Dual-wavelength method and optoelectronic sensor for online monitoring of the efficiency of dialysis treatment

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Abstract. The absorption spectra of effluent dialysate in the ultraviolet region were investigated. A novel dual-wavelength spectrophotometric method for uric acid determination in effluent dialysate and an optoelectronic sensor based on UV LED were developed. Clinical trials of the proposed sensor were carried out in the dialysis unit of St. Petersburg Mariinsky Hospital. The relative error of measurement for the concentration of uric acid does not exceed 10%.

1. Introduction

Hemodialysis (HD) is an extracorporeal method of blood purification by means of a dialysis machine for patients suffering from renal failure. During this life-supporting medical procedure low molecular weight waste products of metabolism and excessive water are removed from patient’s blood circulating through a dialyzer to dialysis fluid (dialysate) via semi-permeable membranes. HD treatment is carried out 3 times a week; every session lasts 3-5 hours. The adequacy (efficiency) of HD treatment is usually estimated by taking blood samples before and after an HD session for laboratory analysis. The concentrations of uremic markers (urea, creatinine, uric acid etc.) in these sampled are measured and so-called dialysis indexes are calculated using special formulae. To make HD more safe and efficient it is necessary to control the concentrations of uremic markers in patients’ blood or effluent dialysate online by means of special HD monitoring systems.

Three types of such devices have been developed and partly introduced to clinical practice: electrochemical sensors for urea monitoring, conductometric systems (ionic dialysance sensors) and optical spectral systems, which measure the spectral transmittance of effluent dialysate in the ultraviolet (UV) region at one or more wavelengths [1-4]. Spectral systems have some advantages over other devices including the possibility to measure the concentrations of several substances simultaneously without having to use any disposables or chemical reagents. In recent years, deep UV light-emitting diodes (LEDs) which are based on aluminum-gallium nitride AlGaN have been developed. These LEDs can emit optical radiation in the spectral range of 240 ... 350 nm, which allows creating compact and low-cost optoelectronic spectral sensors for HD monitoring instead of using large and expensive UV spectrophotometers.

2. Experiment

Previous experimental studies of the UV absorption spectra of spent dialysate have proved the validity of optical spectrophotometry based methods for online HD monitoring [2-3]. However, additional
research work is required to make possible the quantitative control of uremic toxins using UV spectrophotometry.

The maximum of spectral absorption of urea lies at the wavelengths shorter than 200 nm (the spectral region that is not accessible by conventional equipment); the absorption maxima of uric acid (UA) are located at the wavelengths 238 and 293 nm, creatinine - 217 and 234 nm. Therefore UA and creatinine were chosen as marker substances for HD monitoring by optical spectral methods.

Comprehensive analysis of the profiles of the absorption spectra of the dialysate samples from the large group of patients (more than 300) revealed that using of the single wavelength of 293 nm for quantitative analysis of UA in dialysate (so-called single wavelength method) leads to significant errors, since at this wavelength not only UA make significant contribution to dialysate absorption but also other substances. Therefore it is necessary to introduce additional working wavelengths and to evaluate the contribution of other components.

Depending on the character of the UV absorption curve in the region of 260 ... 290 nm the spectra of spent dialysate can be classified into three types (Fig.1): type «A» – absorption spectra that have the maximum at 290 nm (~ 15% of total patients); type «B» - spectra that have “plateau” without distinct maxima (~ 70% of the total number of patients); type «C» - spectra with a slope in the mentioned range (~ 15% of total patients). It should be noted that the profile of dialysate absorption curve for each patient remained virtually unchanged throughout the whole period of the study (more than two years).

Further researches showed that in the wavelength range of 260 ... 290 nm the spectral absorption of dialysate is dominated by UA and the set of identified and unidentified components, which include tryptophan, hippuric acid, pseudouridine, adenosine and other substances associated apparently with individual metabolic processes [5]. The individual concentration of every such component is low, but their combination, conventionally called pseudocomponent (pseudo-NK), determines the characteristic shapes of absorption curves. Spectral analysis in the wavelength range 260 ... 320 nm of dialysis fluid samples taken from patients assigned to different types, and simultaneous biochemical tests made it possible to find the profile of the absorption spectrum for the pseudo-NK which can be used for UA quantitative determination during HD online monitoring.

3. Results
The results of experimental studies and mathematical modeling of spent dialysate absorption spectra in the range of 260...350 nm showed:

- The spectral absorbance of dialysate in 285...295 nm is mainly due to UA;
At shorter wavelengths absorption is due to both UA and pseudo-NK. The region of 260 ... 270 nm is optimal for estimating the absorption of pseudo-NK, where the absorption of UA is minimal.

A novel dual-wavelength spectrophotometric method for UA determination in effluent dialysate and an optoelectronic sensor based on UV LED were developed [6].

The mathematical basis of the method is the law of Bouguer-Lambert for the two-component medium:

\[
k_{\lambda_1} = e_{\lambda_1}^{UrAc} \cdot C^{UrAc} + e_{\lambda_1}^{NK} \cdot C^{NK}
\]

\[
k_{\lambda_2} = e_{\lambda_2}^{UrAc} \cdot C^{UrAc} + e_{\lambda_2}^{NK} \cdot C^{NK}
\]

where \(k_{\lambda_1}\) and \(k_{\lambda_2}\) – absorption coefficients at the respective wavelengths \(\lambda_1\) and \(\lambda_2\), \(e_{\lambda_1}^{UrAc}\) and \(e_{\lambda_2}^{UrAc}\) – molar spectral absorption coefficients of UA at the respective wavelengths \(\lambda_1\) and \(\lambda_2\), \(e_{\lambda_1}^{NK}\) and \(e_{\lambda_2}^{NK}\) – molar spectral absorption coefficients of pseudo-NK at the respective wavelengths \(\lambda_1\) and \(\lambda_2\).

In solving a system of equations (1) for the \(C^{UrAc}\) we find the concentration of UA by the values of the absorption coefficients at wavelengths \(\lambda_1\) and \(\lambda_2\):

\[
C^{UrAc} = \frac{e_{\lambda_2}^{NK} k_{\lambda_1} - e_{\lambda_1}^{NK} k_{\lambda_2}}{e_{\lambda_1}^{UrAc} e_{\lambda_2}^{NK} - e_{\lambda_1}^{NK} e_{\lambda_2}^{UrAc}}
\]

The proposed method is implemented as a compact optical sensor using UV LEDs at the wavelengths 262 and 287 nm, which was designed and manufactured by LDIAMON AS (Tartu, Estonia) in collaboration with Saint-Petersburg Electrotechnical University (Saint-Petersburg, Russia).

The sensor allows measuring the time profiles of UA concentration with extremely high temporal resolution (down to 5 sec).

Clinical trials of the proposed sensor carried out in the dialysis unit of St. Petersburg Mariinsky Hospital. The time profiles of UA concentration were measured for the group of 10 patients with the help of the sensor. The shapes of the absorption spectra of the patients’ dialysate belong to different
types of classification proposed earlier. For validation the samples of effluent dialysate were taken at 0, 30, 60, 150 and 240 min of HD and lab tests for UA were carried out.

The time profiles of effluent dialysate spectral transmittance in two narrow spectral ranges (262 nm and 287 nm) for one of the patients are presented in Fig. 2. Fig. 3 shows the time profiles of UA concentration in effluent dialysate and results of the lab tests for UA. It should be noted that, the sensor allows early detecting of adverse events during HD (see Fig.3 at the middle of the HD session).

4. Conclusion
Clinical trials of the developed sensor were carried out in the dialysis unit of St. Petersburg Mariinsky Hospital. The results of spectral measurements are presented as time profiles of dialysate spectral transmission at two wavelengths and UA concentration in the course of a HD session. The relative error of measurement for the concentration does not exceed 10% (for more than 100 samples).

The correlation coefficient between the UA concentrations is 0.987, standard error of estimate is 4.4 umol/l. The sensor allows early detecting of adverse events during HD.

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