Three-wavelength optoelectronic system for hemodialysis monitoring

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Abstract. Novel spectrophotometric method and optoelectronic spectral equipment for automatic on-line monitoring of hemodialysis treatment are introduced. The method allows determination of the concentrations of uric acid and creatinine in effluent dialysate by measuring ultraviolet (UV) absorption at three wavelengths. An optoelectronic spectral sensor with three deep ultraviolet light emitting diodes (LED), a flow-through quartz cuvette connected to the outlet of a dialysis machine, and a solar-blind UV photodetector was designed. Dedicated software for sensor control, spectral data acquisition, and spectral analysis was developed. The results of preliminary clinical trials of the developed system are presented.

1. Introduction

Hemodialysis (HD) is a life-supporting extracorporeal medical treatment for patients with chronic renal failure (CRF). This procedure helps to eliminate from patient’s body low molecular weight metabolic wastes and excessive water which otherwise are excreted with urine. HD is based on diffusive and convective transfer of small molecules from blood to dialysis fluid (dialysate) via a semi-permeable membrane. Technically HD is realized by means of a dialysis machine – very sophisticated piece of medical equipment which includes a dialyzer with a semi-permeable dialysis membrane, hydraulic elements for pumping blood and dialysis fluids through the dialyzer, the mixing system for preparing fresh dialysate from purified water and concentrate, multiple sensors (pressure, temperature, conductivity, bubbles etc.), and a built-in computer (figure 1).

Usually HD treatment is carried out three times a week and each session lasts 3-5 hours depending on the clinical status of a particular patient. In clinical practice the adequacy (efficiency) of the treatment is estimated using so-called dialysis indexes such as kt/V which indicate the amount of a particular waste substance eliminated during the HD session related to the total amount of this substance in patient’s biological fluids. Such substances are called uremic markers; the most known are urea, creatinine, uric acid, and β-2-microglobuline. To measure dialysis indexes blood samples are taken before and after the treatment, then concentrations of the marker substances are determined in a clinical laboratory by standard biochemical methods; after that dialysis indexes are calculated from the results of the blood tests using special equations or dedicated medical software [1].

Conventional methods for estimation of HD adequacy are expensive, time-consuming and labor-intensive so such clinical tests are usually carried out only once a month or even every three months. Meanwhile it has been noted before that the most representative information about HD treatment could
be obtained by on-line monitoring of uremic markers concentration in effluent dialysate [2]. Different methods of HD monitoring have been developed including electrochemical cells, conductometric and viscosimetric systems. However there are difficulties with implementation of such systems into clinical practice because most of them are based on indirect measurements (conductometric systems) or require disposable materials and high-cost equipment (electrochemical cells).

Optical methods of HD monitoring are based on continuous (on-line) measurement of effluent dialysate spectral transmittance in the UV region, where most of the waste products selectively absorb light [3]. The fact that uric acid and creatinine have the strongest UV absorption among other uremic markers makes them the most suitable for this purpose [4]. It should be noted that urea has little or no absorption for wavelengths longer than 200 nm so it is not possible to monitor urea concentration in dialysate by optical methods despite some earlier reports. There have been attempts to use UV spectrophotometers for HD monitoring but they are too expensive and impractical for hospital conditions [3, 4].

The most cheap and reliable alternative to spectrophotometers is optical spectral sensors with deep UV LEDs [5]. Single-wavelength optical monitoring at 280 nm was introduced in some dialysis machines but they only provide information about overall concentration of waste products in effluent dialysate; the main drawback of these devices is that they do not allow quantitative determination of any individual uremic markers [6]. As further development of this approach the dual-wavelengths technique and optical sensor for uric acid determination was created [7]. It proved to be accurate and reliable but unfortunately uric acid is less clinically significant than other uremic markers such as urea and creatinine.

In this work we introduce novel spectrophotometric method and three-wavelength optoelectronic spectral sensor for automatic on-line monitoring of creatinine concentration in effluent dialysate. In our opinion it could be the next step in the development of optical sensors for HD monitoring.

2. Spectrophotometric method for determination of uric acid and creatinine in effluent dialysate

Direct spectrophotometric method for uric acid and creatinine quantitative determination in effluent dialysate was developed. The assumption was made that dialysate can be considered as three component fluid which contains uric acid (absorption maxima are at 234 nm and 287 nm), creatinine (absorption maximum is at 234 nm) and a pseudocomponent that accounts for all other substances with relatively minor UV absorbance (absorption maximum is at 262 nm). Absorption spectra of the pseudocomponent were found by mathematical modelling using absorption spectra of dialysate samples taken from large group of patients in combination with the results of laboratory analysis. Accordingly three narrow spectral bands were chosen as analytical – 237...247 nm, 260...270 nm and 285...295 nm. The first analytical band (for the 234 nm creatinine and uric acid maximum) was shifted to the longer wavelengths due to two reasons: there are no commercially available LEDs for 234 nm and dialysate absorption at 234 nm is too high for registration in the cuvette with reasonable optical thickness.

Uric acid and creatinine concentration can be relatively easily calculated from spectral absorbance in these three working wavelength regions by solving a system of linear equations. More detailed information about the developed method and mathematical algorithms used for analysis of spectral data can be found elsewhere.

3. Three-wavelength spectral sensor for HD monitoring

The spectrophotometric method was realized in the three-wavelength optoelectronic sensor which can automatically measure spectral absorbance of effluent dialysate in three narrow spectral bands near 247 nm, 262 nm, and 287 nm (figure 1). The sensor consists of three deep UV LEDs in a single package with integrated focusing lens (SETi, Inc), the flow-through quartz cuvette with 3 mm optical thickness connected to the outlet of a dialysis machine, the solar-blind photodetector and corresponding electronics which connects the sensor to a computer via USB interface (figure 2). The LEDs emission spectra are quite narrow (FWHM is about 10...12 nm) so no additional
monochromatization with interferential filters was needed, which makes such sensors very simple and inexpensive.

The UV LEDs are powered by phase shifted pulse current with a period of several hundred milliseconds in such a way that they are switched on and off sequentially and only single light source emitting in one of the three narrow spectral bands is active at a given time point. Output signals of the photodetector when irradiated at all working wavelengths and dark signal are measured continuously; up to 100 samples of both light and dark levels have to be recorded and averaged to achieve photometric accuracy 0.01 Abs and signal-to-noise ratio 200:1.

Reference signal (100% transmission) is measured before the beginning of a dialysis treatment when fresh dialysate is being circulated within the dialysis line of a machine. Because for obvious reasons reference signal cannot be re-measured during a HD session the second photodiode is installed in the vicinity of the LED in front of the cuvette to monitor any fluctuations of incident UV radiation and adjust the output signal correspondingly.

The sensor was designed and manufactured by AS Ldiamond (Tartu, Estonia).

![Normalized emission spectra of UV LEDs](image)

**Figure 1.** Normalized emission spectra of UV LEDs (LED1 – 247 nm, LED2 – 262 nm, LED3 – 287 nm).

Dedicated software HDMonitor was developed for device control, setting measuring parameters, spectral data acquisition, calculating uric acid and creatinine concentrations, and presenting the results of the monitoring in the form of diagrams. It provides simple and convenient for medical staff user interface.
4. Results of preliminary clinical trials

Preliminary clinical trials of the system were carried out in HD unit of Mariinsky City Hospital (Saint-Petersburg, Russia). The sensor was connected to BBraun Dialog dialysis machines; a regular laptop PC with HDMonitor software was used for sensor control and data acquisition via USB 2.0 interface. Measurements were done for 25 HD sessions and 10 patients; for each session a report file which contains patient’s personal data, treatment parameters, effluent dialysate optical transmission at the working wavelengths, and calculated concentrations of uric acid and creatinine was created and saved on the laptop hard disk in ASCII format. The time profiles of uric acid and creatinine concentrations in the course of a dialysis session for one of the patients measured using the sensor are presented on figure 3 and figure 4 respectively.

For validation purpose the samples of effluent dialysate were taken from the outlet of a dialysis machine for laboratory analysis several times during five random HD treatments: at the very beginning, when the concentrations of uric acid and creatinine were at their maxima, and afterwards at 30, 60, 150 and 240 min. Automatic analyzer “Beckman Coulter AU680” was used; because the special analytical protocol for dialysate was not available the protocol for blood plasma was utilized.

The results of the monitoring in comparison with laboratory data are presented on figure 5 and figure 6 for uric acid and creatinine respectively. Statistical analysis using Bland-Altman method [8] showed a good agreement between the results obtained with the sensor and with the automated biochemical analyzer “Beckman Coulter AU680”; the relative error of determination was less than 10% for uric acid and less than 20% for creatinine.
Figure 3. The time profile of uric acid concentration in effluent dialysate measured using the sensor and the results of the lab tests for one of the patients.

Figure 4. The time profile of creatinine concentration in effluent dialysate measured using the sensor and the results of the lab tests for one of the patients.
Figure 5. The scatter diagram for uric acid concentration in the effluent dialysate samples measured with the optical sensor and with the automated biochemical analyzer “Beckman Coulter AU680.

Figure 6. The scatter diagram for creatinine concentration in the effluent dialysate samples measured with the optical sensor and with the automated biochemical analyzer “Beckman Coulter AU680.

5. Conclusion
The presented spectrophotometric method and UV LED based optical sensor proved to be simple, safe, comparatively low-cost and very effective for on-line monitoring of uric acid and creatinine concentrations in effluent dialysate during HD treatment. For uric acid the relative error of
concentration measurement is quite low (less than 10%) and does not exceed the error of routine biochemical laboratory tests which is fully acceptable for clinical use; for creatinine the error is higher (up to 20%) and additional researches are needed to improve the accuracy of the method.

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