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Automated monitoring of hemodialysis adequacy by dialysis machines: potential benefits to patients and cost savings

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Hemodialysis adequacy can be quantified using ultraviolet absorbance of the spent dialysate, or by analysis of dialysate conductivity at the dialyzer inlet and outlet in response to changes in dialysate electrolyte concentration. These measurements can be made at every dialysis, including initial and acute treatments and can help detect access recirculation. No disposables or reagents are required. Cost may be reduced by reducing the need for blood sampling and laboratory analysis.

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In this issue of *Kidney International*, Castellarnau and colleagues[1] describe a method of machine monitoring of hemodialysis adequacy based on analysis of ultraviolet (UV) absorbance of the outflowing dialysate during the dialysis treatment. From this information, the log blood urea nitrogen (BUN) slope can be determined. This slope is the ratio of clearance (K) to urea distribution volume (V). By multiplying session length (t) and adjusting for fluid removal, the ratio of cleared volume to body water (Kt/V) can be estimated. The concept of using dialysate urea analysis[2–8] or UV absorbance[9] to measure adequacy has been described previously (Figure 1).

Certain dialyzable solutes, including uric acid, but not urea, absorb UV.[9,10] The UV absorbance in dialysate can be measured continuously without reagents and so is more suited for integration into a dialysis machine than existing urea sensors. The data of Castellarnau *et al.* suggest that UV absorbance is sufficiently representative of urea concentration that more specific measurement of urea may not be necessary.[1] UV-absorbing solutes are of higher molecular weight (that is, are more slowly dialyzed) than urea, so the method will underestimate urea clearance. Because the UV method detects a range of solutes, it is theoretically susceptible to interfering factors. Larger validation studies in different groups of patients may be needed.

The advantage of this method is that Kt/V is calculated directly from measurements in dialysate, and values for absolute concentrations K and V are not required. A variety of different approaches to estimating urea removal have been proposed, including measurement of urea in recirculating dialysate, which will equilibrate with the concentration in blood.[2]

A disadvantage is that changes in clearance during dialysis due to membrane fouling or changing blood or dialysate flow will disturb the ratio between blood and dialysate concentrations. By integrating the sensor into the dialysis machine, the method of Castellarnau *et al.*[1] has accounted for changes in flow and can include the effect of ultrafiltration. By continuous analysis of the dialysate measurements over time, the post-dialysis rebound may be predicted for calculation of an equilibrated Kt/V. The method also claims to be capable of detecting membrane fouling by detecting unexpected changes in measurements over time, but this probably requires more validation.

Conductivity clearance measurement (CC) is a different approach to machine-monitored hemodialysis adequacy (Figure 2) that has been available in many regions of the world for several years now.[11–13] With CC, the dialysis machine briefly and periodically increases and then reduces the inflowing dialysate conductivity. Mass transfer and clearance can be calculated by analysis of the changes in conductivity at the dialysate inflow and outflow pursuant to these alterations in dialysate electrolyte concentration.[11–13] Because of time delays and the way in which this measurement is performed, CC estimates of dialyzer clearance also

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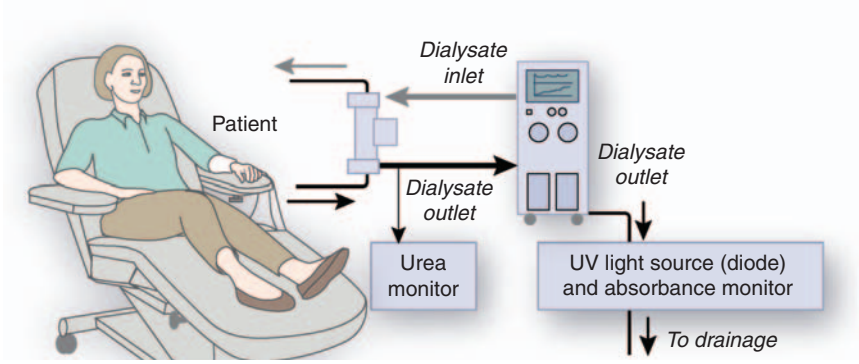

Figure 1 | Schematic showing typical locations for an outflowing dialysate urea monitor or ultraviolet absorbance monitor.

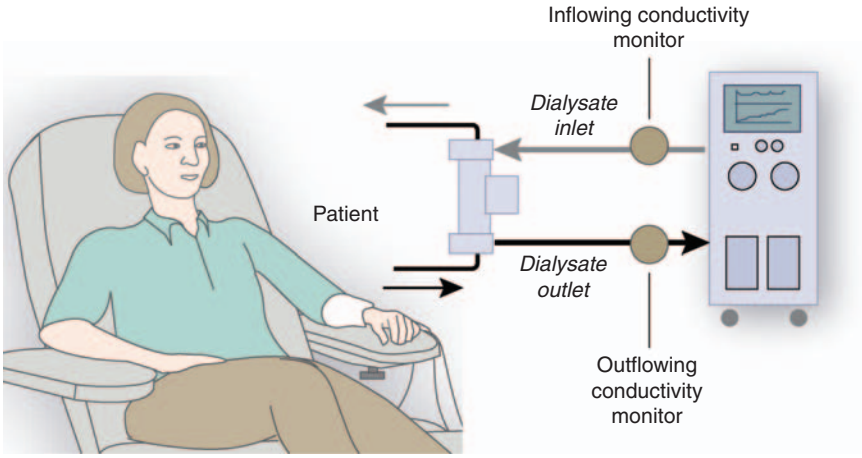

Figure 2 | In the conductivity clearance method, the schematic shows typical locations for conductivity monitors of the inflowing and outflowing dialysate. (The monitors actually are located within the dialysis machine housing.) The conductivity clearance method requires that the machine periodically alter the proportioning of dialysate concentrate with inlet water to change the inflowing dialysate conductivity in a predictable manner.

include the effects of access recirculation if present, and of cardiopulmonary recirculation.[11–13] Unlike the dialysate concentration or UV methods, CC is not able to calculate Kt/V from direct measurement. CC can accurately measure K and t but requires separate measurement and input of the urea distribution volume V in order to calculate Kt/V. The latter can be obtained from a previous urea modeling session in which pre- and post-dialysis BUN values were measured, from bioimpedance, or from an anthropometric estimate of total body water.[14] Each of these methods for calculating V is indirect and prone to error. Conductivity clearance is not the same as urea clearance, though its nature and relationship to urea clearance are well understood.

How can machine monitoring of adequacy be useful? There are several advantages to these techniques.

1. Elimination of pre- and post-dialysis blood urea nitrogen measurements

Dialysis adequacy is usually monitored with the use of monthly pre- and post-dialysis blood samples. These samples require significant resources, including staff time, disposables, logistics, information management, and planning. The sampling may also confer infection risk to the patients and staff, especially if a needle is used. The post-dialysis sample is particularly troublesome, as it has to be paired with the pre-dialysis sample and to be taken at a busy time right at the end of dialysis and by a specific protocol to avoid interference from access recirculation.[15,16]

With the UV method, assuming that validation studies confirm that it reliably reflects urea, there should no longer be any need to measure pre- or post-dialysis blood urea concentrations. As well as calculating Kt/V, the dialysate UV measurements could be used to deduce the urea mass removed, hence the protein catabolic rate (PCR). An accurate value for urea distribution volume (V), for example, using bioimpedance, is required for calculation of normalized protein catabolic rate (nPCR).[5–7]

With CC, pre-dialysis BUN values would still be required, because a BUN value is necessary for the estimation of protein catabolic rate. If V can be measured reliably (for example, by bioimpedance), then the troublesome post-dialysis sample can be avoided. Without a reliable measurement of V, pre- and post-dialysis BUN measurements are still needed to compute V but could be performed at a reduced frequency (for example, three to six monthly).

2. Ensuring that the patient receives the prescribed dose of dialysis each time

Traditional adequacy methods using pre- and post-dialysis blood samples are typically performed monthly under controlled conditions and may not accurately reflect a typical dialysis. There may be a delay of more than a month before an inadequate dialysis is detected and confirmed. With machine-monitored adequacy methods, there is continuous feedback to patients and staff regarding the adequacy of each session. The effects of changes in prescription (for example, reduction of blood flow or time) are immediately apparent. Where K is unavoidably reduced (for example, by access problems), the dialysis can be prolonged until the minimum Kt/V target is delivered.

3. More accurate delivery of a dialysis prescription to new patients

One challenge in providing dialysis to incident patients is that patient urea distribution volume is completely unknown and may differ markedly from anthropometric estimates. K may also be difficult to predict with new vascular access. With dialysate urea or UV monitoring, the delivered Kt/V is displayed as the dialysis progresses, and values for K and V are not needed. With CC, a value for V is still

required, but this can be measured at a convenient time before dialysis (for example, by bioimpedance).

4. Detection of access recirculation

With traditional adequacy methods based on blood samples, access recirculation (AR) is suspected when the urea reduction ratio decreases for no apparent reason in comparison with previous modeled sessions. A more accurate method, taking other factors that may reduce K into account, is to follow changes in V calculated by a urea kinetic model. The model effectively calculates Kt/V directly from pre- and post-dialysis BUN. The actual treatment time (t) and a 'theoretical' value of K, calculated from dialyzer overall mass transfer coefficient (KoA) and blood and dialysate flow rate, are then used to calculate V. Since the model has no knowledge of the actual K, any unexpected fall in measured Kt/V (for example, due to AR) is interpreted by the model as an increase in V. Unexpected increases in calculated V are likely to be caused by AR, especially if V calculated by the model is significantly higher than that calculated from anthropometric data.

With dialysate urea or UV methods, the presence of AR could be deduced by analysis of the way the measurement changes at the start of dialysis. AR causes an abnormally precipitous fall in dialysate urea concentration (and, presumably, UV absorption, though this has not been described in the literature) at the start of dialysis. With CC, actual clearance will be lower than the 'theoretical' clearance when there is AR. AR may be caused by incorrect needle position (for example, arterial needle downstream of the venous needle). This AR could be intermittent, dependent on needling position, and be missed by monthly adequacy measurements. With machine-monitored methods, AR would be detected immediately each time it occurs.

5. Performing quality assurance of reprocessed dialyzers

Reused dialyzers are prone to fiber blockage or membrane fouling, which may reduce clearance. This should be detected and accounted for. When the clearance falls below acceptable levels, the dialyzer is discarded. Measurements of fiber bundle volume are used as an indirect method to detect reductions in dialyzer performance. Monthly adequacy assessment is far too infrequent to reliably detect dialyzer inefficiency, as this can occur suddenly. With machine-monitored methods, dialyzer performance is monitored each treatment in a more direct way and probably more accurately than by fiber bundle volume.

In conclusion, machine monitoring of hemodialysis adequacy using UV, dialysate urea, or CC methods should translate into substantial benefits to patient care and, depending on acquisition and maintenance costs, may also result in considerable cost savings. Conductivity clearance is a well-validated method for assessing dialysis adequacy but does not completely remove the need for BUN measurement. UV has potential advantages over conductivity clearance (including the ability to avoid input of V, and omit BUN measurement altogether) but needs more validation study. Actually, both dialysate urea analysis and CC can be combined to obtain reliable estimates of both pre- and post-dialysis BUN[8] in addition to the standard measures of dialysis adequacy.

Given that guidelines lag behind published literature, and that government-mandated quality assurance measures lag behind guidelines, it is important that early adopters of these new technologies undertake, and publish as rapidly as possible, quality assurance studies comparing use of machine-monitored adequacy with pre- and post-dialysis BUN approaches, focusing on monitoring of changes in Kt/V, nPCR, AR, and performance of reused dialyzers. Current Kidney Disease Outcomes Quality Initiative[15] guidelines mandate that adequacy be assessed at least monthly, by pre- and post-dialysis blood samples. The European Best Practice Guidelines allow for the use of alternative methods of adequacy assessment such as online clearance, as long as the method has been validated and referenced to urea kinetic modeling, but no specific alternative method is endorsed.[16] One would anticipate that the next iteration of dialysis adequacy guidelines will be able to endorse the use of machine monitoring of adequacy as an alternative to the older BUN-based techniques.

DISCLOSURE

All the authors declared no competing interests.

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