European Pharmacopoeia (6th edition, 2007).

Guideline 3.2 – HD: Specification of water treatment system for haemodialysis

We recommend that the complete water treatment, storage and distribution system should meet the requirements of BS ISO 26722:2009 *Water treatment equipment for haemodialysis applications and related therapies* and be shown to be capable of meeting the requirements of BS ISO 13959:2009 *Water for haemodialysis and related therapies at the time of installation*. (1C)

Rationale

An average dialysis patient's blood is exposed to in excess of 300 litres of water per week through a non-selective membrane in contrast to an average 12 litres per week through a highly selective membrane (intestinal tract) in healthy individuals. It is therefore essential that the water used to produce dialysis fluid is of an appropriate chemical and microbiological purity. This is achieved by using:

1. additional water treatment within the renal unit or the patient's home

2. the correct design of the distribution network
3. materials compatible with modern methods of ensuring microbiological quality
4. an effective monitoring and disinfection programme.

Recently there have been incidents arising from the chemical sterilisation of hospital water supplies to minimise the presence of Legionella. The chemicals used are not effectively removed by the water treatment plants in renal units, and to minimise the risk of adverse events from such chemicals:

1. new build renal units should have a direct feed water supply separate from that of the hospital water supply
2. if existing water treatment systems use a hospital water supply there should be awareness of the potential risks that may arise from the introduction of chemicals into the hospital water supply by either renal unit and hospital engineering staff. In this setting addition of chemicals into the hospital water supply should not be undertaken without prior consultation with renal services.

Guideline 3.3 – HD: Chemical contaminants in water used for the preparation of dialysis fluid

We recommend that the concentrations of chemical contaminants in water used to prepare dialysis fluid should not exceed the limits stated either in BS ISO 13959:2009 *Water for haemodialysis and related therapies* or in the European Pharmacopoeia (6th edition, 2007). A programme of improvement should begin immediately if routine monitoring demonstrates that concentrations of chemical contaminants exceed the maximum allowable limits. (1B)

Rationale

Knowledge of the potentially harmful effects of trace elements and chemicals continues to expand and techniques of water treatment are continuously being modified. Recommendations for the maximum allowable concentrations of chemical contaminants have been prepared by a variety of standard developing organisations, professional societies and pharmacopoeias, such as AAMI [2], International Standards Organisation [3] and the European Pharmacopoeia [4]. While there is general agreement concerning the maximum allowable levels of inorganic chemicals with documented toxicity

Table 1. Maximum allowable concentrations of chemical contaminants in dialysis water for which monitoring is mandatory (reproduced from ISO 13959 and EP)

Chemical contaminant	Maximum recommended concentration (mg/l = ppm)
Aluminium	0.01
Calcium	2 (0.05 mmol/l)
Total chlorine*	0.1
Copper	0.1
Fluoride	0.2
Magnesium	2 (0.08 mmol/l)
Nitrate (as N)	2 (equates to 9 mg/l NO$_3$)
Potassium	2 (0.05 mmol/l)
Sodium	50 (2.2 mmol/l)

* All of the above should be tested initially every 3 months apart from total chlorine concentrations which should be tested at least weekly.

Table 2. Maximum allowable concentrations of chemical contaminants in dialysis water which may be omitted from routine monitoring (reproduced from ISO 13959 and EP)

Chemical contaminant	Maximum recommended concentration (mg/l = ppm)
Ammonium	0.2
Arsenic	0.005
Cadmium	0.001
Chloride	50
Chromium	0.014
Lead	0.005
Mercury	0.0002
Sulphate	50

in HD patients (aluminium, chloramines, copper, fluoride, lead, nitrate, sulphate, and zinc) there are some exceptions e.g. the current edition of the European Pharmacopoeia does not explicitly specify maximum allowable levels for copper or chloramines. Of note none of the standards and recommendations includes limits for specific organic chemical contaminants. The rationale for this omission is that organic chemicals with specific toxicity in HD patients have not been identified and that carbon adsorption and reverse osmosis removes most organic compounds. However, there has been a recent report of patient exposure following inadequate removal of organic chemicals in the preparation of dialysis water [5].

Tables 1–3 list all the contaminants for which a maximum allowable limit is defined for water for dialysis in one or more of the standards. With the exception of nitrate, where the standards differ in their recommendations, the most stringent limit has been adopted. An exception has been made in the case of nitrate, for which the European Pharmacopoeia (EP) specifies a maximum of 2 mg/l nitrate whereas the AAMI and ISO 13959 standards recommend a limit of 2 mg/l of nitrate as nitrogen (N), equating to approximately 9 mg/l of nitrate. The more stringent limits may only be met using a double pass reverse osmosis water treatment system which is not universally used and, in view of this, the less stringent recommendation has been adopted for nitrate.

Table 2 defines a group of contaminants for which the drinking water limit is 2 to 5 times the recommended limit for dialysis [6]. In water treated by reverse osmosis, these contaminants will only exceed the limits in Table 2

if they occur at relatively high levels in the water supplied to the unit. These contaminants can be omitted from routine tests if data is available to show that the levels in the water supplied to the unit rarely exceed the limit in the table. These data should be obtained from the municipal water supplier or from tests on the raw water if it is obtained from a private source.

The final group of contaminants (barium, beryllium, silver, thallium, tin and zinc) are those for which a limit has been defined for water for dialysis and there is no limit specified for drinking water in the UK. These trace elements are not considered to occur in levels that give cause for concern and, if low levels are present, they are removed effectively by reverse osmosis. Testing is only required if there is evidence of high levels in the local water supply (zinc, for example, can be introduced in the pipework). Antimony (AAMI limit 0.006 mg/l) and selenium (AAMI and ISO limit 0.09 mg/l) have been excluded from the requirements for monitoring as the limits for drinking water in the UK are lower than the limit for water for dialysis.

Although standard laboratory test methods may be specified to be used to measure chemical contaminants,

Table 3. Maximum allowable concentrations of chemical contaminants in dialysis water which only require monitoring when indicated

Chemical contaminant	Maximum recommended concentration (mg/l = ppm)
Barium	0.1
Beryllium	0.0004
Silver	0.005
Thallium	0.002
Zinc	0.1

any test method validated by the United Kingdom Accreditation Service is acceptable provided the detection limit is not less than 50% of the limits given in Tables 1–3.

The manufacturer or supplier of a complete water treatment system should recommend a system that is capable of meeting the above requirements based on a feed water analysis and allowing for seasonal variation in feed water quality. The complete water treatment, storage and distribution system should meet the requirements of ISO 26722 [7] and be shown to be capable of meeting the requirements of ISO 13959 [3] at the time of installation [8].

Guideline 3.4 – HD: Microbiological contaminants in water used for the preparation of dialysis fluid

We recommend that the concentration of microbiological contaminants in water used for the preparation of the dialysis fluid should not exceed the limits stated in BS ISO 11663:2009 *Quality of dialysis fluid for haemodialysis and related therapies.* (1C)

Guideline 3.5 – HD: Microbiological contaminants in dialysis fluid

We recommend that dialysis fluid is produced by the mixing of treated water, acid and bicarbonate concentrates. The microbiological contaminant levels for acid and bicarbonate concentrates are defined in BS ISO 13958:2009 *Concentrates for haemodialysis and related therapies.* The microbiological quality of the dialysis fluid should not exceed the limits specified in BS ISO 11663:2009 *Quality of dialysis fluid for haemodialysis and related therapies* (100 CFU/ml for bacteria and 0.25 EU/ml for endotoxin). If routine monitoring demonstrates microbiological contaminant levels in excess of 50 CFU/ml and 0.125 EU/ml for bacteria and endotoxin (50% of the maximum permitted levels) a programme of corrective measures should be commenced immediately. (1B)

Guideline 3.6 – HD: Ultrapure dialysis fluid

We recommend that all new water treatment plants should be capable of producing water suitable for the production of 'ultrapure dialysis fluid'. The microbiological contaminant levels of ultrapure dialysis fluid should be <0.1 CFU/mL and <0.03 EU/mL. (1B)

Rationale for 3.4–3.6

The dialysis membrane was regarded as an effective barrier against the passage of bacteria and endotoxin (potent pyrogenic materials arising from the outer layers of bacterial cells) from dialysis fluid to blood. This produced a complacent attitude towards the purity of dialysis fluid. More than 10 years ago, several in vitro studies showed that intact membranes used in dialysers are permeable to bacterial contaminants [9–11].

The pore size of the membrane appears to be less important than the thickness and the capacity of the membrane to adsorb bacterial products. Consequently low flux (standard) dialysis does not necessarily translate into higher microbiological safety than high flux dialysis or HDF. Patients receiving standard dialysis treatment with low flux cellulose-based membranes (thickness 6–8 microns), may therefore be at greater risk of pyrogenic reactions (see below) than those treated using thicker synthetic membranes which have the capacity to adsorb bacterial endotoxin.

In patients treated with high flux membranes, a risk of pyrogen transfer due to backfiltration (a movement of dialysis fluid into the blood pathway of the device due to an inverted pressure gradient rather than the diffusion gradient discussed above) may exist. Lonneman et al., however, concluded that diffusion rather than convection is the predominant mechanism of transmembrane transport of pyrogens, and backfiltration across pyrogen adsorbing membranes does not necessarily increase their passage [12]. It should be emphasised that the adsorption capacity of the synthetic membranes is not infinite and that a breakthrough of pyrogenic substances can occur in the event of excessive water contamination.

A raised C-reactive protein (a sensitive marker of activation of the acute phase response) is associated with a significantly increased risk of death [13, 14] and has led to speculation that micro-inflammation associated with transmembrane transfer of endotoxins and bacterial fragments may contribute to raised serum levels of CRP in patients undergoing regular HD. Impure dialysis fluid has also been implicated in the pathogenesis of dialysis-related amyloidosis and an increased rate of loss of residual renal function. Ultrapure dialysis fluid is produced by ultrafiltration of dialysis fluid in dialysis machines and is used as an on-line substitution fluid in convective therapies such as HDF or haemofiltration. It may also be used in high flux HD. A number of clinical studies have shown that the use of ultrapure dialysis fluid is associated with a range of clinical benefits [15–18]. Its use for HD has been associated in the short term with lower indices of inflammatory response (serum CRP and IL-6), in the medium term with better preservation of residual renal function, nutritional status and correction

of anaemia and in the longer term may reduce the risk of complications due to dialysis-related amyloidosis. In a prospective 30 month observational study patients with combined high levels of CRP and pro-inflammatory cytokines showed an increase in all-cause mortality (RR = 2.57, p < 0.001) and cardiovascular death (RR = 1.9, p < 0.001) [17]. Although the clinical benefit of ultrapure dialysis fluid has not been established in a large scale randomised trial it would seem prudent to ensure that water is as pure as reasonably possible and the European Best Practice Guidelines recommend the use of ultrapure water for all dialysis treatments [19].

New water treatment systems have the capability of producing water suitable for the production of ultrapure dialysis fluid but the fluid requires further treatment if it is to be used as infusion fluid in convective therapies. In some dialysis units up to 100% of treatments are performed with such techniques. Modern dialysis machines permit the production of substitution fluid on site and on-line allowing large reinfusion volumes to be used. Prior to the introduction of on-line production of reinfusion fluid, the permitted endotoxin level was relatively high (0.25 EU/ml). However current standards specify much lower levels although variability among recommendations exists [20]. Reinfusion fluid used in haemofiltration and HDF must be sterile and non-pyrogenic; a final filter is used to achieve this and the line downstream of the filter must be sterile [21].

The tests used for monitoring microbial contamination of water for dialysis should be appropriate to the type of organisms found in water. A low nutrient agar, such as Tryptone Glucose Extract Agar or Reasoner's 2A, should be used [22–24] and samples should be incubated for at least 7 days at 20–22°C [25]. These conditions have been shown to give good recovery for most environmental bacteria found in purified water. Some species are better adapted for growth at a higher temperature and/or on richer media, but the long incubation time will allow most of these to grow. Details of methods for sampling and culturing of water for dialysis are available in the Appendix of European Best Practice Guidelines for Haemodialysis Part 1 [19] and in the EDTNA/ERCA Guidelines on Control and Monitoring of Microbiological Contamination in Water for Dialysis [26], which also gives specific test conditions for fungi.

Detailed procedures for the collection and analysis of samples of water and dialysis solution for microbiological analysis also form part of ISO 23500.

Guideline 3.7 – HD: Monitoring of feed and dialysis water for haemodialysis

We recommend that a routine testing procedure for water for dialysis should form part of the renal unit policy. Each unit should have standard operating procedures in place for sampling, monitoring and recording of feed and product water quality. The operating procedures should include details of the procedures to be followed if the prescribed limits are exceeded. (1C)

Rationale

The manufacturer of the water treatment plant and distribution system should demonstrate that the requirements for microbial contamination are met throughout the complete system at the time of installation [8]. No specific recommendations regarding the frequency of monitoring are made but it should be performed at least monthly in respect of the product water and after any maintenance work on the water treatment system. The frequency of monitoring of the feed (or raw water) quality may be performed less frequently. For home installations it may be impractical to maintain a monthly testing programme and to ensure adequate patient safety the dialysis machine should be fitted with point of use filtration.

The laboratory tests required to demonstrate compliance with the recommendations for monitoring of chemical contamination of dialysis water should be carried out during commissioning and thereafter monthly or following alterations to the water treatment plant. The frequency of testing may be modified once local trends have been established, but should not fall below annually. An initial full test on the supply water may be advisable and regular monitoring of water quality data from the supplier is essential when tests are omitted based on low levels of contamination in the water supply.

The absence of any type of bacteriostat in the water following treatment makes it susceptible to bacterial contamination downstream of the water treatment plant. Microbial contamination may be enhanced by stagnant areas within the distribution network or irregular cleaning. The presence of microbial contamination contributes to the development of biofilm which may also be found in the dialysate pathway of the proportionating system, particularly when non-sterile liquid bicarbonate concentrate is used. Such biofilm is difficult to remove and results in the release of bacteria and bacterial fragments (endotoxins, muramylpeptides,

and polysaccharides). The dialysis membrane prevents transmembrane passage of intact bacteria but bacterial fragments have molecular weights that allow them to pass across the membrane into the bloodstream. Considerable differences exist in the adsorption capacity of such membranes, which may permit the passage of short bacterial DNA fragments [27–29]. Current pro-portionating systems incorporate filters for the removal of such fragments on the basis of size exclusion and hydrophobic interaction. The aim of implementing a disinfection programme is to prevent formation rather than elimination of biofilm and a routine testing procedure for microbiological contaminants in dialysate, dialysis water and feed water should form part of the renal unit policy. It is unnecessary to perform micro-biological monitoring of dialysate or substitution fluid if production paths are fitted with validated micro-biological filters operated and monitored within the manufacture's instructions.

Testing for chemical contaminants will normally include continuous conductivity monitoring of the water leaving the reverse osmosis system, and regular in-house checks of hardness and total chlorine [30]. There is increasing use of chlorine dioxide to prevent growth of Legionella bacteria in hospital water systems. There is currently no guidance on the control and monitoring of chlorine dioxide in water for dialysis. Confirmation that the standard DPD test used to monitor chlorine and chloramines gives an accurate measure of the levels of chlorine dioxide and its breakdown products (chlorite and chlorates) is needed as is data on the carbon filter empty bed contact time that is required for the effective removal of these compounds.

Records should be kept of all chemical and micro-biological test results and remedial actions [26].

Guideline 3.8 – HD: Bicarbonate dialysate for haemodialysis

We recommend that the dialysate should contain bicarbonate as the buffer. (1B)

Rationale

One of the critical functions of dialysis is the correction of the metabolic acidosis caused by the failure of the diseased kidneys to excrete non-volatile acids and to regenerate bicarbonate. Bicarbonate is the natural buffer normally regenerated by the kidneys and was the initial choice as dialysate buffer. If, however, sodium bicarbonate is added to a calcium- or magnesium-containing dialysate, their respective carbonate salts will precipitate unless the dialysate is maintained at a low pH level. Since it does not precipitate calcium or magnesium, acetate was used as an alternative buffer [31] because of its rapid conversion to bicarbonate in the liver. In the late 1970s and early 1980s, a number of studies suggested that some of the morbidity associated with HD could be attributed to the acetate component of the dialysate [32, 33]. This appears to have been unmasked by the introduction of high-efficiency and short-duration dialysis, using membranes with large surface areas. Acetate intolerance led to the reappraisal of bicarbonate as a dialysis buffer in the early 1980s and, following the solving of the issue of precipitation, to its reintroduction. A systematic review of 18 randomised trials indicated a reduction in the number of treatments complicated by headaches, nausea/vomiting and symptomatic hypotension when bi-carbonate was used [34]. Economic evaluations showed the cost of self-mix bicarbonate buffer to be similar to that of acetate. It should be noted, however, that even 'bicarbonate' dialysate contains moderate amounts of acetate [35]. Increased interest in the UK is being shown in the NxStage machine which uses lactate as a buffer and cannot be used with bicarbonate.

It is not possible to set evidence-based standards for other components of the dialysate. However there is recent evidence that non-diabetic HD patients using glucose-free dialysate have a surprisingly high rate of asymptomatic hypoglycaemia without an associated counter-regulatory response [36, 37] The long-term effects of repeated dialysis-induced hypoglycaemia are uncertain. Hypoglycaemia is not observed if the dialysate contains glucose, but glucose-containing dialysate is slightly more expensive. Currently many dialysis units retain the dialysate glucose concentration at 200 mg/L. In elderly and diabetic patients higher insulin levels coupled with the higher glucose levels impair potassium removal during HD. Hyperglycaemia also activates inflammatory pathways and contributes to the pro-inflammatory state of HD patients. For these reasons a reduction in the dialysate glucose concentration may be useful. A recent study by Burgmeister et al. suggested that a level of around 100 mg/L would be appropriate for both diabetic and non-diabetic patients [38]. Individua-lisation of dialysate potassium may be required in patients with hypokalaemia and adjustment of dialysate sodium concentrations during HD (sodium profiling) may be beneficial in some patients with haemodynamic instability.

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4. Haemodialysis (HD) (Guidelines 4.1–4.5)

Guideline 4.1 – HD: Biocompatible haemodialysis membranes

We suggest that haemodialysers with synthetic and modified cellulose membranes should be used instead of unmodified cellulose membranes. (2C) The proven benefits of low flux synthetic and modified cellulose membranes over unmodified cellulose membranes are limited to advantages arising from different aspects of improved biocompatibility rather than better patient outcomes.

Rationale

Synthetic membranes, which can have more porous characteristics (high flux) than standard cellulose membranes, started to be used in the mid-1980s with a view to increasing the depurative capacity of HD.

Clinical use increased with the subsequent discovery that a number of these membranes (e.g. polysulphone, polyamide, polyacrylonitrile) had markedly less ability to activate complement, leucocytes and other cellular elements than standard cellulose and hence decrease the inflammatory response. That is they were more bio-compatible. Cellulose membranes have been modified to make them both more biocompatible and of slightly higher flux (semi-synthetic membranes e.g hemophan or cellulose triacetate), and synthetic membranes with lower flux properties have also been produced (e.g. low-flux polysulphone). The more biocompatible membranes may have other advantages as a result of reduced activation of the systemic inflammatory response during dialysis but this is less certain [1].

A systematic Cochrane review in 2005 showed no evidence of clinical benefit (patient mortality or reduction in dialysis-related adverse symptoms) when synthetic membranes were used compared with cellulose/modified cellulose membranes [2]. Comparison between unmodified cellulose and modified cellulose membranes was not undertaken. Despite the relatively large number of randomised controlled trials undertaken in this area, none of the studies that were included in the review reported any measures of quality of life. Plasma triglyceride values were lower with synthetic membranes in the single study that measured this outcome in this systematic review but a subsequent randomised study has shown no difference in serum lipid levels in the patient group treated with high-flux biocompatible membranes [3]. Serum albumin was slightly higher at certain time points in some studies when synthetic membranes of both high and low flux were used and this may be an important finding given the adverse prognostic impact of hypoalbuminaemia in dialysis patients [4, 5].

In summary the more biocompatible dialysis membranes have potentially beneficial biological effects (lower complement and leucocyte activation; greater adsorptive capacity for cytokines and beta-2-microglobulin) but have not been shown so far to provide better patient survival rates than unmodified cellulose membranes [6]. Synthetic and modified cellulose dialysers are now no more expensive than unmodified cellulose dialysers and the use of these more biocompatible dialysers instead of unmodified cellulose therefore seems justifiable on the basis of evidence of biological benefits and equivalent costs.

Currently there are no dialysers on the market in Europe which retain the use of unmodified cellulose membrane (Cuprophan).

Guideline 4.2 – HD: High flux haemodialysis membranes

We suggest that high flux dialysers should be used instead of low flux dialysers to provide HD. Evidence of improved patient survival with the use of high flux membranes is restricted to incident patients, who have lower serum albumin concentrations (<40 g/L) or have diabetes mellitus, and prevalent patients, who have been on haemodialysis for more than 3.7 years. (2B)

Rationale

Treatments with better clearance of middle molecules include HD with high flux synthetic membranes and haemodiafiltration. The proven benefits of high flux synthetic membranes in randomised trials arise from improved biocompatibility and enhanced removal of middle molecules, such as beta-2-microglobulin, rather than better patient survival rates. Dialysis-related amyloidosis is a disabling, progressive condition caused by the polymerisation within tendons, synovium, and other tissues of beta-2-microglobulin, a large (molecular weight (MW) 11,600) molecule, which is released into the circulation as a result of normal cell turnover but is not excreted in renal failure and is not removed by cellulose membranes. Exposure to bio-incompatible membranes may increase beta-2-microglobulin generation. Symptoms are typically first reported 7–10 years after commencing HD although tissue accumulation of dialysis-related amyloid can be demonstrated much earlier. A systematic review of 27 randomised trials

comparing cellulose, modified cellulose and synthetic membranes, showed a significant reduction in end of study beta-2-microglobulin values when high flux synthetic membranes were used and one small study showed amyloid occurred less frequently with this treatment [7]. High flux HD membranes remove beta-2-microglobulin by a combination of diffusive clearance and adsorption and haemodiafiltration removes substantially more as a result of convective clearance. Both treatments are thought to reduce the risk of developing dialysis-related amyloid.

The effect of dialyser membrane flux was examined in the HEMO study, which was a prospective randomised trial of prevalent HD patients who had been on dialysis for a median of 3.7 years at the time of recruitment to the study [8, 9]. After a mean follow-up period of 2.8 years, during which 871 of the 1846 randomised patients died, no significant difference was observed in all cause mortality or secondary endpoints (the rates of first cardiac hospitalisation or all cause mortality, first infectious hospitalisation or all cause mortality, first 15% decrease in serum albumin or all cause mortality, or all non-vascular access-related hospitalisations) between the high and the low flux treatment groups in spite of a ten fold increase in beta-2-microglobulin clearances in the high flux group (beta-2-microglobulin clearances of at least 20 ml/min). Secondary analyses of the patients who had been on HD for greater than the median of 3.7 years before enrolment showed that the patients on high flux dialysis membranes had a 32% reduction in all cause mortality (CI 14–47%; p = 0.001) and 37% reduction in cardiac death (CI 37–57%; p = 0.016) compared with the low flux patients [10]. However, when the number of prevalent years on HD was analysed as a continuous variable, the interaction of flux and years of dialysis on patient survival was not significant.

The HEMO study was designed to have adequate power to detect a 25% reduction in the predicted baseline all cause mortality rate with the interventions [11]. However the limited benefit observed with high flux membranes has been attributed to several factors in the design of the HEMO study such as the inclusion of prevalent rather than incident patients, the exclusion of patients with major co-morbidity, the failure to utilise ultrapure water whilst using dialyser reuse and the high and low flux groups may have been separated inadequately since predialysis beta-2-microglobulin levels were only 19% lower in the high flux group.

Most of these confounding factors have been addressed in the Membrane Permeability Outcome (MPO) study which is a prospective, randomised, multi-centre, European study comparing the use of high flux and low flux membranes in 738 incident HD patients who have few exclusion criteria and do not reuse dialysers [12]. This study stratified patients on enrolment into two groups with serum albumin < or >40 g/L and reported significantly greater patient survival in the high flux group treated with high flux membranes after a medium term follow up, ranging between 3 and 7.5 years (p = 0.032). A post hoc analysis showed that there was a significant survival advantage in the diabetic patients treated with high flux membranes but the reduced mortality risk associated with the use of high flux membranes may have been associated with an interaction between low serum albumin and a diagnosis of diabetes mellitus. Other studies have shown improved survival [13] or no difference in survival [14] of diabetic patients treated with high flux membranes.

There was no survival advantage associated with the use of high flux membranes in the total MPO study population [12] and no survival advantage with the use of high flux membranes was observed in hypoalbunaemic patients in the HEMO study [15].

However, other studies have shown conflicting results. The J-DOPPS research group failed to show any effect of the biocompatibility or membrane flux of the dialyser on all-cause mortality or control of anaemia in Japanese HD patients treated by non-reuse dialysis [16]. A multicentre, randomised controlled trial has failed to show a beneficial effect on anaemia in stable HD patients using a high flux biocompatible membrane compared with conventional cellulose membranes over a 12 week study period [17]. A multivariate Cox proportional hazards analysis of a prospective non-randomised study of 1,610 prevalent HD patients from 20 centres in France showed that age, diabetes, lower serum albumin and the use of low-flux dialyser membranes were associated with poorer survival [18]. The patients on high-flux dialysers had a 38% lower risk of death (p = 0.01) than patients on low-flux membranes. One small prospective study has shown better preservation of residual renal function when using high flux membranes combined with ultrapure water [19]. Preservation of residual renal function is desirable as residual renal function is a predictor of survival in HD patients [20], decreases beta-2-microglobulin levels and lessens the need for ultrafiltration. The clinical utility of super flux dialysers which provide even greater removal rates of beta-2-microglobulin remains uncertain [21]. Although lower beta-2-microglobulin concentrations are associated with lower all

cause mortality [22] and lower infection related mortality [23] this association does not indicate causality with the use of high flux membranes as other factors such as the level of residual renal function, survival bias, use of ultrapure water or confounding co-morbidity may be implicated [22, 23].

In summary the MPO study [12] and post hoc analysis of the HEMO study [10] provide evidence that long-term HD patients have better survival with the use of high flux dialysers and support the routine use of high flux instead of low flux dialysers.

Guideline 4.3 – HD: High flux HD and haemodiafiltration

Both modalities are effective extracorporeal techniques for established renal failure but haemodiafiltration can provide higher rates of removal of small and middle molecules and may lower the risk of developing complications due to dialysis related amyloidosis. Haemodiafiltration would be the preferred mode of extracorporeal renal replacement therapy in patients with established renal failure if it was shown in randomised controlled trials to provide better patient outcomes than high flux HD. We suggest that high flux HD using ultrapure water provides non-inferior patient outcomes to haemodiafiltration. (2C)

Rationale

Both modalities are effective extracorporeal techniques for established renal failure. 'Middle molecules' (MW 200–20,000) diffuse only slowly into dialysis fluid and so lower treatment times have a proportionately greater deleterious effect on their clearance. Theoretically, reductions in sessional dialysis time can be more safely pursued if there is a concomitant improvement in middle molecular (MM) clearance, a goal which cannot be achieved by high blood flow rate or dialysis fluid flow rate and large surface areas of membranes impermeable to middle molecules. While the use of high flux membranes can increase this, a more effective way of promoting MM clearance is to superimpose convection upon standard diffusive blood purification technique using haemodiafiltration (HDF). In this technique approximately 20 litres of 'extra' fluid, over and above the patients' interdialytic fluid gain, is removed through the dialyser and an equal volume of physiological 'replacement' fluid is returned to the blood before (pre-dilutional) or after (post-dilutional) the dialyser. High volume HDF can therefore provide higher removal rates of all MM, phosphate and other small solutes. For example, the reduction ratios of

beta-2-microglobulin after HDF were 75%, after high flux HD were 60% and after low flux HD were 20% [24].

However a systematic review of the existing 18, albeit mainly small, randomised trials in 2005 showed no difference in patient outcomes between HD, HDF and haemofiltration [25]. The authors have acknowledged that there was a small arithmetic error in this systematic review although this did not alter its main conclusion [26]. Haemodynamic variables were found to be similar in a further recent study comparing HDF and low-flux HD under conditions of equivalent dialysis dose, ultrafiltration volume and core temperature [27]. In a retrospective observational study of 2,165 patients from 1998–2001 in five European countries, stratified into 4 groups (low-flux HD, high-flux HD, low-efficiency HDF and high-efficiency HDF), the subgroup on high-efficiency HDF had a 35% lower mortality risk compared with patients on low-flux HD after adjusting for the dialysis dose and co-morbidity (p = 0.01) [28]. In view of the potential influence of selection bias and other confounding factors the authors of this study stated that a controlled clinical trial was required to document the benefits of HDF before it can be recommended in clinical practice guidelines [28].

The Dutch CONvective TRAnsport STudy (CONTRAST) is a prospective, randomised study that addresses if all cause mortality and/or fatal and non-fatal cardiovascular events differ between haemodiafiltration and low flux HD in almost 800 HD patients after 3 years follow up and the estimated completion date of this study is December 2010 [29]. Another study in Italy is underway also comparing patient outcomes in patients treated with HDF/HF and low flux HD [30]. A study in Turkey comparing outcomes between on-line HDF and high flux HD in 780 patients over a 2 year period is due to be completed in March 2010 [31] and the results will be of great clinical interest as HDF is being compared directly with high flux HD, which is considered to be the optimal mode of standard HD. There is also a French study underway comparing dialysis tolerance in 600 patients randomised to either HDF or high flux HD [32].

At present there is no data to support the use of haemofiltration or HDF instead of high flux HD in the management of established renal failure [33, 34]. If HDF is shown to provide better patient outcomes than high flux HD, HDF will become the default therapy for all patients with established renal failure. A survey of nephrologists' opinion showed that high flux HD was the preferred mode of RRT in the USA and Asia and high volume HDF was the most common therapy of

choice in Europe [35]. Moreover most respondents indicated they wished to have hard evidence of better patient outcomes, such as patient survival, before considering one form of dialysis to be superior to another and that evidence based on improvements in surrogate markers was inadequate [35].

Guideline 4.4 – HD: Haemodialysis membranes

We recommend that the use of dialysers sterilised with ethylene oxide should be avoided. (1C)

Rationale

Chemical sterilisation of dialysers and tubing with ethylene oxide has been associated with anaphylactoid reactions [36] and this risk can be avoided by using alternatives, such as steam or gamma radiation, for the sterilisation of dialysers [37].

Guideline 4.5 – HD: ACE inhibitors and haemodialysis membranes

We recommend that ACE inhibitor drugs should not be prescribed in patients who are receiving HD with synthetic membranes which are capable of generating bradykinin. (1B)

Rationale

With the widespread use of ACE-inhibitors within the dialysis population, a novel type of hypersensitivity reaction has been recognised, which may occur not only during HD but also during other forms of extra-corporeal therapy [38]. Such reactions are triggered by negatively charged biomaterials such as Polyacrylonitrile (AN69) capable of activating factor XII, leading to the generation of bradykinin. Normally this is rapidly degraded by serine proteinase kininase II but in the presence of ACE inhibition plasma bradykinin levels increase and can cause anaphylaxis [39]. In view of this interaction the ACE inhibitor should be changed to an angiotensin II antagonist in patients starting dialysis with a synthetic membrane which is capable of generating bradykinin. Alternatively a different dialysis membrane may be used and the ACE inhibitor continued [37].

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5. Haemodialysis (HD) (Guidelines 5.1–5.10)

Guideline 5.1 – HD: Minimum frequency of haemodialysis

We recommend that HD should take place at least three times per week in nearly all patients with established renal failure. Reduction of dialysis frequency to twice per week because of insufficient dialysis facilities is unacceptable. (1B)

Rationale

The most powerful determinant of solute removal is dialysis frequency rather than duration. Twice per week HD is no longer regarded as adequate and should be avoided. The frequency of twice weekly dialysis has decreased world wide, including in the USA where it fell from 12.9% to 3.6% of new patients between 1990 and 1996. Some patients who live at far distances from a HD unit remain on twice weekly HD and this small subgroup of patients should be kept to a minimum and receive much longer duration sessions.

Twice weekly HD without an increase in treatment time may be acceptable if patients have a significant level of residual renal function, such as either a combined urinary urea and creatinine clearance or eGFR above 5 ml/min/1.73 m^2, provided that residual renal function is monitored at least every 3 months and the frequency of dialysis is increased when renal function decreases.

Twice weekly HD as a long-term form of chronic renal replacement therapy should be discouraged. Some patients may be only willing to travel for HD twice weekly for reasons of geography but they should receive a higher sessional dose of dialysis. A wider distribution of small satellite HD units would help reduce the need to accept twice weekly HD for lifestyle reasons. Twice weekly HD effectively means that the patient will require longer duration HD, usually at least 6 hours twice per week. It should be acknowledged if this cannot be achieved. Patients who are receiving twice weekly HD without an increase in treatment time should be informed explicitly that this is a compromise between the practicalities of dialysis delivery and their long-term health.

Audit measure 5

The proportion of patients in the main renal unit and its satellite units who are on twice weekly haemodialysis.

Guideline 5.2 – HD: Method of measuring dose of haemodialysis

We recommend that a standard method of measuring dialysis dose is adopted to permit effective comparative audit within each regional network and national registry. (1B)

Rationale

Dialysis adequacy is a global concept that includes the clinical assessment of general well-being, nutrition, the impact on the patient's quality of life, anaemia, blood pressure and fluid status as well as measures of clearance of putative uraemic toxins by the dialysis process. The molecular weights of the solutes to be cleared by dialysis range over three orders of magnitude, from small (water, urea) to large (beta-2-microglobulin). Adequate clearance of the whole range of molecules by dialysis is important and in the future monitoring of beta-2-microglobulin levels may be used to assess dialysis adequacy. For practical reasons HD adequacy, thus far, has been measured using small, easily measured solutes such as urea [1–3].

Three methods of assessing urea removal are in current use [1, 2]:

(a) The URR [4] is the simplest. The percentage fall in blood urea achieved by a dialysis session is measured as follows:

$$\frac{\text{pre-dialysis (urea)} - \text{post-dialysis (urea)}}{\text{pre-dialysis (urea)} \times 100\%}.$$

The URR is easy to perform and is the most widely used index of dialysis dose used in the UK. URR does not take solute removal via ultrafiltration or residual renal function or urea generation during dialysis into account [5, 6] and hence total urea removal can be significantly higher than predicted from the percentage reduction in blood urea. However these drawbacks are not important if the main aim of measuring small solute removal by HD is to ensure that a minimum target dialysis dose is delivered consistently. A number of large observational studies in populations of HD patients have shown that variations in URR are associated with major differences in mortality and have led to recommendations that the URR should be at least 65% [7–10].

(b) Kt/V urea can also be predicted from one of several simple formulae requiring as input data the pre- and post-dialysis urea concentrations, the duration of dialysis, and the weight loss during dialysis. Kt/V can be calculated using several formulae giving different

results [11] and hence, if Kt/V is being used for comparative audit, it is important that the raw data are collected to allow calculation of URR and estimated Kt/V using a single formula. The second generation formula validated and reported by Daugirdas is recommended [12]. Kt/V is closely related mathematically to URR ($Kt/V = -\ln(1 - URR)$) and has been shown to be no better than URR in predicting patient outcomes in observational studies.

(c) Urea kinetic modeling (Formal UKM), the most complex measure, involves analysis of the fall in (urea) during HD, the rise in (urea) in the interdialytic period, clearance of urea by residual renal function, and the total clearance predicted from the dialyser clearance, blood and dialysate flow, time on dialysis, and fluid removal during dialysis. Therefore UKM requires collection of additional data on dialyser clearance, an interdialytic urine collection for measurement of urea concentration and volume, and measurement of pre-dialysis urea concentration on the subsequent dialysis. These data are fed into a computer programme which, assuming steady state, calculates Kt/V urea and normalised protein catabolic rate [5]. Kt/V measured by formal UKM is more accurate than URR, particularly at high values of URR and Kt/V [3]. Its use allows accurate prediction of the effects of changing one particular component of the dialysis prescription (e.g. dialyser size, dialysis duration, blood flow rate) on the delivered dialysis dose although this benefit has been overstated given the limited number of practical options for changing the dialysis prescription. UKM also may give valuable information on urea generation rate and protein catabolic rate. If the patient is in a steady state nutritionally, this gives information on current protein intake, and may be a useful adjunct to other methods of assessment of nutritional status.

However doubts have been raised whether Kt/V is a good index of dialysis dose since survival rates on HD are higher in patients with larger body size and better nutrition even though this patient group tends to have lower Kt/V values [13, 14]. Non-normalised dialysis dose (Kt) has been proposed as an alternative and better index of dialysis dose adequacy to Kt/V since the former index obviates the trend for smaller patients with poorer nutritional status to be accorded a higher dialysis dose [15, 16]. In a large cross-sectional analysis using Kt as the index of dialysis dose mortality risk was observed to fall if the delivered dialysis dose was a minimum Kt of 42 litres in women and 48 litres in men [16]. A further difficulty with the use of the Kt/V

index for other than thrice weekly HD is that the significance of any weekly Kt/V value depends on the frequency of dialysis since more frequent dialysis therapies, such as daily HD, will deliver greater small solute removal at the same weekly Kt/V.

Most UK haemodialysis units only collect pre- and post-dialysis urea concentration, and only a very few perform UKM. For comparative audit, the choice therefore currently lies between calculation of URR and estimation of Kt/V urea from such data. Recent data from a survey in Europe showed that URR was used as the only measurement of dialysis dose in 37% of responding dialysis centres (46% in association with another method), spKt/V by 25% (35% in association with another method), eKt/V by 10% (13% in association with another method) and on-line clearance by 4% (12% associated with another method) [17].

This report indicates the need for implementation of a standard approach at regional and national level to allow effective comparative audit.

Guideline 5.3 – HD: Minimum dose of thrice weekly haemodialysis
We recommend that every patient with established renal failure receiving thrice weekly HD should have consistently:

- either urea reduction ratio (URR) >65%
- or equilibrated Kt/V of >1.2 (or sp Kt/V of >1.3) calculated from pre- and post-dialysis urea values, duration of dialysis and weight loss during dialysis. (1A)

To achieve a URR above 65% or eKt/V above 1.2 consistently in the vast majority of the haemodialysis population clinicians should aim for a minimum target URR of 70% or minimum eKt/V of 1.3 in individual patients. Aiming for these target doses also addresses the concerns raised by recent data that suggest that women and patients of low body weight may have improved survival rates if the URR is maintained above 70% or eKt/V is at least 1.3.

Rationale
The optimal dialysis dose has not yet been well defined but minimum targets of delivered dose measured by URR and Kt/V have been established. A retrospective analysis of the National Co-operative Dialysis Study suggested that a Kt/V of 1.0 was the watershed between 'good' dialysis (Kt/V >1.0) and inadequate dialysis (Kt/V <1.0). Thereafter Kt/V survived as an index of

dialysis adequacy [18]. More recent studies [19–24] have shown a reduction in mortality rates with increases in dialysis dose measured in various ways with some of the studies adjusting for co-morbidity [20, 24]. One study has shown no further reduction in mortality above Kt/V of 1.3 or URR of 70% [19]. Many commentators, however, believed that some further improvement in mortality risk could be achieved with Kt/V up to 1.6 or even higher [25–27].

The HEMO trial was a prospective randomised controlled trial in which 1846 patients were randomised to achieve a standard-dose goal of an equilibrated Kt/V of 1.05 (URR circa 65%) or a high-dose goal of an eKt/V of 1.45 (URR circa 75%) and to synthetic or semi-synthetic membranes of high or low flux in a 2×2 factorial design [28]. The HEMO study showed no difference in patient survival or secondary end-points between the two groups after a mean follow-up period of 2.8 years. No difference in patient outcomes was observed in the two groups even although dialysis doses were well separated with achieved eKt/V of 1.16 in the standard-dose group (spKt/V 1.3 ± 0.1; URR $66.3 \pm 2.5\%$) and eKt/V of 1.53 in the high-dose group (spKt/V 1.7 ± 0.1; URR $75.2 \pm 2.5\%$). Subgroup analysis of the HEMO study showed that survival rates in women randomised to the higher dose group were higher than women in the lower dose group (relative risk 0.81; p = 0.02) and this association persisted after adjusting for different indices of body size [29]. An association between higher dose and lower mortality rates in women but not in men was confirmed using the average URR of incident HD patients in the USA and eKt/V of HD patients in the DOPPS data from 7 countries [30]. Further analyses of the HEMO study showed that differences in dialysis dose and membrane flux had no effect on the proportion of infection-related deaths [31].

Time-dependent Cox regression analysis of the HEMO study has shown that mean pre-dialysis serum beta-2-microglobulin levels but not dialyser beta-2-microglobulin clearances were associated with all cause mortality with a relative risk of 1.11 per 10 mg/L rise in the beta-2-microglobulin concentration above a reference value of 27 mg/L (CI 1.05–1.19; p = 0.001) after adjusting for residual renal function and pre-study years on dialysis [32]. This evidence provides support for the use of beta-2-microglobulin to assess adequacy of HD in future both as an indicator of patient outcome and a surrogate marker of middle molecule removal [33]. The apparent disparity between the prognostic effects of serum beta-2-microglobulin levels and dialyser beta-2-microglobulin clearances [32] is most likely due to the limited mass removal of beta-2-microglobulin in high-efficiency dialysis due to intercompartmental transfer resistance within the patient which results in rebound of serum beta-2-microglobulin levels at the end of therapy [34]. This observation on beta-2-microglobulin intra-dialytic kinetics provides further support for the use of longer duration and/or more frequent dialytic therapies.

In summary, based upon the above dialysis doses achieved in the low dose group in the HEMO study we have retained the standard dose as a URR of 65% or eKt/V of 1.2 which should be regarded as the minimum dialysis dose delivered thrice weekly. The ERBP guidelines on HD adequacy recommend the same minimum eKt/V [35] although the CARI, CSN and KDOQI guidelines recommend a slightly lower minimum target dialysis dose (spKt/V >1.2) which is below the delivered dialysis dose in the low dose group of the HEMO study [36–38]. A recent European survey has reported that URR is the most common method used to quantify small solute removal in HD patients and eKt/V was used by a minority of centres [39]. To ensure as many patients as possible achieve this standard consistently the target dose should be a URR of 70% or eKt/V of 1.3. These higher target doses allow to some extent for the risk of overestimating HD dose in women and small men when using URR and eKt/V [40].

As with all performance indicators, achievement is dependent on patients' concordance with treatment. This includes the agreement of the patient to increase treatment duration if the delivered dialysis dose is inadequate after the dialyser blood flow rate, dialysate flow rate and dialyser performance have been increased to the maximum that can be achieved. Increased understanding amongst patients of the benefits of an adequate dialysis dose may help to improve outcomes. The proportion of dialysis sessions that are missed or shortened by the patient should be audited in each unit.

Audit measure 6
Cumulative frequency curves of urea reduction ratio measured using a standard method of post-dialysis sampling.

Guideline 5.4 – HD: Minimum duration of thrice weekly haemodialysis
We recommend that the duration of thrice weekly HD in adult patients with minimal residual renal function should not be reduced below 4 hours without careful consideration. (1B)

Rationale

The three times per week HD schedule has evolved from empirical considerations in the belief that it reconciles adequate treatment with adequate breaks between treatments to provide the patient with a reasonable quality of life within a 7 day treatment cycle. Furthermore, all outcome data from randomised prospective trials have so far been derived from patient groups undergoing such dialysis schedules. The National Cooperative Dialysis Study (NCDS), an historical US randomised trial where cellulose membranes and acetate dialysate were used, has addressed the issue of optimal dialysis time. This study randomised non-diabetic patients to one of four dialysis regimens, two with short (2.5–3.5 hour) and two with longer (4.5–5.0 hour) dialysis times, and two different time-averaged urea concentrations in each arm [41]. Longer dialysis gave a better outcome [41, 42]. A combination of better patient tolerance using improved machines and higher efficiency HD, economic constraints and patient preference for shorter times has resulted in a gradual reduction in the average length of dialysis sessions around the world.

It is difficult to separate the influence of dialysis time and dose on patient outcomes [43]. Early studies showed that the risk of death is associated with short dialysis duration [44]. Dialysers with higher mass transfer area coefficients in combination with higher blood and dialysis fluid flow rates have been used to provide higher efficiency HD than in the past. The urea clearance will depend on whichever is the lowest of the blood flow rate, dialyser urea mass transfer coefficient and dialysate flow rate. Since small solute urea removal can be formally quantified by validated techniques, dialysis times have been reduced while maintaining 'equivalence' in the degree of blood urea purification. A crossover study of standard and higher efficiency HD prescriptions delivering equal dialysis dose (urea removal) measured by direct dialysate quantification has shown lower phosphate and beta-2-microglobulin removal and less bicarbonate absorption during the shorter duration, higher efficiency prescription [45]. Improved clearance of iohexol was also observed on longer duration HD with similar Kt/V. Thus, when short and standard duration HD provide equal urea clearances, delivered dialysis therapy should not be regarded as equivalent. Alternatively changing to treatment modalities that provide both convective and diffusive removal of solutes such as haemodiafiltration have been used to lower treatment times although shortening the duration of haemodiafiltration will tend to negate its benefits of providing higher middle molecule clearances.

Retrospective data from a large Japanese population have shown that dialysis duration up to 5.5 hours was associated with improved patient survival after adjusting for dialysis dose [46]. Very low mortality rates were observed in Tassin in patients treated with long duration thrice weekly HD with mean spKt/V of 1.67 ± 0.41 [47]. However, a Cox analysis showed that patient survival was linked to improved blood pressure control and lower cardiovascular mortality related to the achievement of better long-term control of dry body weight [47]. Conversely high efficiency HD has been associated with poor blood pressure control. In the USA patients who received dialysis for less than 3.5 hours per session three times per week had approximately twice the risk of death of patients on HD for more than 4 hours three times per week [44]. Cox regression analyses of data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) and the Australian and New Zealand Dialysis and Transplant Registry have shown that patient survival was greater in patients if treatment times were above 4 hours and 4.5 hours, respectively [48, 49] and both of these observational studies have concluded that a randomised controlled study of longer dialysis sessions in thrice weekly HD is needed.

Small solute removal (URR or eKt/V) higher than the above minimum targets can be achieved in adults of small body weight with shorter HD treatment times which then compromises adequate removal of sodium and water, phosphate and middle molecules. This may explain why small adults have higher than expected mortality rates with small solute removal rates above the minimum target [29].

All of these observations suggest that the duration of thrice weekly HD should not be reduced below 4 hours unless the patient has significant residual renal function. The KDOQI 2006 Haemodialysis Update workgroup has also recommended that an adequate dialysis means achieving the minimum target small solute removal rates whilst avoiding ultrashort HD treatment times [36]. The KDOQI and EBPG guidelines on dialysis strategies recommend that total duration of HD should be at least 12 hours per week unless the patient has significant residual renal function [35, 36]. The EBPG guideline also advocates an increase in treatment time and/or frequency for high risk patient groups such as patients with cardiovascular instability, refractory hypertension, hyperphosphataemia or malnutrition [35]. These observations support the conclusions of previous

reviews which highlight the importance of treatment time in delivering adequate HD [50, 51].

Delivered treatment times and hence weekly dialysis dose are reduced if either the patient requests to discontinue the dialysis session early or if the patient attends for dialysis irregularly. Non-adherence to the prescribed dialysis schedule should be kept to a minimum and monitored.

Audit measure 7
The proportion of patient non-attendances for dialysis and the proportion of dialysis sessions shortened at the patient's request.

Guideline 5.5 – HD: Weekly haemodialysis dose
We suggest that adequate HD three times per week should be defined as a combination of the minimum recommended dialysis dose (URR >65% or eKt/V >1.2) <u>and</u> a minimum recommended treatment time per session (240 mins). (2C)

Rationale
There is evidence that HD thrice weekly should deliver a minimum removal of small solutes per treatment and observational data which indicates that the dialysis treatment time should not be less than 240 minutes per session. Increasing treatment time is a surrogate for delivering higher removal rates of middle molecules, sodium and water and/or lower rates of ultrafiltration per hour. Whilst maintaining the same Kt/V and increasing treatment time from 4 to 6 and 8 hours, phosphate removal was increased by 20 and 40% respectively and beta-2-microglobulin by 50 and 70% respectively [52]. It is therefore intuitive that HD staff recommend to patients that they receive an adequate dialysis dose over a minimum treatment time. The provision of a minimum treatment time also provides a safeguard against underdialysis in small adults, particularly small women; target Kt/V is more readily achieved in women because V in women is lower than in men and in small adults as Kt scaled for V is disproportionately lower than Kt scaled for body surface area.

Several methods have been used to assess weekly solute removal in different dialysis modalities. Standard Kt/V (std Kt/V) is a measure of weekly urea clearances normalised to body water, allows comparison of dialysis dose in PD and HD treatment schedules of differing frequency and duration and has been regarded as a dose measure of weekly clearances of both water-soluble and protein-bound toxins [53, 54]. A significant increase

in dialysis dose is demonstrated when standardised Kt/V is utilised to calculate the weekly dialysis dose in treatments of increasing duration and frequency instead of the sum of the Kt/V of all treatments per week [55].

The significant increase in std Kt/V by increasing duration of dialysis suggests that renal units should adopt the approach of defining an adequate dose of HD as a combination of delivery of both an adequate dialysis dose and adequate treatment time.

Audit measure 8
The proportion of thrice weekly haemodialysis sessions which have prescribed treatment times less than 4 hours.

Guideline 5.6 – Increased frequency and/or duration of haemodialysis
We suggest that an increase in treatment time and/or frequency of HD should be considered in patients with refractory fluid overload, uncontrolled hypertension, hyperphosphataemia, malnutrition or cardiovascular disease. (2C)

Rationale
Weekly removal of small solutes, phosphate and middle molecules is enhanced greatly by increasing the frequency or duration of treatment sessions [56]. The HD product (number of HD sessions per week squared × treatment hours per session) has been proposed as a simple index of dialysis adequacy and highlights the impact of a combination of increased time and increased frequency on solute clearances [57]. Studies of long duration HD three times per week in Tassin have reported excellent patient survival rates while using predominantly low flux membranes and the DOPPS study showed that patient survival improved by 7% for every 30 minute increase in the treatment time three times per week [47, 48].

The benefits of increasing treatment frequency and/or duration on solute clearances, blood pressure and fluid balance have stimulated interest in daily short and nocturnal HD (either thrice weekly or daily).

Several forms of more frequent HD have been re-evaluated recently. The most common approach so far is to perform dialysis for around two-three hours per day for five–six days per week (often termed short daily HD) [58–63]. Small observational studies of daily short HD has been associated with shortened recovery time after dialysis sessions, better fluid balance and blood pressure control, regression of left ventricular hypertrophy and fewer episodes of intradialysis

hypotension but control of anaemia and phosphate are similar to thrice weekly HD [58–63]. Most patients do not wish to switch back to thrice per week HD once established on short daily HD. Daily HD may also be indicated in the short term when patients develop an acute intercurrent illness or pericarditis. Apart from the additional cost of 6 times per week dialysis, which may be offset by fewer drugs and hospital admissions, the only theoretical disadvantage of daily HD is the potential for a higher incidence of vascular access complications (more frequent fistula/graft punctures or more frequent opening of central venous catheter lumens) but this has not been reported as yet.

The other approach is a renewed interest in slow overnight treatment for 5–7 nights per week (often termed nocturnal daily HD). The combination of increased frequency and longer session times provide a much greater weekly removal of small solutes and middle molecules. Nocturnal daily HD can [64–68]:

a. deliver very large doses of dialysis (weekly Kt/V of almost 6 and much greater removal of middle molecules)
b. remove sodium and water so that anti-hypertensive treatment can be reduced to a minimum
c. permit regression of left ventricular hypertrophy
d. allow patients to follow an unrestricted diet
e. improve appetite and nutritional status
f. permit phosphate binders to be discontinued (may need phosphate supplementation)
g. improve sleep disturbance and sleep apnoea
h. better control of anaemia.

Both regimes have been reported to give improved clinical outcomes such as higher quality of life and fewer hospital admissions when compared with the more conventional regime of three sessions per week each of four hours but this may be due to patient selection and no randomised data on patient survival is available [61–68]. On the basis of the successful reports from these observational studies of short daily and nocturnal daily HD the National Institutes of Health (NIH) has sponsored 2 prospective randomised studies in 250 patients to compare each form of 'daily' or frequent HD with standard thrice weekly HD. These NIH studies (Frequent Haemodialysis Network Studies) are due to be completed in 2010 [69]. The prospective multicentre FREEDOM study is underway in the USA to compare the health and economic benefits of daily home HD with matched patients on thrice weekly HD

[70]. Similar patient benefits have been reported in a small crossover trial comparing thrice weekly HDF with short daily HDF in 8 patients [71]. The benefits of daily HD have been summarised in a recent systematic review [72].

Daily short or nocturnal HD is impractical for most in-centre HD patients but we suggest that high risk in-centre patients may be prescribed more frequent or longer duration HD. The EBPG guideline advocates an increase in treatment time and/or frequency for patient groups such as patients with cardiovascular instability, refractory hypertension and fluid overload, hyperphophataemia or malnutrition [35]. The need for adequately powered trials which evaluate patient outcomes on more frequent HD modalities has been highlighted in recent reviews [72, 73]. The measurement of dialysis dose in more frequent dialysis schedules can be compared using standard Kt/V (std Kt/V) as the index of dialysis dose.

Audit measure 9
The proportion of hospital (main and satellite unit) and home haemodialysis patients who are prescribed more frequent than thrice weekly haemodialysis.

Guideline 5.7 – Frequency of monitoring of haemodialysis dose
We suggest that measurement of the 'dose' or 'adequacy' of HD should be performed monthly in all hospital HD patients and may be performed less frequently in home HD patients. (1C)

Rationale
Monthly measurement of dialysis dose in hospital HD patients should be used to optimise the HD prescription and may facilitate early detection of poorly functioning vascular access. Monitoring of dialysis dose in home HD patients on a monthly basis is impractical and may be performed on a less frequent basis such as every 3 months. All dialysis units should collect and report data on dialysis adequacy to their regional network and the UK Renal Registry. Meaningful comparative audit within a renal unit or regional network requires the use of the same methodology of measurement of dialysis dose and blood sampling during a mid-week HD session in the census week. However routine monthly monitoring of HD dose is not performed uniformly in all centres despite regular monitoring being recommended in hospital HD patients to achieve consistent delivery of a minimum dialysis dose [39].

Guideline 5.8 – HD: Haemodialysis post-dialysis blood sampling

We recommend the use of a standardised method of post-dialysis blood sampling. Post-dialysis blood samples should be collected by the stop-dialysate flow method or, alternatively, the slow-flow or the simplified stop-flow methods may be used. The method used should remain consistent within renal units and should be reported to the Renal Registry. (1B)

Rationale

With the exception of on-line methods the measurement of dialysis dose requires an accurate measurement of pre-dialysis and post-dialysis urea concentrations on a mid-week dialysis session. Full urea kinetic modelling also requires:

- measurement of dialyser clearance
- measurement of weight loss during dialysis
- collection of an inter-dialytic urine
- pre-dialysis blood urea concentration from the subsequent dialysis session.

Contamination of the post-dialysis sample with blood returning from the dialyser or heparin, or sampling from a fistula or other access device in which there is recirculation of dialysed blood will lead to falsely low measurements of the post-dialysis blood urea concentration, and thus to over-estimation of dialysis dose. True venous blood urea concentration rises rapidly in the first few minutes after dialysis as the effects of access and cardiopulmonary recirculation dissipate [74]. It continues to rise at a rate higher than that expected from urea generation for up to 30 minutes, as a consequence of continued transfer of urea from peripheral body compartments into the bloodstream [75–79]; the earlier the sample is drawn, the higher the apparent delivered dialysis dose. Small variations in the timing and technique with which post-dialysis blood samples are drawn can, therefore, result in clinically important errors in the estimated dose of dialysis. Such variation has been shown to be common in the USA [80] and in the UK [81, 82]. Techniques of post-dialysis blood sampling that involve taking the sample immediately at the end of the HD session were used commonly in the USA in the past [80], generate a higher apparent URR and may have contributed to the rise in the URR deemed necessary for optimum survival in observational studies.

Several methods of post-dialysis blood sampling are in use in the UK

(a) Stop dialysate flow method. This method was validated by Drs. Geddes, Traynor and Mactier, NHS Greater Glasgow and Clyde and has been used by all of the HD units in Scotland since 1999 [81–83].

- At the end of the dialysis time stop dialysate flow but keep the blood pump running.
- After 5 minutes with no dialysate flow take a blood sample from anywhere in the blood circuit.

(b) Slow-flow method. This method was developed by F Gotch and M Keen, Davis Medical Centre, San Francisco and has been used by Lister Renal Unit, East and North Herts NHS Trust since 1990 [76].

- At the end of the dialysis time turn the blood pump speed down to 100 ml per min.
- Override alarms to keep blood pump operating.
- Wait 15–30 seconds and take samples from the 'arterial' line sampling port.
- If more than one blood sample is required, the sample for urea should be the first one taken.

(c) Simplified stop-flow method. This was developed by EJ Lindley, V Osborne, S Sanasy, D Swales and M Wright at Leeds Teaching Hospitals NHS Trust.

- When you are ready to take the sample turn the blood pump speed slowly down to 50 ml per min.
- Start counting to five; if the venous pressure alarm has not already stopped the blood pump when you get to five stop the pump manually.
- Disconnect the arterial line and take a sample from the needle tubing (or the arterial connector of the catheter) within 20 seconds of slowing the blood pump speed to 50 ml per min.
- If more than one blood sample is required, the urea sample should be the first one taken.

The stop dialysate flow method avoids the dilutional effects of access and cardiopulmonary recirculation and is a 2 step process involving switching off the dialysate flow for 5 minutes at the end of the HD session and then taking a blood sample from the arterial or venous port [81]. The stop dialysate flow method is simple, easily reproducible, suitable for all forms of vascular access, validated in haemodiafiltration as well as HD [81, 82] and is currently the most widely used method in the UK. The slow-flow method and the stop-flow method were devised to give early post-dialysis measurements which avoid the effects of access re-circulation but

do not allow for cardiopulmonary recirculation which continues for the first 2 minutes after the end of HD using a fistula or graft as vascular access [74]. The stop-flow and slow-flow methods will underestimate post-dialysis 'equilibrated' blood urea concentrations more than the stop dialysate flow method and consequently overestimate urea removal by HD.

Post-dialysis rebound in venous blood urea concentration results from continued return of blood from poorly dialysed body 'compartments', and is particularly marked after high efficiency dialysis. Accurate comparison of delivered dialysis dose therefore requires estimation of the equilibrated blood urea concentration, allowing calculation of 'equilibrated' Kt/V. Full re-equilibration takes about 30 minutes, but it is impractical to ask patients to wait this long for post-dialysis blood sampling on a routine basis. The amount of rebound is determined by several factors including the efficiency of dialysis and the size of the patient. Formulae have been validated for predicting 30 minute post-dialysis or 'equilibrated' blood urea from blood samples using either the stop dialysate flow method [83] or similar sampling methods to the slow flow and stop flow methods [12, 76, 79].

A standardised approach to post-dialysis blood sampling is preferable for comparative audit [84]. The stop-flow method is the only method validated in HD and haemodiafiltration and which requires no change in sampling practice with different forms of vascular access. The stop dialysate flow method was adopted by all of the adult renal units in Scotland since it is simple, practical, well validated and the least likely method to overestimate the URR or Kt/V. The stop dialysate flow and slow-flow methods are the two methods included in Guideline 3.4 of the latest update of the KDOQI Clinical Practice Guidelines on Haemodialysis Adequacy [36].

Guideline 5.9 – HD: Residual renal function

We suggest that the management of HD patients should include dialysis strategies that attempt to preserve their residual renal function. As a minimum policies and procedures should be in place to reduce intradialysis hypotension or excessive ultrafiltration and avoid the use of nephrotoxins. (2B)

Rationale

The importance of residual renal function is now well documented in HD as well as PD patients [85–90]. Residual renal function helps maintain fluid and electrolyte balance and greatly enhances removal of middle molecules resulting in lower pre-dialysis beta-2-microglobulin concentrations in HD patients with preserved residual renal function. The CANUSA study documented that the level of residual renal function rather than PD dose was an independent predictor of risk of death [86] and emerging evidence from observational studies suggests that residual renal function also provides a survival advantage in HD patients [87–90]. The NECOSAD study of 740 incident patients showed that each increase of 1 per week in renal Kt/V urea was associated with a significant reduction in the relative risk of death [87]. The NECOSAD study also showed that both renal and dialysis components of urea clearance were associated with better patient survival (for each increase of 1 per week in renal Kt/V the relative risk of death was 0.44; p = 0.0001 and for dialysis Kt/V was 0.76; p = 0.01) but the effect of dialysis dose on mortality was strongly dependent on the presence of residual renal function. Consequently the delivery of weekly dialysis Kt/V less than 2.9 was associated with higher mortality rates only in the patients who were anuric and patients with high interdialytic weight gains had increased mortality rates independent of dialysis dose [87]. A smaller prospective observational study of 114 HD patients has also shown a reduced relative risk of death (0.44) in the patient subgroup with preserved renal function estimated from mean urinary urea and creatinine clearances in 24 hour collections [88]. An observational study of 650 incident HD patients has shown that the subgroup of HD patients who maintained residual renal function (defined as renal urea clearance >1 ml/min) had lower erythropoietin requirements, better nutritional indices (higher serum albumin and nPCR), lower ultrafiltration volumes and lower mortality rates [89]. There is also evidence in a small randomised trial that the use ultrapure water for dialysis preserves residual renal function [90]. In PD it has been reported that technique and patient survival are lower in the patients with higher rates of decline in residual renal function [91]. It remains unclear whether the better clinical outcomes observed in patients with preserved residual renal function are maintained if their estimated residual renal function is offset by a reduction in the weekly dialysis dose.

The observations reported in these studies suggest that residual renal function improves clinical outcomes of HD patients and that dialysis strategies to preserve residual renal function of all dialysis patients are warranted. As a minimum, strategies in haemodialysis units should address:

a. reduction in intradialytic hypotensive episodes, hypovolaemia or excessive ultrafiltration
b. avoidance of the use of nephrotoxins whenever possible
c. reduction in infection complications, especially the rate of vascular access related infections
d. the use of ultrapure water for dialysis.

Whilst it is important to avoid excessive ultrafiltration when attempting to maintain residual renal function in HD patients, there is the ever present trade off of needing to avoid subclinical chronic fluid overload and uncontrolled hypertension [92]. The rationale and need for dialysis strategies to preserve residual renal function in HD as well as PD patients has been reviewed in detail in recent publications [93, 94].

Guideline 5.10 – HD: Haemodialysis dose and frequency in acute kidney injury

We suggest that patients with acute kidney injury and multi-organ failure, who are treated by intermittent HD, should receive either alternate day HD at a dose at least equal to the dose for established renal failure (URR >65% or eKt/V >1.2) or daily HD. Haemodynamically unstable patients with AKI may be treated by a continuous modality of RRT and the minimum recommended dose of continuous renal replacement therapy is 20 ml/kg/hour. (2C)

Rationale

At present there is no evidence to show whether continuous or intermittent renal replacement therapies or whether haemofiltration or HD provide better survival in patients with acute kidney injury (AKI). In a randomised, risk stratified, dose equivalent prospective comparison of continuous veno-venous HD (CVVHD) versus intermittent HD in 80 intensive care unit patients with AKI the CVVHD group had greater daily fluid volume removal but no improvement in patient survival, preservation of urinary output or recovery of renal function [95]. A randomised study of extended daily HD and continuous HD in intensive care patients with AKI showed no difference in haemodynamic stability [96]. However there is evidence that survival in patients with AKI is better with daily than alternate day renal replacement therapy [97]. In this randomised prospective study of 160 critically ill patients with AKI the mortality rate using an intention-to-treat analysis was 28% with daily HD and 46% with alternate day HD (p < 0.01). The frequency of renal replacement therapy may be reduced once the metabolic syndrome and fluid status of patients with AKI is stable. Initial randomised studies showed that the use high flux biocompatible membranes were associated with improved patient survival rates in patients with AKI but this has not been confirmed in follow-up studies [98]. 58% of the 90 patients randomly assigned to bioincompatible Cuprophan dialysers survived compared with 60% of the 90 patients assigned to polymethylmethacrylate membranes [98]. A randomised study of continuous veno-venous haemofiltration in AKI has shown improved patient survival in patients prescribed at least 35 ml/hour/kg body weight [99]. In contrast to the above smaller randomised studies [97, 99] the recent ATN study has reported no survival benefit in patients with AKI treated with higher doses or with daily therapy [100].

In summary, in the setting of AKI, randomised trials have shown conflicting results regarding survival benefit from the use of biocompatible membranes, daily or continuous therapies or enhanced dialysis dose. Nevertheless extended daily HD and post-dilutional continuous veno-venous haemofiltration are widely utilised in the management of AKI in intensive therapy units in the UK and both provide long duration therapy to help maintain fluid balance with minimal adverse haemodynamic effects in this critically ill patient group.

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6. Haemodialysis (HD) (Guidelines 6.1–6.8)

Guideline 6.1 – HD: Standardisation of the method of pre-dialysis blood sampling

We recommend that blood sampling for biochemical and haematological measurements should be performed before a mid-week HD session using a dry needle or syringe. (1C)

Rationale

Too much emphasis may have been placed in the past on achieving a given standard of small solute clearance at the expense of addressing a wide range of other important clinical and laboratory parameters of dialysis adequacy. A global assessment of dialysis adequacy includes achievement of good control of:

- hyperkalaemia and metabolic acidosis
- bone metabolism
- anaemia
- hypertension and fluid balance
- traditional and non-traditional cardiovascular risk factors
- nutritional status.

Variability in interdialysis fluid weight gains after the 1 or 2 day intervals between HD sessions may be expected to cause differing degrees of haemodilution and so influence pre-dialysis haemoglobin and albumin concentrations. A recent study has shown higher pre-dialysis serum calcium and phosphate concentrations after the longer interdialysis interval in the absence of evidence of different levels of haemodilution between short and long interdialysis intervals [1]. These findings indicate that time-interval related interdialytic and non-dialytic factors may influence pre-dialysis biochemical and haematological results and reinforce the need for standardisation of timing of pre-dialysis blood sampling in HD patients.

The UK Renal Registry and Scottish Renal Registry have employed audit measures using measurement of laboratory values from samples that were collected before commencing HD after a one day interdialysis interval. To avoid blood sampling at weekends blood sampling is effectively limited to either a Wednesday or Thursday dialysis session. This restricted timing of blood sampling allows standardisation of interpatient and intrapatient interdialysis fluid weight gains and it is important that all samples are taken using a dry needle or syringe to ensure dilutional sampling errors are avoided.

Guideline 6.2 – HD: Frequency of monitoring of biochemical and haemotological indices

We recommend that monitoring of pre-dialysis biochemical and haematological parameters should be performed monthly in hospital HD patients and at least 3 monthly in home HD patients. (1D)

Rationale

Standardised analytical methods of measuring laboratory indices are required if comparative audit against performance indicators is to be meaningful. Difficulties still arise since laboratories across the UK use different methods to measure serum albumin and PTH as well as different correction factors for adjusting serum calcium levels [2]. The UK Renal Registry and Scottish Renal Registry have workgroups trying to harmonise these differences in analytical methodology.

Guideline 6.3 – HD: Pre-dialysis serum bicarbonate concentrations

We suggest that pre-dialysis serum bicarbonate concentrations, measured with minimum delay after venepuncture, should be between 18 and 24 mmol/l. (2C)

Rationale

The main causal factors of metabolic acidosis in stable HD patients are inadequate dialysis delivery, excessive animal protein (sulphur containing amino acid) intake and high interdialysis weight gains. Whole-body base balance studies in 18 anuric HD patients have highlighted the importance of interdialysis dilution in the aetiology of predialysis acidosis [3]. In ill patients metabolic acidosis may also be due to increased protein catabolism, hypotension or hypoxia induced lactate production or bicarbonate losses associated with co-morbid illness. Pre-dialysis metabolic acidosis has a range of adverse consequences: an increase in protein catabolism and anti-anabolic effects, a negative inotropic effect, loss of bone mineral, insulin resistance, growth retardation in children, reduced thyroxine levels, altered triglyceride metabolism, hyperkalaemia, lower serum leptin levels and greater accumulation of beta-2-microglobulin.

Pre-dialysis venous bicarbonate levels between 17.5 and 20 mmol/l were associated with the lowest risk of death in a large cohort study of 13535 HD patients whilst the relative risk of death was increased threefold if the pre-dialysis venous bicarbonate was <15 mmol/l [4]. In a DOPPS study of more than 7000 unselected HD patients the corrected mid-week serum bicarbonate

concentration averaged 21.9 mmol/l and serum bicarbonate concentrations correlated inversely with the nPCR and serum albumin [5]. The adjusted risk of death, hospitalisation or malnutrition was higher in patients with serum bicarbonate levels less than 16 or above 24 when compared with patients in the reference group with moderate pre-dialysis acidosis [5]. Short-term benefits of correcting pre-dialysis acidosis from below 19 mmol/l to 24 mmol/l, by either increasing the dialysate bicarbonate concentration [6–9] or the addition of oral bicarbonate supplements [10], have been shown in several small crossover studies. Correction of acidosis reduced whole body protein degradation in a study of 6 patients [6], increased the sensitivity of the parathyroid glands to serum calcium in studies of 21 and 8 patients [7, 8], improved triceps skin thickness as an index of nutritional status in 46 patients [9] and increased serum albumin after 3 months in 12 patients without any change in body weight, Kt/V, and nPCR [10]. Other studies have shown no increase in serum albumin after correction of acidosis.

Complete correction of pre-dialysis metabolic acidosis in HD patients may lead to post-dialysis metabolic alkalosis and consequently hypoventilation, phosphate transfer into cells and a higher risk of soft tissue and vascular calcification. The prerequisite additional oral or dialysate bicarbonate (and sodium) load may contribute to higher sodium (and fluid) retention and hypertension. In a large observational study the risk of death was lowest in HD patients with pre-dialysis serum bicarbonate concentrations within the 18.0–24.0 mmol/l range [11]. Review of the target pre-dialysis serum bicarbonate levels set by international clinical practice guidelines indicates that a mild degree of pre-dialysis acidosis is recommended to minimise the risk of adverse events.

Guideline 6.4 – HD: Pre-dialysis serum potassium concentration

We suggest that the pre-dialysis serum potassium should be between 4.0 and 6.0 mmol/l in HD patients. (2C)

Rationale

The risk of developing hyperkalaemia is inversely related to renal function. Hyperkalaemia is a common indication for emergency dialysis in patients already on HD and 3–5% of deaths in dialysis patients have been attributed to hyperkalaemia [12]. Non-compliance with the HD prescription and/or diet is the main cause of hyperkalaemia in dialysis patients but drug therapy, such as ACE inhibitors, angiotensin receptor blockers, non-steroidal anti-inflammatory drugs, beta-blockers and potassium supplements may be implicated.

HD is the most reliable and immediate treatment of hyperkalaemia in dialysis patients and the serum potassium will usually fall by 1 mmol/l after the first hour of HD and a further 1 mmol/l after the next 2 hours of HD [13]. The rate of potassium removal may be enhanced by an increase in the dialyser blood flow rate, a rise in the dialysate bicarbonate concentration or a decrease in the dialysate potassium concentration [14]. A recent review paper [15] has highlighted the benefit in performing an urgent electrocardiogram to guide management in patients with serum potassium above 6 mmol/l and help decide which patients need emergency administration of intravenous 10 ml 10% calcium chloride over 5 minutes. A Cochrane meta-analysis of non-dialytic emergency interventions for hyperkalaemia concluded that intravenous glucose with insulin and nebulised or inhaled salbutamol were effective in reducing serum potassium levels but the studies were limited by the absence of data on cardiac arrhythmia or mortality rates [14]. Whilst the combination of salbutamol and intravenous glucose with insulin was probably more effective than either therapy alone the evidence for efficacy of intravenous bicarbonate or potassium exchange resins in this Cochrane review of randomised or quasi-randomised trials was equivocal and neither should be used as monotherapy for severe hyperkalaemia.

Pre-dialysis serum potasium levels less than 4.0 mmol/L or greater than 5.6 mmol/L were associated with higher mortality rates in HD patients when compared to a reference group with serum potassium concentrations between 4.6 and 5.3 mmol/L [16]. In another large observational study the risk of death was lowest in HD patients with pre-dialysis serum potassium concentrations within the 4.0–6.0 mmol/l range [11].

Hypokalaemia towards the end or immediately after HD is not uncommon and may be corrected by relaxing dietary potassium restriction or, if necessary, by increasing the dialysate potassium concentration [17, 18].

Audit measure 10

Cumulative frequency curves of pre-dialysis serum potassium concentration.

Guideline 6.5 – HD: Pre-dialysis serum phosphate concentration

We suggest that pre-dialysis serum phosphate, if elevated, should be lowered towards the normal range such as between 1.1 and 1.7 mmol/l. (2C)

Rationale

The clinical risks associated with abnormal serum phosphate concentrations have been reported only in observational studies. Although phosphate binders have been shown to be effective in reducing serum phosphate levels in patients with renal failure, it has not been shown that lowering time-integrated serum phosphate concentrations reduces the risk of patient death [19]. High and low serum phosphate concentrations are associated with an increased risk of death but defining the optimal target range for control of serum phosphate is difficult in the absence of randomised clinical trials with evidence of benefit in hard clinical end-points. However monitoring and clinical audit of serum phosphate concentrations should continue to be performed regularly as part of routine clinical practice as very high and low serum phosphate concentrations are associated with poor outcomes and clinical interventions are used to try to correct hyperphosphataemia and malnutrition.

Guideline 6.6 – HD: Pre-dialysis serum calcium concentration

We suggest that pre-dialysis serum calcium, adjusted for serum albumin, should be within the normal range. (2C)

Rationale

The KDIGO guideline on Mineral Bone Disorders recommends that hypercalcaemia in HD patients should be avoided and documents that the risks of complications and death in HD patients that are caused by pre-dialysis serum calcium levels below the normal range are not established [19].

Audit measure 11

Cumulative frequency curves of pre-dialysis serum calcium and phosphate concentrations.

Guideline 6.7 – HD: Serum aluminium concentration

We suggest that serum aluminium concentration should be measured every three months in all patients receiving oral aluminium containing phosphate binders. (2C)

Guideline 6.8 – HD: Pre-dialysis haemoglobin concentration

We recommend that pre-dialysis haemoglobin concentration should be 10.0–12.0 g/dl. (1B)

The target haemoglobin concentration should be at least 10.5 g/dl to allow for the normal distribution around the mean haemoglobin value of the patient population and intra-individual variation of laboratory measurements and hydration status.

Audit measure 12

Cumulative frequency curves of pre-dialysis haemoglobin concentration.

Rationale

Defined ranges of several laboratory variables (Guidelines 6.3–6.6 and 6.8) have been associated with better survival rates of HD patients in large observational studies [20–29]. These laboratory indices, which have been associated with improved patient outcomes in large datasets of hospital HD patients, were used to develop the audit measures and clinical practice guidelines for thrice weekly HD within this update. The laboratory based guidelines that are recommended for thrice weekly HD in this update are consistent with previous versions of the Renal Association HD guidelines, the UK Renal Registry, Scottish Renal Registry and Quality Improvement Scotland (QIS) and also with the clinical practice guidelines for HD that have been generated in Europe, Australasia and North America. There are no evidence-based guidelines for these laboratory parameters in patients with end-stage chronic renal failure on other than thrice weekly HD or in patients with dialysis dependent acute renal failure. The standards set in this module apply equally to home and hospital HD patients. Similar audit measures have been used in the preparation of previous UK Renal Registry Annual Reports [2].

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7. Haemodialysis (HD) (Guidelines 7.1–7.4)

Guideline 7.1 – HD: Anticoagulation without added risk of bleeding

We recommend that patients without increased bleeding risk should be given unfractionated heparin or LMWH during HD to reduce the risk of clotting of the extracorporeal system. (1A)

Rationale

Extracorporeal anticoagulation is usually required to prevent thrombosis of all forms of dialyser and extracorporeal circuit. Unfractionated heparin may be used as the standard anticoagulant in view of its proven efficacy, ease of use and safety record unless the patient has a history of recent or active bleeding or heparin induced thrombocytopenia [1, 2]. Heparin with a mean half-life of 1.5 hours is best administered as a loading dose followed by a continuous infusion of 500–1,500 units/hour that is discontinued approximately 30 minutes before the end of the dialysis session. Monitoring when required can be performed by measuring the activated partial thromboplastin time or the whole-blood activated clotting time aiming for around 150% of predialysis or normal values. The dosage of heparin may need to be increased if there has been a substantive rise in the haematocrit after correction of renal anaemia or reduced if the patient is on warfarin or antiplatelet drugs. Low molecular weight heparin (LMWH) is an alternative agent that has been associated with lower risk of bleeding, less frequent episodes of hyperkalaemia and an improved lipid profile compared with standard heparin. However a systematic review of 11 trials comparing the use of LMWH and unfractionated heparin in HD patients concluded that there was no difference in the incidence of bleeding complications, bleeding from the vascular access after HD or thrombosis of the extracorporeal circuit [3]. Although no difference has been observed in thrombotic or haemorrhagic complications during HD with either unfractionated heparin or LMWH, renal units' uptake of LMWH is increasing because of its ease of use and convenience for HD nursing staff.

Guideline 7.2 – HD: Anticoagulation with significant risk of bleeding

We recommend that systemic anticoagulation should be avoided or kept to a minimum in patients with a significant risk of bleeding. This may be achieved by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15–30 minutes or regional citrate infusion. Low-dose unfractionated heparin may be used with caution in patients with intermediate risk of bleeding. (1C)

Rationale

For patients with a risk of bleeding anticoagulation should be avoided or kept to a minimum by using a high blood flow rate and regular flushing of the extracorporeal circuit with saline every 15–30 minutes [2]. Alternatively heparin may be replaced by a prostacyclin infusion or regional citrate anticoagulation [4]. The former may induce hypotension and is expensive whilst the latter requires careful replacement of calcium and magnesium, monitoring of serum calcium and magnesium levels during HD and is too complex for routine use. The use of regional citrate infusion has been shown to reduce the incidence of bleeding complications compared to the use of standard heparin for anticoagulation during HD [5]. Low-dose unfractionated heparin may be used with caution in patients with intermediate risk of bleeding.

Guideline 7.3 – HD: Anticoagulation in patients with HIT type 2 or HITTS

We suggest that patients with HIT type 2 or HITTS should not be prescribed unfractionated heparin or low molecular weight heparin (LMWH). (2B)

Rationale

Heparin induced thrombocytopenia type 1 usually occurs early after starting heparin, is non-immune mediated and associated with mild thrombocytopenia and resolves without stopping heparin [2]. For patients with heparin induced thrombocytopenia (HIT) type 2 or heparin induced thrombocytopenia and thrombotic syndrome (HITTS) anticoagulation with either Argatroban, heparinoids (danaparoid) or recombinant hirudin (lepirudin) should be utilised instead of heparin or LMWH [6]. Patients with HIT type 2 or HITTS should not be prescribed either unfractionated heparin or LMWH in future as there is a high cross-reactivity (>90%) between unfractionated heparin and LMWH.

Guideline 7.4 – HD: Anticoagulation and catheter lock solutions

We suggest that each unit should have policies and procedures for administration of catheter locking solutions to maintain catheter patency and keep systemic leak of the catheter lock solution to a minimum. (2C)

Rationale

There have been multiple reports to the National Patient Safety Agency (NPSA) of episodes of life threatening haemorrhage due to systemic anticoagulation arising from central venous dialysis catheter locks [7]. The NPSA has issued guidance that all catheter lock solutions should only be administered if there is a prescription or patient group direction [7].

There are also reports of a systemic anticoagulant effect even if the volume of heparin catheter lock solution is equal to the internal volumes of the catheter lumens stated by the catheter manufacturer [8–12]. In a study of administering heparin lock solutions after heparin free HD sessions the mean aPTT increased by 126 seconds at 15 minutes after catheter locks were inserted and 71 seconds 1 hour after catheter locks were inserted [11]. In vitro studies have shown that there is leakage of the catheter lock solution through the holes near the tip of the catheter when the volume of catheter lock solution used is the same as the internal volume of each lumen the catheter [9, 10]. The estimated leak of heparin lock solution averaged 0.61ml and ranged from 0.46 to 0.85ml in the different catheters studied when 80–120% of the catheter lumen volume was injected, which would cause a significant systemic anticoagulant effect if 5000 u/ml heparin is used as a catheter lock solution [10]. The reports of adverse events emphasise the need for each renal unit to have detailed policies and procedures plus adequate training of staff in the correct use of catheter locks containing anticoagulants (heparin or citrate) to maintain catheter patency.

As patients with HIT type 2 or HITTS should not be prescribed either unfractionated heparin or LMWH the options for suitable catheter lock solutions for such patients include 30% trisodium citrate, taurolock, urokinase or tissue plasminogen activator. 30% citrate has also been shown to reduce the risk of catheter-related bacteraemia compared with the use of unfractionated heparin [13].

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8. Haemodialysis (HD) (Guidelines 8.1–8.3)

Guideline 8.1 – HD: Symptomatic dialysis-related hypotension

We recommend that data on the frequency of dialysis-related hypotension, defined as an acute symptomatic fall in blood pressure during dialysis requiring immediate intervention to prevent syncope, should be collected and audited. (1C)

Rationale

Dialysis-related hypotension is the most frequent symptomatic complication of HD and historically in some studies occurred in more than 15% of HD sessions [1]. As well as being extremely unpleasant hypotensive episodes can shorten the time on dialysis and reduce the efficiency of delivered dialysis [1]. Dialysis-related hypotension also has been shown to be an independent predictor of poor patient survival [2]. The frequency of this event is, therefore, an important indicator of the quality of dialysis from the patient's perspective. It is caused by a reflex withdrawal of sympathetic tone resulting from decreased left ventricular filling, and is therefore dependent on the rate of fluid removal from the vascular space, the rate of re-filling from the interstitial space, venous tone, and many other variables [3]. Patients experiencing frequent dialysis-related hypotension are at higher risk of death [4] and this may be because dialysis-related hypotension is a marker for severe cardiac disease [5]. A recent audit in London has shown that achieving blood pressure targets during HD is associated with a higher incidence of developing symptomatic intradialysis hypotension (r = 0.8; p = 0.003) [6]. In this study of 2,639 HD patients 15% of the patients developed symptomatic hypotension requiring intravenous fluid resuscitation during a 1 week observation period, equivalent to 7% of all HD sessions. The high incidence of intradialysis hypotension occurred despite only 26% of patients meeting both of the targets for blood pressure control (pre-dialysis BP <140/90 and post-dialysis BP <130/80) [6].

Audit measure 13

The incidence of symptomatic hypotensive episodes during dialysis sessions.

Guideline 8.2 – HD: Prevention of symptomatic dialysis-related hypotension

We recommend that a stepwise approach is adopted to minimise the incidence of intradialysis hypotension: restrict dietary sodium intake to reduce interdialysis weight gains and review 'dry' weight and antihypertensive drugs; increase duration of HD to reduce the hourly ultrafiltration rate; trial use of cool temperature dialysis. (1C)

Rationale

Adjustment of the rate of fluid removal, dialysate sodium concentration and dialysate temperature during dialysis, or combinations thereof, can reduce the incidence of this complication [7–10]. Interdialysis weight gains can be reduced if dietary sodium intake is kept below 100 mmol/day and thereby reduce thirst and subsequent fluid intake. Dialysate sodium modeling or ramping can reduce intradialysis cramps and hypotension but incurs the risk of greater problems with interdialysis thirst, weight gain and hypertension [8]. A recent randomised trial of intradialytic blood volume monitoring and conventional monitoring showed no difference in weight, blood pressure or frequency of dialysis-related complications whilst hospitalisation and mortality rates were lower in the group assigned to conventional monitoring [11]. However the conventional monitoring group had atypically low hospitalisation and mortality rates in comparison with local prevalent HD patients [11]. There is also the question of increased cost if on-line monitoring of changes in relative blood volume (by measurement of changes in optical density of blood) is used to assess dry body weight in an attempt to reduce the incidence of intradialytic hypotension [12]. A recent systematic review of 22 studies has concluded that a reduction in dialysate temperature is effective in decreasing the incidence of intradialytic hypotension without affecting dialysis adequacy [13]. Increasing the dialysis treatment time to reduce the fluid ultrafiltration rate or decreasing the dialysate fluid temperature are the most reliable and practical methods of reducing the incidence of intradialytic hypotension without causing adverse sequelae.

Guideline 8.3 – HD: Maximum hourly ultrafiltration

We suggest that the maximum hourly ultrafiltration rate during haemodialysis should not exceed 10 ml/kg/hour. (2C)

Rationale

Symptomatic hypotension during HD is more common if the patient has higher interdialysis weight gains. A DOPPS international observational study of 22,000 HD patients has shown that the risk of intradialysis hypotension (RR = 1.3; p = 0.045) and the risk of

death (RR = 1.1; p = 0.02) were significantly higher in the patient group with ultrafiltration rates above 10 ml/kg/hour after adjusting for patient demographics, co-morbidities, dialysis dose (including residual renal function) and body size [14]. Treatment time >4 hours was independently associated with a lower risk of death (RR = 0.81; p = 0.0005) and treatment time lowered mortality rates at all levels of Kt/V [14]. Patient survival rates at any given treatment time were worse in the USA than Europe which in turn were worse than Japan but the data should be interpreted with caution as it is an observational study with potential unknown confounding variables and patients in Japan with cardiac disease or a history of hypotensive episodes are usually prescribed lower ultrafiltration rates.

Prolonging treatment time and so reducing the ultrafiltration rate has been shown to improve survival in other studies [15, 16]. Data from a large Japanese population have shown that dialysis duration up to 5.5 hours was associated with improved patient survival after adjusting for dialysis dose [15]. Patients in Tassin treated with long duration thrice weekly HD with mean spKt/V of 1.67 ± 0.41 have been observed to have very low mortality rates [16] and a Cox analysis showed that patient survival was linked to improved blood pressure control and lower cardiovascular mortality due to the achievement of better long-term control of dry body weight [16]. A randomised crossover trial comparing 4 hours and 5 hours HD has shown a reduction in the incidence of hypotensive episodes during 5 hour treatment sessions [17]. All of these studies suggest that lower rates of ultrafiltration result in better patient outcomes. Reducing the hourly ultrafiltration rate on HD may be an indication to extend the duration of HD. Alternatively the addition of periods of isolated ultrafiltration without HD has been employed to reduce the risk of developing hypotension.

Audit measure 14

The proportion of haemodialysis patients who have ultrafiltration rates in excess of 10 ml/kg/hour.

Guideline 8.4 – HD: Prevention and detection of venous fistula needle or venous line disconnection

We suggest that all haemodialysis staff should follow standard operating procedures to minimise the risk of accidental venous needle/line disconnection. In patients who are restless or undergoing haemodialysis at home consideration should be given to the use of commercially available monitoring systems. (2C)

Rationale

Patient safety on HD is paramount. HD machines have reliable alarms to detect air embolism, blood leaks, low arterial pressure, dialysate conductivity or temperature outwith the specified range and high venous pressure. The importance of securing and monitoring the fistula needles or central venous catheter during HD is well recognised. Dislodgement of vascular access needles or catheters or disconnection of the dialysis lines should be very uncommon complications of HD and should be detected quickly if they do occur. Patients are at greater risk of exsanguination following dislodgement of the venous needle as the patient will continue to lose blood at the same rate as the blood pump flow rate unless the HD venous pressure alarms are activated. The venous pressure alarms may not be triggered as the venous pressure falls only to a small extent if there is a disconnection of the venous fistula needle or venous dialysis line from the patient's low venous pressure system as the bulk of the resistance to blood flow is in the dialysis needle and tubing, especially if HD is performed using high blood flow rates and smaller gauge venous return needles. If a disconnection is not noted by the patient, nursing staff or carer life threatening haemorrhage can occur without the venous pressure alarm being activated.

A survey of UK renal units in 2007 identified 4 fatal and 38 non-fatal episodes of haemorrhage since 2000 due to venous needle/line dislodgement and this is almost certainly an underestimate of the true incidence of this serious adverse event [18]. The EDTNA/ERCA has produced recommendations for renal nurses to highlight awareness of this life threatening complication, provide a consistent approach to securing and monitoring of the fistula needles/catheter and dialysis lines during HD and advocate best practice of asymmetric setting of the venous pressure alarms [19]. Asymmetric setting of the venous pressure alarms at $-30\,\mathrm{mmHg}$ and $+70\,\mathrm{mmHg}$ around the prevailing setting of the patient's venous pressure may optimise the detection of the small decreases in venous pressure that occur if the venous fistula needle, catheter or dialysis line become disconnected. Blood leak detection devices may be used if the patient is deemed at high risk of venous needle/line disconnection, such as agitated or confused, or the patient is self caring at home without assistance [20]. Daily nocturnal HD does not require high blood flow rates and vascular access is often achieved using a single needle to prevent the risks associated with venous needle dislodgement.

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9. Haemodialysis (HD) (Guidelines 9.1–9.3)

Guideline 9.1 – HD: Home haemodialysis and patient choice

We recommend that all patients who may be suitable for home dialysis should receive full information and education about home HD. (1B)

Rationale

HD may be performed in a variety of settings, including hospital-based units, free-standing units, and in the home. Patient survival and quality of life adjusted for co-morbid risk factors has been reported to be higher on home than hospital HD [1, 2]. Home HD is more cost-effective than hospital HD if patients remain on dialysis for more than 14 months to offset training and setup costs [3]. The choice between home and hospital HD for patients assessed as able to perform dialysis at home should be determined mainly by patient preference rather than economic grounds. Patients performing HD at home require to be motivated to perform self dialysis, have a spare room or a home cabin for conversion for home HD and have reliable vascular access and most will have a helper or carer at home [4].

Audit measure 15

The proportion of dialysis patients in the main renal unit and its satellite units who are on home haemodialysis.

Guideline 9.2 – HD: Home haemodialysis training and technical support

We suggest that some patients may need to travel to a sub-regional or regional centre to pursue their choice to train for home HD as HD training is not available in all renal units. (2C)

Rationale

The number of patients on home HD in the UK has continued to decline. Not all UK units provide home HD and, based on a review of the clinical-effectiveness and cost-effectiveness of home, satellite and hospital HD, the National Institute of Clinical Excellence (NICE) has recommended that the option to train to perform home HD should be available to all patients [4, 5]. NICE recommended that more than 10% of dialysis patients should be treated by home HD and, whilst this recommendation is achieved in Australasia [6], very few centres in the UK have more than 5% of dialysis patients on home HD [7]. Higher prevalence rates of home HD may be achieved by having a designated home HD training centre serving several renal units within a region akin to current service provision for renal transplantation.

Guideline 9.3 – HD: Daily home haemodialysis

We recommend self-treatment at home as the best way to perform daily short or daily nocturnal HD. (1D)

Rationale

Daily short and daily nocturnal HD have been reported in small observational studies to improve patient well being and reduce recovery times after HD and have been associated with improved control of anaemia and blood pressure, better nutritional status and regression of left ventricular hypertrophy [8–15]. However the delivery of daily HD at a hospital or satellite unit is impractical for a significant proportion of HD patients. Patient travel to and from a HD unit on a daily basis makes in centre or satellite daily HD less suitable for most patients wishing to perform daily short or nocturnal HD. In centre or satellite daily HD requires increased HD facilities and also an increase in trained HD staff unless the patient is self-caring. For these reasons daily short or nocturnal HD is suited ideally to be performed by the patient at home.

Audit measure 9

The proportion of hospital (main and satellite unit) and home haemodialysis patients who are prescribed more frequent than thrice weekly haemodialysis.

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