DOI: 10.15825/1995-1191-2019-4-41-44

CONVECTION FLOW OPTIMIZATION IN ONLINE HEMODIAFILTRATION

A.G. Strokov, I.L. Poz

Shumakov National Medical Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation

Objective: to evaluate the dependence of the magnitude of convection flow in online hemodiafiltration (OLHDF) on ultrafiltration control method and patients' individual characteristics. **Materials and methods.** The study included 36 stable dialysis patients (20 male and 16 female). The substitution rate was conducted manually based on transmembrane pressure (TMP). In some cases, devices with automatic filtration rate control unit AutoSub *plus* were used. The filtration rate (FR), TMP, blood flow rate (Qb), specific filtration rate (SFR, ml/min/mm Hg^{-1}) were recorded. **Results.** The maximum SFR in various patients ranged from 0.51 to 0.80 ml/min/mm Hg^{-1}; average value was 0.62 ± 0.07 ml/min/mm Hg^{-1}. There was significant correlation of SFR with hemoglobin level ($r = -0.55$). SFR reduced during hemodiafiltration (on average – by $23 \pm 4\%$). SFR was significantly affected by Qb ($r = 0.70$). Maximum SFR was achieved with a TMP of 140–220 mm Hg; with TMP over 250 mm Hg, a decrease in SFR was noted, an increase in Qb was required for further increase in FR. Individual stability of SFR was noted during serial observations; fluctuations in a particular patient did not exceed 10%. Substitution volume for the HDF session was 18.0 ± 3.3 L, the FR/Qb ratio was $24.7 \pm 5.2\%$. Substitution volume of 21 L was not achieved in 17 of 36 patients. The use of automatic FR adjustment system made it possible to increase the substitution volume (SV) by 12–18%. **Conclusion.** Achieving maximum convection volume in OLHDF requires individualizing treatment parameters. The use of FR automatic control allows maximum possible convection flow.

Keywords: online hemodiafiltration, specific filtration rate, substitution volume.

Online hemodiafiltration (OL-HDF) is a technique incorporating all modern technological achievements. It is mostly considered as the gold standard in renal replacement therapy requiring hemodialysis [1]. The main advantage of OL-HDF from the point of view of a more complete correction of uremia is the possibility of active transmembrane transfer of substances with significant molecular weight when creating high-speed filtration flow of water molecules from the blood circuit to the dialysate circuit. With a known membrane and a known high sieving coefficient with respect to the substance, the filtration volume achieved during treatment session can be considered a surrogate indicator of treatment efficacy with respect to elimination of this substance [2]. Thus, modern dialysis membranes used in OL-HDF have a sieving coefficient for β2-microglobulin (11,800 Da) of at least 0.6. The assumption that more significant elimination of medium- and high-molecular-weight uremic substances should have a positive effect on the outcomes of long-term hemodialysis has been confirmed in recent studies. It was demonstrated that higher survival rates are achieved with high filtration volume – over 20 liters per treatment session [3]. In real clinical practice, ensuring such high ultrafiltration rate is often fraught with several difficulties caused by both the parameters of the procedure and the patient's features [4].

The objective of this study is to evaluate the dependence of convection flow on ultrafiltration adjustment method and on patients' individual characteristics.

PATIENTS AND RESEARCH METHODS

The study included 36 patients (20 men and 16 women) aged 21 to 82 (59.6 years average). The subjects were treated with programmed hemodialysis for at least 6 months. Vascular access was achieved through arteriovenous fistula or vascular prosthesis in 29 patients, and through tunneled dual-lumen catheters in 7 patients. Four-hour OL-HDF sessions were performed on Fresenius 4008 and 5008 devices and FX60 and FX80 hemodiafilters (Fresenius Medical Care, Germany) at a fixed dialysis fluid flow rate of 500 mL/min and there was post-dilution introduction of substitution fluid. The substitution rate was controlled in manual mode based on TMP indicators. Here, FR, TMP and actual Qb were recorded. During treatment sessions, we also investigated the SFR corresponding to the filtration flow value (FR, mL/min) and the actual transmembrane pressure (TMP, mmHg). In some cases, automatic dialysate flow control systems with 1.5 coefficient with respect to Qb and automatic FR adjustment unit AutoSub plus were used. AutoSub plus was based on constant measurement of pressure pulsation in the air trap of the venous line, as

Corresponding author: Poz Iakov L'vovich. Address: 1, Shchukinskaya str., Moscow, 123182, Russian Federation.
Tel. (499) 158-22-33. E-mail: dr.poz@list.ru

part of Fresenius 5008 dialysis machines. The data was statistically processed using a Microsoft Office Excel spreadsheet.

RESULTS AND DISCUSSION

With fixed duration (4 hours) of therapy session and average Qb = 322.5 ± 27.1 mL/min, maximum SFR for different patients ranged from 0.51–0.80 mL/min/mmHg^{-1}, the average value was 0.62 ± 0.07 mL/min/mmHg^{-1}. There was significant correlation of SFR with hemoglobin level (r = –0.55). There was no dependence of SFR on proteinemia, albuminemia, glycemia and total cholesterol levels. During treatment sessions, decreased SFR (on average by 23 ± 4%) was observed. This can be explained both by systemic blood concentration amidst decreased volume of circulating blood and by compaction of secondary protein membrane on the surface of the dialysis membrane. The secondary protein membrane is actively formed precisely at high filtration rate [2]. Among the parameters of the procedure, the value of SFR was significantly influenced by Qb (r = 0.70).

Maximum SFR values were achieved in TMP 140–220 mm Hg. Further increase in filtration rate, and accordingly, TMP value, led to exponential decrease in SFR value (see figure).

With TMP >250 mm Hg, a fall in SFR levels became especially noticeable and subsequent increase in FR often led to alarming levels of TMP. In such situation, increasing Qb was required to restore FR.

During serial observations, individual SFR stability was noted, session-to-session fluctuations in a particular patient did not exceed 10%. Average substitution volume per HDF session was 18.0 ± 3.3 L, while filtration fraction (FR/Qb ratio) was 24.7 ± 5.2%. In 17 of the 36 patients, substitution volume 21 L was not achieved during HDF. This observation was primarily due to the fact that in this group of patients, there were no reserves for increasing the blood flow rate. Use of automatic FR adjustment system based on blood viscosity measurement allowed increasing the total convection volume by 12–18%, while SFR was not observed below 0.4 and no TMP alarms were noted. At the same time, in 4 out of the 12 patients who used this system, the threshold substitution volume for treatment session was not achieved because Qb could not be increased.

According to current research, the substitution volume achieved during HDF session is a key factor in improving the final outcomes of program dialysis [2]. At present, the threshold value is 21 L without taking into account the ultrafiltration volume aimed at eliminating interdialytic hyperhydration [3]. In routine clinical practice, achieving such high FR requires intense treatment regimens, including creating a high transmembrane pressure gradient [4]. It is known that HDF with high TMP values increases the number of alarms requiring the intervention of medical staff [5]. In addition, in this situation, the sieving of high molecular weight substances, including albumin, significantly increases [6]. Although several authors consider albumin elimination as a positive factor contributing to removal of protein-bound uremic toxins [7], significant albumin loss can reduce plasma albumin concentration. SFR and TMP levels help in evaluating convection flow intensity. With these two indicators, excessive hemoconcentration in the extracorporeal circuit and significant albumin sieving are avoided. Increasing blood flow rate is the main reserve to ensuring adequate (or maximum for a given patient and given duration of HDF session) substitution volume without resorting to extreme filtration regimes and, accordingly, significant drop in SFR. Clear, meaningful management of FR is becoming increasingly important, given the permanent tendency towards increase in hydraulic permeability and sieving coefficients of high molecular weight membranes used in wide clinical practice. In this regard, improvement and widespread introduction of automatic substitution rate control systems that increase the volume achieved during a therapy session, and also provide stable procedure requiring no human intervention, seems a promising approach.

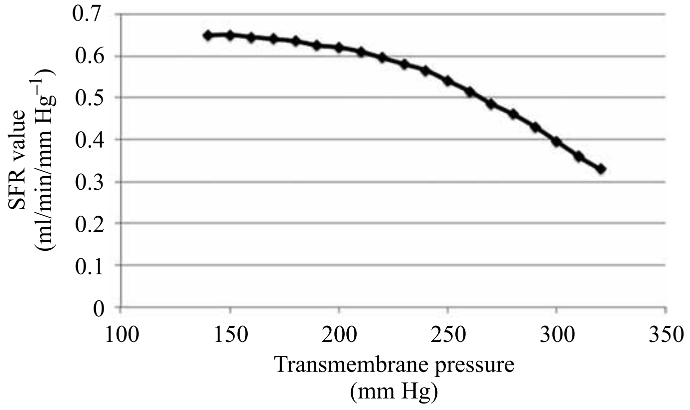

Fig. SFR dependence on TMP during OL-HDF session with progressive increase in FR

CONCLUSION

Achieving maximum convection volume in HDF requires individualizing treatment prescription. At the same time, it is optimal that filtration is done in the most efficient rank of transmembrane pressure of up to 250 mmHg. The main limitation in total substitution volume in HDF is the inability to ensure adequate blood flow rate.

With modern automatic filtration rate control systems, maximum possible convection flow is provided in specific conditions in real time without episodes of excessively high TMP and extracorporeal blood flow stops.

Identifying the substitution volumes required for patients of different sexes and ages with various anthropometric and clinical data, as well as the effect of intense filtration regimes on treatment outcomes, require further investigation.

The authors declare no conflict of interest.

REFERENCES

1. *Mostovaya IM, Blankestijn PJ, Bots ML, Covic A, Davenport A, Grooteman MP. et al.* EUDIAL1 – an official ERA-EDTA Working Group. Clinical evidence on hemodiafiltration: a systematic review and a meta-analysis. *Semin Dial*. 2014; 27: 119–127. doi: 10.1111/sdi.12200.
2. *Tattersall JE, Ward RA.* EUDIAL group. Online haemodiafiltration: definition, dose quantification and safety revisited. *Nephrol Dial Transplant.* 2013; 28: 542–550. doi: 10.1093/ndt/gfs530.
3. *Maduell F, Moreso F, Pons M, Ramos R, Mora-Macià J, Carreras J. et al.* ESHOL Study Group. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. *J Am Soc Nephrol*. 2013; 24: 487–497. doi: 10.1681/ASN.2012080875.
4. *Kim YW, Park S.* Confronting practical problems for initiation of on-line hemodiafiltration therapy. *Electrolyte Blood Press*. 2016; 14: 1–4. 10.5049/EBP.2016.14.1.1.
5. *Gayrard N, Ficheux A, Duranton F, Guzman C, Szwarc I, Vetromile F et al.* Consequences of increasing convection onto patient care and protein removal in hemodialysis. *PLoS One.* 2017; 12 (2): e0171179. doi: 10.1371/journal. pone.0171179.
6. *Fournier A, Birmele B, Francois M, Prat L, Halimi JM.* Factors associated with albumin loss in post-dilution hemodiafiltration. *Int J Artif Organs*. 2015; 38: 76–82. doi: 10.5301/ijao.5000389.
7. *Nagai K, Tsuchida K, Ishihara N, Minagawa N, Ichien G, Yamada S. et al.* Implications of albumin leakage for survival in maintenance hemodialysis patients: a 7-year observational study. *Ther Apher Dial*. 2017; 21: 378–386. doi: 10.1111/1744-9987.12526.

The article was submitted to the journal on 4.10.2019