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ORIGINAL ARTICLE

Interventions to improve hemodialysis adequacy: protocols based on real-time monitoring of dialysate solute clearance

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Abstract

Background: The monitoring of dialysate ultraviolet (UV) absorbance is a validated technology to measure hemodialysis adequacy and allows for continuous and real-time tracking every session as opposed to the typical once-monthly assessments. Clinical care guidelines are needed to interpret the findings so as to troubleshoot problematic absorbance patterns and intervene during an individual treatment as needed.

Methods: When paired with highly structured clinical care protocols that allow autonomous nursing actions, this technology has the potential to improve treatment outcomes. These devices measure the UV absorbance of dialysate solutes to calculate and then display the delivered as well as predicted clearance for that session. Various technical factors can affect the course of dialysate absorbance, confound the device's readout of clearance results and thus lead to challenges for the dialysis unit staff to properly monitor dialysis adequacy. We analyze optimal and problematic patterns to the device's 'clearance' display (e.g. due to thrombosis of hollow fibers, inadequate access blood flow or recirculation) and provide specific interventions to ensure delivery of an adequate dialysis dose. A rigorous algorithm is presented with representative device monitor display profiles from actual hemodialysis sessions. Procedural rationale and interventions are described for each individual scenario.

Conclusion: Real-time hemodialysate UV absorbance patterns can be used for protocol-based intradialytic interventions to optimize solute clearance.

Key words: dialysis adequacy, *Kt/V*, recirculation, urea modeling, vascular access

Introduction

Real-time monitoring of dialysis adequacy has been made possible by the development and marketing of hemodialysis machines that monitor solute clearance. Currently this is accomplished by two different technological approaches, both of which depend on measuring fluxes of substances from blood into the dialysate: monitoring the effluent for moieties that are urea surrogates by either electrical conductance or ultraviolet (UV) absorption. Recent focus has been on validating the effectiveness of current methodologies. Despite concerns that results could be confounded by such problems as interfering substances, inappropriate urea modeling, solute rebound or errors in calculating urea

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volume (V), the dialyzer clearance of urea (K), dialysis time (t) and urea reduction ratio (URR) clearance calculations from the different modalities have generally had excellent correlation.

Nevertheless, these estimations of dialysate urea 'appearance' have not been universally accepted for the purposes of quality assurance for dialysis adequacy. The efficacy of hemodialysis treatments thus still needs to be confirmed by blood tests for urea 'clearance'. Given the fact that these blood-based urea clearance tests are preformed infrequently, on the order of one per month, there is much practical value from using a real-time device that is available for every treatment. The ability to monitor the pattern of intradialytic solute removal, detect problems and immediately intervene [1, 2] enhances the provider's ability to react to direct therapy variables. Although such a benefit has been proposed, this is the first report of how to use this technology for protocol-driven changes to impact each dialysis session's prescription so as to achieve dosing adequacy.

Since the ionic conductance technology is limited to intermittent monitoring, typically every 45 min, it is theoretically inferior to the continuous nature of the UV absorbance technique for the immediate detection and resolution of problems. Therefore, nursing protocols were developed based on UV absorbance technology, which are driven by comparing the calculated delivered dialysis dose (*Kt*/*V* or URR) profile to that of the ideal trajectory. Because minute-to-minute changes in treatment efficacy cannot practically be addressed by offsite physicians, nurses would now have a new tool to independently implement physician-driven protocols to improve patient care. For example, immediate recognition of low or decreasing clearance can trigger interventions that increase dialysis time, alter blood or dialysate flow rate, adjust needle position, improve anticoagulation or replace the dialyzer. Additionally, patterns from the continuous device readouts suggestive of access recirculation were identified. Patients with patterns suggestive of recirculation underwent verification by blood-based testing or imaging studies. Real-time continuous monitoring is particularly important for patients using catheters as their primary access, since intermittent erratic flow may otherwise not be detected.

The goal of this article is to use the findings from the multiple published device-validation studies to describe clearance profiles (calculated from the dialysate UV absorption) that can prompt real-time changes in the treatment prescription to overcome problems with achieving dialysis adequacy, access function or technical difficulties involving the extracorporeal circuit. Clinical care guidelines and protocol-driven clearance interventions based on continuous data allow the nursing staff a new opportunity to be nimble and empowered so as to provide optimal high-quality dialysis.

Materials and methods

Hemodialysis and online clearance devices

Hemodialysis was performed using machines equipped with continuous monitoring of effluent dialysate by UV absorbance at 280 nm (Adimea device integrated in the Dialog hemodialysis machine, B. Braun, Bethlehem, PA, USA). Clearance is calculated by analysis of the decrease in the dialysate's solute absorption (UVAbs) over time. A logarithmic decline in dialysate moieties is expected as they are removed from the blood compartment. Characterization of exponentially falling solutes in the effluent yields the dialysis dose expressed as either *Kt*/*V* or URR using single-pool analysis. While the machine measures absorbance, it graphically displays the calculated clearance, which increases over time. The software also adjusts the total clearance so as to include the component achieved by convective losses through ultrafiltration. The calculated *Kt*/*V* and URR curves are shown as predicted (dotted line) and as achieved (solid line). The display also shows the user-set target values for these parameters (red line) over the prescribed treatment time (e.g. 1.4, 75% in 4 h, respectively). At any point, the user can discern how the achieved clearance varies from the predicted trajectory and whether the patient will reach the adequacy goal. The machine can be set so as to alarm and thereby notify the staff when the patient is projected to not reach the clearance target. Patients received their hemodialysis therapy as part of their routine clinical care as outpatients or inpatients at the University of Florida Shands Hospital, Gainesville, FL and the dialysate UV absorbance technology was utilized for every patient at every treatment. Hemodialyzers were made of polysulfone [F160, F200 or F16NF (Fresenius, Worcester, MA, USA) or cap15 or cap 20 (B. Braun, Bethlehem, PA, USA)]. This report adheres to the policies of the University of Florida Institutional Review Board.

Nursing protocol to reach dialysis adequacy goal

As per physician orders and the dialysis adequacy policy, nurses are empowered to follow the protocol (Figure 1) and react to treatment variances to reach the prescribed dose target. Using the protocol, nursing actions are based on whether the achieved clearance pattern is above or below the desired trajectory. Variables include the choice of dialyzer (e.g. based on clearance specifications), blood and dialysis flow rates, treatment time, the degree of anticoagulation (e.g. dose of heparin), replacement of a clotted dialyzer, repositioning of cannulation needles and thrombolysis of access catheters. Images of the problematic clearance curves were obtained during various clinical scenarios when patients were off trajectory, as well as improved displays of the profiles after remediation by appropriate nursing interventions.

Results

The dialysate UV absorption-based patient care protocol was well-accepted by the nursing staff and physicians. When indicated, the efficacy of the protocol-driven changes to the dialysis prescription was verified by blood-drawn URR determinations. Anecdotally, the nurses, technicians and physicians reported better patient compliance with staying for their prescribed HD time by showing the patients the underdialysis graphic. The staff was often able to dissuade the patients from leaving early (staying 'until the blue line reaches the red line'). Specific clearance pattern scenarios were identified and are described below.

Dialysate-based clearance curve follows predicted trajectory

Dialysate-based clearance pattern on track to meet prescribed dose
Figure 2A demonstrates dialysis sessions in which the dialysate clearance based on UV absorbance follows the anticipated trajectory so as to achieve the prescribed dose. In Figure 2A, a *Kt*/*V* goal of 1.4 is reached in a patient weighing 67.8 kg after 4 h using a blood flow (Qb) of 450 mL/min and dialysate flow (Qd) of 500 mL/min. The delivered-dose curve is essentially superimposable on the anticipated trajectory. Staff need to stay vigilant that there can be concurrent processes with opposite effects on the displayed curve, although the net effect is unlikely to culminate in a tracing that consistently tracks the projected trajectory over the course of the entire dialysis treatment.

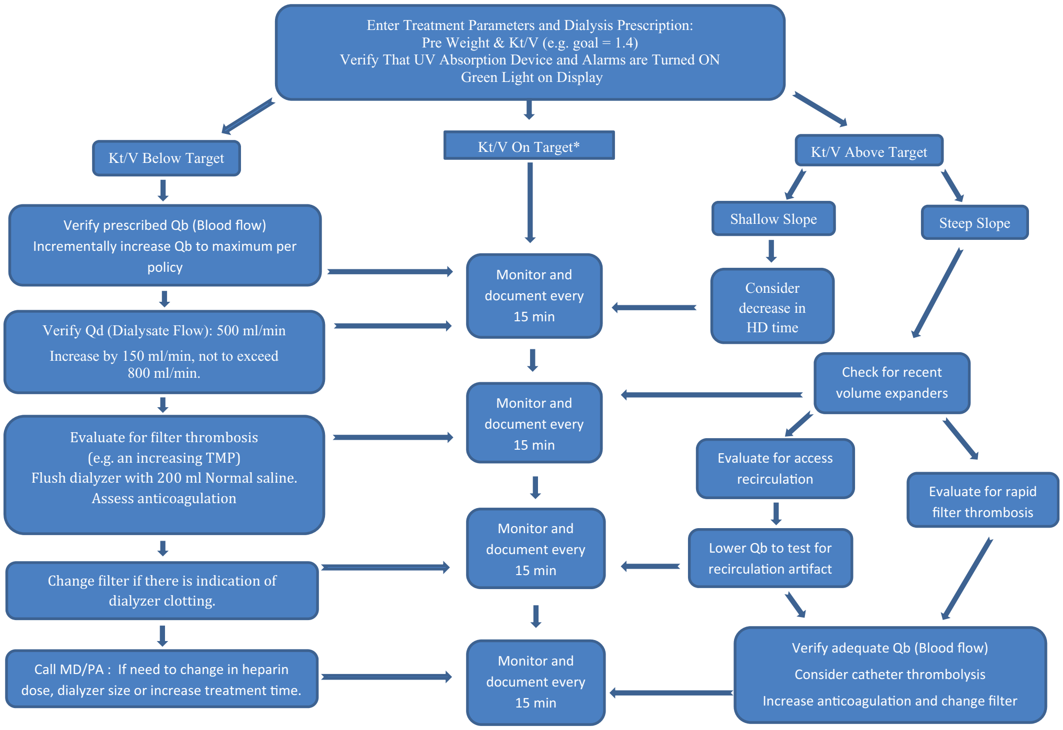

Fig. 1. Flow diagram of nursing protocol using solute clearance calculated from real-time dialysate UV absorption measurements. Decisions are based on the real-time (measured) clearance curve differing from the projected trajectory. *Signifies the need of the staff to stay vigilant wherein there can be concurrent processes with opposite effects on the displayed curve.

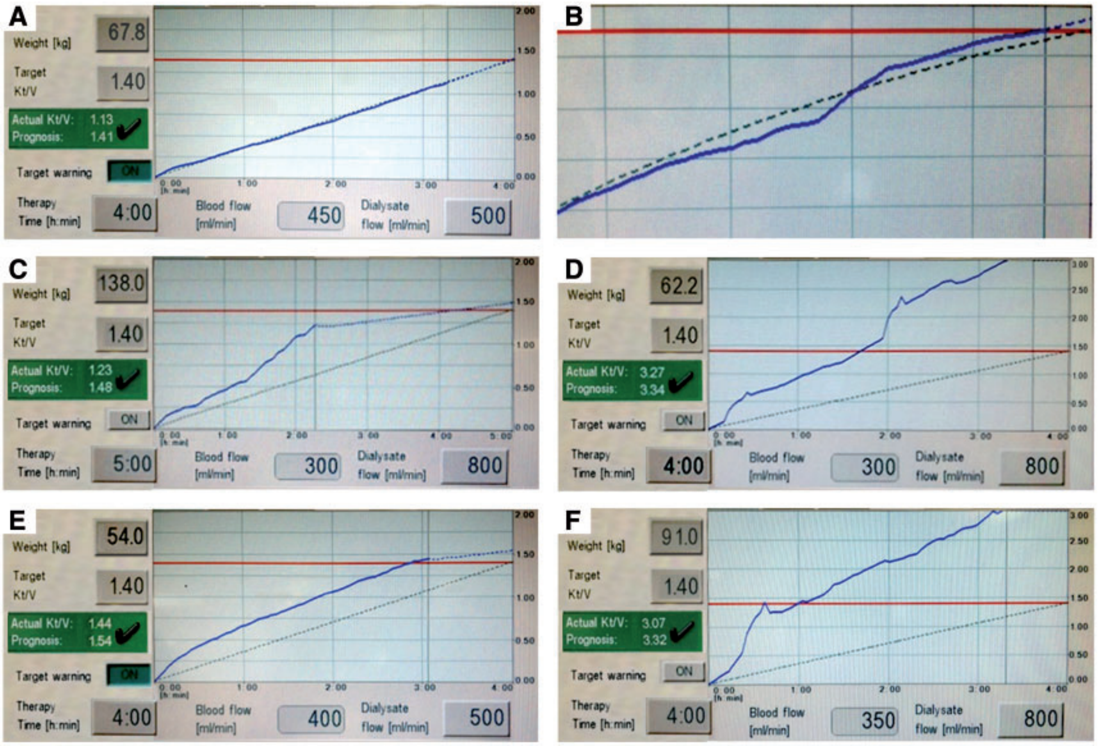

Fig. 2. (**A**) Clearance curve (based on UV absorption) for a patient weighing 67.8 kg who can meet the target clearance in the prescribed 4 h. (**B**) Clearance curve below prescription with gradual clotting of the dialyzer and improved trajectory after increased dialysate flow rate. (**C** and **D**) Clearance curves erroneously high due to artifact caused by access recirculation. (**E**) Clearance curve in a former pediatric patient weighing 54 kg who can reach clearance targets in less than the prescribed 4 h. (**F**) Clearance curve erroneously high due to artifact caused by rapid volume expansion from intravenous albumin.

Dialysate-based clearance pattern initially adequate, then falling below the desired trajectory

In Figure 2B, a patient is initially on target for dialysis adequacy and then the trajectory falls below the desired adequacy at ∼2 h due to what was discerned to be gradual clotting of the hollow fibers. As per the protocol, the Qd was increased to 800 mL/min and the dialysate clearance curve shifted upward to again match the desired trajectory, achieving the prescribed dose.

Dialysate-based clearance curve higher than predicted or prescribed trajectory

Steep upward slope yet actual clearance is inadequate due to access recirculation

Figure 2C and 2D demonstrates two examples of inadequate clearance due to access recirculation that had not been otherwise suspected or detectable during the treatment session. As described below, the greater the recirculation of the extracorporeal circuit, the faster the decrease in its concentration of uremic solutes. This misleading rapid decline in solutes due to the recirculation phenomenon is erroneously interpreted by the software as a high dialysis dose; the calculated dialysate clearance curve rises greatly above the machine's predicted curve. Reversed needles are a potential cause and easily remedied. In Figure 2C, a patient weighing 138 kg with catheter access and a Qb of 300 mL/min was prescribed 5 h at a Qd of 800 mL/min. Recirculation was not clinically detected by the staff and was only suspected when the calculated clearance curve was unexpectedly greater than anticipated, with a pronounced steep slope: this heavyweight patient was erroneously predicted to reach a 1.40 *Kt*/*V* goal in just over 2 h. Blood sampling confirmed an ∼20% access recirculation. Figure 2D demonstrates how recirculation not only raises the curve but also causes an erroneously high numerical *Kt*/*V* to be displayed (∼3.3 in this example).

Dialysate-based clearance pattern on trajectory but dialysis dose consistently higher than the prescribed goal

As shown in Figure 2E, a lesser weighing former pediatric patient on multiple dialysis sessions had reached the adequacy goal more quickly than the 4 h initially prescribed. At 54 kg, a Qb of 400 mL/min and Qd of 500 mL/min, the *Kt*/*V* of 1.4 was attainable at just 3 h. This permitted cautious reduction in the dialysis time with verification of adequacy by blood testing.

Sudden steep upward slope, then curve parallel to predicted trajectory

This phenomenon is due to sudden hemodilution caused by volume expanders such as saline or albumin infusions. The diluted blood passing through the dialyzer results in an immediate decrease in uremic solutes appearing in the dialysate effluent. The dramatic decrease in dialysate UV absorbance is incorrectly interpreted by the software as being due to a higher dialysis dose, yielding erroneously high *Kt*/*V* and URR values. Figure 2F demonstrates this happening immediately following infusion of 50 g of albumin.

Dialysate-based clearance curve lower than predicted trajectory

Common causes of the achieved dialysate clearance being below the desired trajectory are inadequate prescription (blood or dialysate flows, time, choice of dialyzer) clearance characteristics in relation to the patient's size and *Kt*/*V* goal, problematic access causing low blood flows and gradual clotting the hollow fibers due to inadequate anticoagulation. Sudden severe thrombosis of the fibers causes a somewhat different pattern. The rapid decrease in UV absorption by dialysate solutes is incorrectly attributed to high dialysis clearance (displayed as an upward slope in calculated clearance), then the curve flattens out (as solute removal remains low). The curve then gradually declines further and further below expectation.

Discussion

The ability to monitor a real-time dialysis dose holds great promise to ensure the delivery of optimal treatments. The first commercially available technology utilized electrical conductance of effluent dialysate. These devices are based on the premise and evidence that sodium fluxes across the dialyzer membrane are an excellent surrogate for urea dialysance and that they can be measured by changes in dialysate conductivity [3, 4]. As currently marketed (Fresenius, Waltham, MA, USA), the hemodialysis machines intermittently alter dialysate sodium and calculate a predicted urea clearance (*K*). Although technically possible to be done frequently, with this popular device it is typically done only every 45 min, or six times over the course of a 4-h treatment. Based on the presumption that those few values are representative of the entire session, the device estimates the clearance for the whole treatment (*Kt*). However, for determination of the dialysis dose (*Kt*/*V*), the urea volume (*V*) must be established separately by various empirically derived equations (e.g. using weight, height, gender) or independent technology (e.g. bioimpedance). The two major weaknesses of conductance-based dose monitoring are missing the problems that occur between the intermittent tests and errors in calculating volume. The latter can be >20%, depending on the methodology chosen for the *V* estimation [5–8].

Monitoring clearance in dialysate effluent can overcome the deficiencies of conductance-based devices. As any particular solute is dialyzed from the blood, the rapid decrease in its plasma concentration will be reflected by a similar decrease in its appearance in the used dialysate. The UV absorbance technology continuously measures certain solutes in the effluent, which will thus exponentially decrease in concentration over the treatment time. By mathematically characterizing the logarithmic decline in dialysate solute (e.g. curve fitting), the equation yields the *Kt*/*V* value using single-pool analysis. For example, when the natural logarithm of the absorbance is plotted against time, the slope of the resultant line is determined by the *Kt*/*V*. Hence the advantage of the direct measure approach is that urea volume does not have to be independently determined; this is the potential major source of error as described above. Since treatment efficacy can change over the course of the treatment (e.g. from clotting or changing flow rates), errors in curve fitting are overcome by the software performing the analyses every 20 min and not being confounded by alarm conditions (e.g. blood leaks, conductivity problems).

The theoretical weakness of using UV methods, however, is that absorbance at any particular wavelength is not unique for a single substance. Each molecule will not only have an optimal or peak wavelength but will also absorb over a range of values, and thus the various moieties found in human blood will be expected to have overlapping absorbance spectra. For example, one study characterized 40 absorption peaks [9]. Thus, choosing the wavelength based on the urea molecule (285 nm) would be nonspecific and has the additional shortcoming that it has relatively limited UV absorbance compared with other waste products appearing in the dialysate [10]. Wavelengths in the range of ∼200–285 nm have been studied in relation to how they characterize many common solutes [11–13], using the 280 nm Adimea device. Multiple investigations have established that small-molecule absorption in that spectral range is an excellent surrogate for urea removal and primarily includes such substances as uric acid and creatinine. Small solutes with high clearance rates account for ~95% of UV absorbance [9, 11]. This is analogous to sodium being used as a surrogate for urea in the conduction-based technologies. Important for clinical use, there is neither negligible confounding from UV absorbance by the low concentrations of small and large proteins in the dialysate nor by commonly used medications [9]. The effect of medication clearance would be attenuated by their typically having much lower plasma concentrations than that of uremia moieties such as urea. A rigorous study across the wide spectrum of pharmaceuticals has not been done.

Theoretically, errors in predicting urea removal could be introduced if the various substances have different volumes of distribution and different mass transfer coefficients between the extracellular fluid compartments. As pointed out by Daugirdas and Tattersall [14], molecules that could confound absorption calculations tend to be large and have slow removal by hemodialysis and thus UV absorption calculations would be expected to underestimate urea clearance. Nevertheless, monitoring of moieties absorbing in this wavelength range has been shown to be satisfactory for clinical purposes. Kt/V_{urea} calculations have reportedly been very similar when comparing blood, conductance and UV absorption techniques, with differences from 0 to 0.1 [2, 5–7, 15, 16]. UV absorption clearance correlated well with blood testing [17] not just with urea, but also with potassium and phosphate [1]. Some of the discrepancy may be due to deficiencies in the mathematical modeling of single- versus double-pool urea kinetics for the blood-based methodology. In that, continuous absorbance measurements are preferable to fewer sampling points and the UV absorbance device can be used to more rigorously assess postdialysis rebound, which is consistent with two-compartment kinetics [18]. It has also been reported that what has been described as a 7% lower clearance from the UV methodology is actually due to some overestimation from the two-pool blood-based methodology [2].

Importantly, the potential disadvantages of all of these devices that use urea surrogates for curve-fitting clearance calculations could be overcome by technology that would precisely measure urea concentration in dialysate. Highly sensitive and selective urea assays would also permit mass clearance calculations, but those machines are complex, require calibration and have not been practical or economically feasible for mass marketing. For example, results from using the Biostat 1000 device (Baxter Healthcare, McGaw Park, IL, USA) supported the use of dialysate measurements for determinations of adequacy [19, 20], but the machine was not made commercially available.

In this article we have demonstrated the usefulness of continuous real-time monitoring of dialysis clearance for maintaining and achieving adequacy goals. While it remains imperative to verify these estimations with blood-based urea determinations, those measurements cannot be performed instantaneously and thus real-time UV absorbance technology can guide nimble intradialytic changes to the prescription: adjusting blood or dialysate flow, prolonging dialysis time, repositioning needles, checking for access recirculation, optimizing anticoagulation of the extracorporeal circuit and replacing dialyzers impaired by thrombosed fibers. Clearance curves (calculated from the dialysate UV absorption measurements) that unexpectedly deviate from the predicted trajectories can also prompt unscheduled postdialysis laboratory testing, which in turn could prompt extra dialysis sessions, a change in the dialysate composition, imaging or revision of the dialysis access. This is important in that the shape of the displayed Kt/V or URR curve can thus provide information beyond that of traditional intermittent adequacy parameters that are calculated using postdialysis data; the curve can be of particular value for the detection of access recirculation. As long as the intra-access blood flow is more than the extracorporeal pump rate, there would not be any recirculation and the UV absorbance–generated clearance curve would be reliable. Once the pump flow exceeds the capacity of the malfunctioning access, dialyzed blood begins to loop back into the dialyzer. Thus this 'clean' blood from the dialyzer outlet returns to mix with the fresh blood ('recirculates') and solute concentrations at the dialyzer inlet are lower (and decrease more rapidly) than anticipated. The recirculation-induced steep decline in the extracorporeal circuit's solutes results in a similar rapidly decreasing pattern in the dialysate (and UV absorption). The software incorrectly interprets this phenomenon as having been caused by a high dialysis dose. For example, with substantial recirculation the solute concentration can decline so quickly in the dialysate that patients can appear to achieve Kt/V values of >1.4 in <2 h, which is clearly not physiologically possible. Properly trained staff can recognize the atypical steep shape of the displayed clearance curves, which greatly differ from the anticipated (dotted line) trajectory. As long as the access is still patent and has a minimally acceptable flow rate (e.g. 200 mL/min), the nurse will be able to decrease the pump rate so as to eliminate the clearance curve's recirculation artifact. Blood testing would be needed to verify an adequate URR. We believe that the ability to detect recirculation as well as other causes of low clearance has particular clinical importance in the setting of catheters. There have been a number of patients in whom we discerned recirculation from malfunctioning femoral vein catheters. The problem was unanticipated from the flow and pressure profiles and would have been missed if not suggested by the UV absorption device, confirmed by blood testing and resolved by replacement with a new longer catheter. We also fear that catheter flow can be so erratic that problems, and thus inadequate dialysis, could be missed by the intermittent nature of the conduction-based devices.

It is important for the staff to also appreciate how sequential remedies to abnormal dialysate absorption-based clearance curves can reveal more than one problem in a dialysis treatment. For example, an abnormal curve may persist after replacing a dialyzer and could thus unmask a second problem. From a practical standpoint, this would be a circumstance in which this technology could make it difficult to discern access recirculation. Users thus need to be cognizant of the possibility that simultaneous unrelated problems could have opposite effects on the displayed curve, wherein one could increase the displayed curve (e.g. recirculation) while a second malfunction decreases it (e.g. partial clotting). We believe it would be theoretically possible, but rare, for these combined effects to culminate in a resultant curve precisely following the trajectory over the full course of many hours of treatment; deviations would provide the opportunity for a trained operator to detect both problems. Another example of complications with opposing effects on the dialysate absorption curve would be an ultrafiltration-associated decrease in cardiac output and an increase in cardiopulmonary recirculation and hemoconcentration. The limitations of both absorbance- and ionic conductance-based technologies emphasize that they cannot replace traditional measures of clearance and dialysis adequacy.

Lastly, the behavioral benefits of using real-time clearance monitoring are not to be underestimated. Anecdotally, many patients have been convinced to not sign off dialysis early by showing them their clearance curves. This educational tool has led some recalcitrant patients to stay on treatment until the 'blue line hits the red line'; however, this is only a partial solution to the nonadherence wherein ultrafiltration goals may still not be met. High fluid removal volumes will also increase solute removal by convection, so that the adequacy predictions that do not incorporate ultrafiltration will underestimate actual total clearance. The ability of the staff to detect problems in real time, troubleshoot, intervene and thus improve dialysis has important implications for nursing care. Not only is the quality of dialysis care improved, but we believe there is a morale and career satisfaction benefit from enhancing nursing autonomy related to improved clinical outcomes.

In conclusion, continuous dialysate UV absorption–based monitoring of hemodialysis clearance is a very promising technology to achieve and maintain treatment adequacy goals. Real-time intradialysis quality assurance for every session is far superior to the typical monthly assessments. Protocol-driven modifications to treatment parameters are valuable nursing tools for optimizing patient therapy outcomes.

Conflict of interest statement

None declared.

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