On-line haemodiafiltration: state of the art

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Abstract. Faced with the shortcomings of conventional dialysis on a long-term basis, as illustrated by the dialysis-related pathology, a need for a new strategy exists to improve the overall quality of treatment in end-stage renal failure (ESRF) patients. On-line haemodiafiltration (HDF) seems to be the best therapeutic option to achieve this goal at the present time. By enhancing convective clearances through highly permeable membranes, HDF offers the greatest solute fluxes both for low and higher molecular weight uraemic toxins. As for example, in our routinely performed HDF programme based on 3 weekly sessions lasting 3–4 h each, double-pool urea Kt/V achieved was 1.55 ± 0.20 and β2-microglobulin Kt/V was 0.91. By producing substitution fluid from fresh dialysate, the technique of HDF is simplified and becomes economically affordable. By improving the haemodynamic tolerance, HDF allows more elderly and high risk cardiovascular patients to be treated more safely. By using bicarbonate-buffered infusate, HDF facilitates the correction of acidosis. Both by using ultrapure bicarbonate dialysate and down-regulating the membrane reactivity via a ‘protein cake’, HDF introduces the first step for a full haemocompatibility concept. Finally, by giving access to virtually unlimited amounts of sterile and non-pyrogenic fluid, HDF should introduce new therapeutic options such as a totally automated and feed-back-controlled machine. Today’s on-line HDF is already a step forward to enhance the overall efficacy of renal replacement therapy and to improve the global care of ESRF patients.

Key words: end-stage renal failure; on-line haemodiafiltration; renal replacement therapy; dialysis

Introduction: rationale for on-line haemodiafiltration

Renal replacement therapy (RRT) by dialysis has become, over the last three decades, a fully accepted and routinely performed treatment modality for end-stage renal failure (ESRF) patients. Long-term dialysis is a basic therapeutic option in the armamentarium of the nephrologist: in many instances, it is by necessity an alternative to renal transplant. On the other hand, it must be remembered that any dialysis modality, regardless of performance and efficacy, will only partially and periodically restore the composition of the internal milieu of the ESRF patient. Despite such a limitation, RRT is presently supporting the life of about one million patients worldwide.

The success of dialysis as a long-term treatment is weighted by the increasingly reported incidence of dialysis-specific morbidity. Dialysis-related pathology (DRP), including β2-microglobulin (β2M) amyloidosis, accelerated atherosclerosis, hypertrophic cardiomyopathy, aortic stenosis and nutrition, is prevalent after 10 years on RRT. Obviously, DRP marks the boundary limits for long-term RRT by dialysis. Taking a simplistic approach, one might speculate that DRP has multiple causes belonging to several categories with possible overlap. These categories can be identified as follows: the low overall efficiency of any intermittent RRT option when compared with native kidneys; the lack of selectivity in solute removal capacity, with a particularly low capacity in removing high molecular weight substances; the relative shortfall in correcting metabolic abnormalities due to the complexity of the internal milieu and the patient–dialysis interaction; and the haemobiologic incompatibility of the dialysis system resulting in the periodic activation of proinflammatory proteins and cell systems.

In as much as nephrologists are concerned both with survival and quality of life of ESRF patients, they must acknowledge that conventional dialysis is not satisfactory for RRT on a long-term basis (more than a few years). Clearly, a need exists to improve the overall quality of treatment in ESRF patients. Fifteen years ago, following the pioneering studies on haemodiafiltration (HDF) [1–3], we hypothesized that on-line HDF was the best therapeutic option to achieve this goal.

By enhancing convective clearances through a highly permeable membrane, HDF offered the highest solute fluxes per membrane surface area both for low and higher molecular weight solutes [4]. By producing substitution fluid from fresh dialysate via ultrafilters and a
cold sterilizing process as proposed by Henderson [5], the technique of HDF was simplified and became economically affordable [6]. The instantaneous and permanent ‘on-line’ production of infusate not requiring storage was an efficient approach to prevent bacterial contamination and growth. Following this rationale, we developed simplified equipment specially designed for the routine use of on-line HDF. The aim of this report is to propose standards of good medical practice for on-line HDF, to summarize our clinical experience with this technique and to look at its future.

Technical prerequisite and hygiene handling

The safety of on-line HDF relies on strict and permanent conditions of use and handling. Compliance with these guidelines is the only way to prevent adverse effects and to warrant the highest probability for success with this RRT option.

The use of ultrapure water (UPW) to feed HDF machines is a basic and common requirement for on-line HDF [7]. Several studies have provided useful information and updated our knowledge concerning the water treatment system required [8]. UPW is a high grade quality water which has been developed mainly to satisfy the needs of the semiconductor industry. In this definition, a strong emphasis was given to a greater chemical purity expressed in terms of water resistivity $\geq 5$ MOhms/cm and more stringent requirements concerning the degree of bacterial contamination, with $<100$ c.f.u./l, and undetectable levels of polysaccharides. For HDF purposes, UPW refers to (RO)-treated water (one or two stages of RO in series) with a resistivity in the range of 0.1–0.5 MOhms/cm, and a very low level of bacterial and endotoxin contamination [e.g. $\leq 100$ c.f.u./l, undetectable levels of endotoxin with Limulus amoebocyte lysate (LAL) assay]. The production and distribution of UPW to HDF machines may be achieved with several water treatment options. Distribution pipes must be adequately designed to prevent stagnation and to eliminate dead arms and other recontamination sites. Permanent recirculation of treated water through a closed loop circuit with a microfiltration process is required when a buffer tank is used. Such a water treatment system is particularly suitable for a hospital-based dialysis unit. A typical example of a water treatment system used in our unit to produce UPW for on-line HDF is presented in Figure 1. Ultrapurity of water produced and delivered to HDF machines has been obtained for >10 years with this configuration. A summary of the microbiology of water for dialysate is presented in Figure 2.

The use of a specifically designed HDF machine is necessary for safety reasons. In this case, dialysate filter units (ultrafilters or microfilters) incorporated into the hydraulic circuit of the machine are disinfected with each disinfection procedure. Moreover, a recent model of an HDF machine (4008D, Fresenius AG, Bad Homburg, Germany) includes a pressure test (bubble point) that is performed automatically by the HDF machine to check the integrity of ultrafilter membranes. The infusate module consists of an adjustable pump running up to 200 ml/min, with a counter calculating the total amount of fluid infused to the patient. The safety of the infusate module is linked to the general alarms of the HDF monitoring system. Fresenius 2008–4008 machines have been used in our unit to drive our HDF programme. An on-line HDF machine based on 2008C–4008E machines is represented schematically in Figure 3. In such a configuration, a fraction of fresh dialysate (100/600 ml/min) produced by the proportioning system is diverted by the infusion pump and infused to the venous bubble trap of the patient (post-dilutional HDF) after three-stage filtration. Ultrapure dialysate flowing into the dialysate compartment of the haemodiafilter is produced from an ultrafilter ($UF_1$) placed just at the exit site of the dialysate [9,10]. Ultrapurity of the infusate is secured by a two-stage filtration, firstly through an ultrafilter ($UF_2$) and secondly through a disc microfilter (0.45 $\mu$m) before infusion to the patient. In this configuration, infusate flow diverted from the inlet dialysate is compensated by an equivalent ultrafiltration flow taken from the patient through the haemodiafilter with the fluid balancing chamber. Ultrafilters and tubing sets are considered as part of the hydraulic circuit of the HDF machine, kept and used for 2–3 months according to the number of sessions performed monthly.

On-line cold sterilization of biological fluids is based on a membrane filtration process (ultrafilter). However, it is important to remember that the retentive capacity of an ultrafilter is restricted to certain conditions of use [11,12]. The titre of reduction achieved with microbiological contaminants present in the inlet solution is an index of efficacy. A sterilizing filter may be able to reduce by 6 log the number of colonies of an incoming contaminated solution. However, the endotoxin removal capacity of an ultrafilter is dependent on several factors: (i) the nature and permeability of its membrane; (ii) the conditions of use including the time of exposure; and (iii) the amount of endotoxin challenging the filter. In this respect, an interesting study shows that different brands of polysulfone (PS) challenged with steadily increasing endotoxin concentrations have different retentive capacities. Two different brands of PS were studied: a leakage appeared soon after starting the challenge test with PS-B while nothing passed through PS-A up to very high endotoxin concentrations [13]. The retentive capacity of a single ultrafilter was maintained over time up to 7 days in a continuous high concentration endotoxin challenge [14]. For the sake of safety, ultrafilters installed on the HDF machine should be changed every 2–3 months according to the number of sessions performed and the quantity of dialysate produced. The use of UPW and sterile electrolyte concentrates, and frequent disinfection of the HDF machine to reduce bacterial contamination are basic requirements to prevent ultrafilter bacterial overflow.
Hygiene handling is the most crucial measure to ensure permanent safety of the HDF system. Measures needed to maintain the bacterial contamination at a low level have two targets: one is to maintain the ultrapurity of water feeding the HDF machines by means of frequent disinfection of the water treatment system, destruction of biofilm by chemical agents, change of filters and disposable tubings at regular intervals and by permanent recirculation of UPW in the distribution system (hydraulic loop); the other is to prevent recontamination and bacterial proliferation in the HDF machine by means of frequent disinfection, use of sterile liquid concentrate or powder and periodic changes of ultrafilters. In our unit, water treatment system disinfection is performed weekly using a peracetic acid-based solution (Dialox, Air Liquide, Paris-F) with a dual bactericidal and cleansing activity. Bacteriological filters installed at the head of the recirculation loop which ensure the final sterility of treated water should be replaced every 6 months. HDF machines are disinfected after each run with a rapid and long-acting bactericidal agent (Dialox). HDF machines are also maintained using the same agent at an appropriate concentration during the non-functioning periods of the machine (night-time, days off). Ultrafilters and infusate tubing sets should be changed every 2 months.

Frequent quality monitoring of the dialysate and the infusate is mandatory to detect early microbiological contamination of the system. A microbiological inventory of water, dialysate and infusate is performed regularly by a pharmacist member of our group. The sampling method, culture media and delay for observation have been validated and published elsewhere [15, 16]. Membrane filtration and culture on a poor nutrient media (R2A) has been our standard for 5 years. Cultures are kept at room temperature and observed daily for 7 days, and a bacteria colony count is performed at 7 days. Bacteria are identified by appropriate methods. The endotoxin content (infusate and dialysate) is assayed using the kinetic LAL assay dilution with a threshold detection limit of 0.005 EU/ml.

Extremely high sensitivity methods based on blood monocyte activation and cytokine-inducing activity which can detect non-endotoxin substances have been described [17]. However, because of their complexity and in the absence of clinical relevance in the presence of sterile dialysate, these were not performed in our unit. The patient’s body temperature should be checked before and after each HDF session: usually no temperature change is observed. If pyrogenic reactions occur during the post-HDF period, they should be reported to the dialysis team. Any fever occurring during or immediately after a HDF session should raise serious doubts about the sterility of the infusate preparation and distribution system: it should trigger a careful microbiological, re-evaluation of the system to detect bacterial contamination and to eradicate its cause.

All information concerning the microbiological monitoring must be recorded in order to confirm a posteriori the quality of treatment delivered to the patient. Such rules must be considered as a part of the good medical practices for on-line HDF.

**HDF: treatment schedule and patient indication**

To illustrate our experience, we will focus on 56 ESRF patients (34 males, 22 females, age 62 ± 15 years)
regularly treated by on-line HDF for at least 12 months. On-line HDF was performed in two different units under the same conditions and with the same follow-up. The dialysis schedule consists of 3 weekly sessions lasting 3–4 h each (9–12 h/week) according to metabolic needs and cardiovascular stability. The mean time spent on RRT at the time of this study was $22 \pm 28$ months (1–31 months). Two patients had a residual glomerular filtration rate of 0.5 ml/min.

No selection for patients was done. Underlying nephropathies were as follows: chronic glomerulonephritis in 22 patients (45%), hypertension or nephroangiosclerosis in 13 patients (23%), autosomal polycystic kidney disease in six patients (11%), diabetes mellitus in three patients (5%) and miscellaneous including unknown in 12 patients (21%).

Thirty patients (64%) had native fistula, 10 (18%) had PTFE graft, the last 10 patients (18%) had double-lumen permanent catheters (TwinCath). The mean dry weight of these patients was $62.7 \pm 11.9$ kg. Two needles (15 gauge) were used to puncture the AV fistula or graft. Blood flow prescribed was set to $300–400$ ml/min.

General anticoagulation was obtained by means of unfractionated heparin with an i.v. bolus and maintenance continuous i.v. infusion.

On-line HDF was performed using specially equipped Fresenius 2008–4008 machines. Haemodiafilters were HF80s (Fresenius, 1.8 m², high-flux PS membrane), steam sterilized. Until January 1995, haemodiafilters were reconditioned automatically on a Renatron machine using a peracetic acid solution and reused up to 13 times. Single use of HF80s has been performed for the last 2 years.

Effective HDF operational conditions delivered to patients were checked monthly during a HDF test session. Blood flow was $361 \pm 29$ ml/min. HDF session duration was $206 \pm 26$ min, global recirculation was $11 \pm 4\%$ and total dialysate flow spent was $650 \pm 25$ ml/min. According to the fraction of the fresh dialysate diverted to produce infusate (100 ml/min, 6 l/h), the net dialysate flow through the haemodiafilter was $500–550$ ml/min. The net ultrafiltration rate required to control the extracellular fluid volume was $2.4 \pm 0.7$ l/session while the total amount of fluid exchanged was $23–27$ l per session.

**HDF: efficacy and ‘dialysis dose’ delivered in clinical practice**

HDF efficacy relied on treatment schedule, effective operational conditions and patient characteristics. Short-term treatment adequacy was evaluated according to conventional clinical and biochemical criteria. The clinical status of patients was assessed at each dialysis session by a physician. Standard chemistries and haematology were performed monthly at mid-week with pre- and post-HDF blood samples. Chest and bone X-ray, and ultrasound cardiography were performed at least once a year.

Dialysis quantification using urea and creatinine...
kinetic modelling was performed monthly at mid-week using a complete dialysis cycle as pre-/post-HDF samples and prior to the next session. Instantaneous body clearances for urea and creatinine were evaluated 1 h after the start of dialysis. The precision of solute mass transfer occurring in the dialyser relied on a blood–dialysate solute mass balance. For urea, the dialysis period was used to calculate Kt/Vdp (double-pool) while the inter-dialytic period was used to calculate the protein catabolic rate (nPCR) [18].

‘Dialysis dose’ evaluated using a double-pool equivalent model was 1.55 ± 0.27, and the solute removal index was 73 ± 3%. The percentage reductions of urea, creatinine and phosphorus were 78 ± 4%, 72 ± 4% and 59 ± 8% respectively. Urea TAC and creatinine TAC were 13.6 ± 4.0 mmol/l and 521 ± 136 μmol/l respectively. As shown in Figure 4, Kt/Vdp remains very stable with time over a 2 year follow-up. In summary, on-line HDF delivered, in a relatively short treatment time, a high dialysis dose which has been suggested as a factor minimizing morbidity and mortality in ESRF patients [19–21].

The nPCR normalized to dry weight obtained from the urea generation rate was 1.12 ± 0.25 g/kg/day. The creatinine index and lean body mass/dry weight ratio calculated from the creatinine generation rate were 19.9 ± 5.5 mg/kg/day and 0.75 ± 0.13 respectively.

Because of its clinical relevance, β2M (11.8 kDa) removal was studied particularly. The percentage reduction of β2M achieved in our patients was 78 ± 2%, corresponding to a β2M Kt/V of 0.91. The β2M time-averaged concentration was maintained at 17.2 ± 7.5 mg/l, a value lower than the β2M serum concentration reported in continuous ambulatory peritoneal dialysis (CAPD) patients and considered at reduced risk [22].

The spectrum of uraemic toxins include higher molecular weight substances which must be cleared during RRT [23,24]. Solute markers of various molecular weights are used to evaluate the clearance capacity of any dialysis modality. All studies comparing high-flux haemodialysis with HDF have confirmed the greater capacity of convective-based methods to remove medium or high molecular weight substances [25,26].

More recently, it has been speculated that advanced glycosylated end-products (AGEs) [27,28] and advanced oxidized protein products (AOPP) [29] may constitute a novel class of uraemic toxins with direct implications on long-term DRP. Interestingly, recent studies have indicated that high-flux HDF with a PS Superflux dialyser was the only method capable of removing AGEs (mol wt 15 kDa) in a significant amount [30]. This confirms the major importance of convective fluxes in removing high molecular weight and long-lasting uraemic toxins. If confirmed by further studies, such facts would be of a major clinical importance in reducing the risk of vascular diseases in ESRF patients.

**HDF: metabolic control and internal milieu correction**

Bicarbonate-buffered infusate facilitates the correction of acidosis [31]. Direct i.v. infusion added to the bicarbonate dialysance of the haemodiafilter occurring in the dialyser increases the bicarbonate mass delivered to the patient. Bicarbonate kinetics show that blood titration is much faster during on-line HDF. Bicarbonate serum concentration increases in a logarithmic fashion, reaching a plateau close to the dialysate concentration within 3–4 h, according to body weight. It is also of interest to mention that after 6–9 months of regular on-line HDF treatment, bicarbonate concentration in the dialysate had to be reduced (35 vs

![Fig. 4. Two year follow-up of urea Kt/Vdp in a group of 56 patients regularly treated by HDF.](image-url)
39 mmol/l) to prevent occurrence of post-dialysis metabolic alkalosis. Alkalotic progression usually observed in the post-HDF period seems to be associated with the large amount of bicarbonate infused during the HDF session responsible for a bicarbonate flux overflow. Another explanation could be the delayed metabolism of the acetate (4 mmol/l) transferred during the session from the dialysate and infusate. Bicarbonate concentrations from the arterial side of the AV fistula were 22.8 ± 4.3 and 29.9 ± 2.3 mmol/l in the pre- and post-HDF session respectively.

Phosphate mass removal per HDF session was 30 ± 7 (12–60) mmol/session. The percentage reduction of phosphate per session was 53%. Mean concentrations of phosphate were 1.63 ± 0.25 and 0.75 ± 0.25 mmol/l in pre- and post-HDF respectively. Calcium carbonate was used in all patients as phosphate binder and prescribed at a dose of 2.5 ± 0.5 g/day.

The calcium content in the infusate contributes to the calcium load achieved in an HDF session. When calcium salts are used regularly as phosphate binders, it seems advisable to reduce the calcium concentration of the dialysate. In our unit, the calcium dialysate concentration was reduced progressively. Over time, 1.5 mmol/l has become the new standard for the dialysate calcium concentration in our on-line HDF programme. Occasionally, in cases of hypercalcaemia, induced by calcium salts used as phosphate binders, alfacalcidol prescription or both, the dialysate calcium concentration had to be reduced to 1.25 mmol/l for a short period of time. On average, blood calcium concentration increased from 2.36 ± 0.12 to 2.63 ± 0.16 mmol/l during an HDF session.

Anaemia correction was performed to achieve a target haematocrit of 33%. The mean haematocrit obtained was 32.6 ± 4.1%, while recombinant human erythropoietin was used in 50% of the HDF population.

Extracellular volume control was easily achieved in all patients. Net ultrafiltration per session was 2.4 ± 0.7 l. Arterial pressure control was satisfactory for the whole group. The mean arterial pressure was 98.5 ± 11.6 and 89.5 ± 10.9 mmHg in the pre- and post-HDF period respectively, but 12/56 (21%) patients used antihypertensive drugs to achieve this goal.

Haemodynamic tolerance was excellent. In a 1 year survey, the incidence of symptomatic hypotension and/or related symptoms was 2%, while the frequency of nurse intervention for any reason was 12%. In a previous prospective and comparative study involving elderly and cardiac high-risk cardiovascular patients, it has been shown that arterial pressure was better preserved in HDF than in high-flux haemodialysis despite a more important net ultrafiltration. Apart from bicarbonate-buffered dialysate/infusate, several factors may contribute specifically to the haemodynamic stability usually associated with HDF [32,33] and more generally with convective methods [34]. Among them are the cooling effect of the infusate due to the calorie loss in the circuit, the high sodium concentration achieved in the venous return line due to the direct infusion of the substitution fluid [35], the high fluxes of calcium that may contribute to increase the cardiac output and the vascular resistance, the low bioreactivity of the HDF system preventing release of vasodilating agents and lastly the removal by convection of nitric oxide synthase inhibitors [36]. From a mechanistic point of view, one can speculate that HDF acts in several ways: it increases the peripheral vascular resistance and facilitates the vascular refilling in enhancing fluid recruitment from the interstitial space while preserving the ejection fraction. Further studies are required to elucidate the beneficial effect of HDF on cardiovascular stability.

HDF: full haemocompatibility concept

To our present knowledge, on-line HDF provides the most haemocompatible system for RRT. UPW used on a long-term basis has been shown to reduce the risk of carpal tunnel syndrome independently of the type of the dialyser [37]. The long-term use of AN69 membranes used for high-flux haemodialysis and HDF reduces the blood–membrane interaction. Use of highly permeable membranes (AN69) has been associated with a reduced risk of incidence of amyloidosis [38]. A high ultrafiltration rate concentrating proteins onto the membrane [39], inducing the formation of a 'protein cake' called the 'second layer', would add two more beneficial effects: one is to 'passivate' the artificial membrane [40]; the other is to prevent back-diffusion (Figure 5) of dialysate contaminants [41]. The pressure profile achieved in the filter cell (Figure 5) with HDF is the best way of preventing dialysate back-filtration [42,43]. Ultrapure dialysate flowing in the haemodilution suppresses the potentiating effect of dialysate contaminants on blood monocyte activation. On-line HDF limits the patient–dialysis system interaction to the contact of blood with the arterial and venous tubing of the extracorporeal circuit. It provides the first approach to reach the full haemocompatibility concept.

HDF: microbiological safety

Cold sterilization of dialysate by ultrafiltration was first introduced by Henderson. Since then, several studies have confirmed the efficacy and reliability of the sterilizing filtration process [44,45]. Challenge tests performed with bacteria and endotoxin in controlled conditions have shown the high retentive capacity of ultrafilters [46]. However, it should be borne in mind that an ultrafilter acts only as a sieve, with some limits of efficacy. To reduce the risk of failure (bacteria or pyrogen overflow, leakage) it has been suggested to proceed by a two-stage filtration process. The cold sterilization concept has been extended to on-line production of i.v. quality fluid used in several therapeutic options: home haemodialysis [47], haemofiltration [48] and HDF. On-line production of sterile and
non-pyrogenic fluid precludes fluid storage thus eliminating the risk of bacterial growth after contamination due to fluid stagnation in a container [49].

On-line HDF used for > 10 years by our group has been proved to be safe and reliable provided that the technical requisites are satisfied [50,51]. To illustrate the safety aspect of on-line HDF, we selected microbiological data collected during 1996. During this period, 8600 HDF sessions were performed. The body temperature of patients was 36.5 ± 0.3 and 36.6 ± 0.3 °C during the pre- and post-HDF session respectively. No pyrogenic reaction (temperature > 38 °C not explained by any type of infection) was observed during this period in spite of the large amount of fluid infused to our patients. These data contrast with the incidence of pyrogenic reactions observed in the US dialysis population among patients treated with high-flux haemodialysis and a dialysate of poor microbiological quality [52]. Dialysate and infusate contamination are summarized in Figures 2 and 6 respectively. Due to the low contamination of our fluid, the bacteria count is expressed in terms of c.f.u. per litre. Endotoxin detection by the LAL assay remained negative in most infusate samples; eventually, a few samples had detectable endotoxin remaining in the very low range of 0.05 EU/ml.

**HDF: new perspectives for RRT**

On-line production of i.v. fluid from dialysate gives access to virtually unlimited amounts of sterile and non-pyrogenic fluid. The consequences of this technological advance for the future of RRT are economic, technical and legal.

From an economic point of view, using the infusate instead of pharmaceutical saline to prime, rinse or compensate patient hypotension, will reduce significantly the overall cost of haemodialysis; producing large amounts of substitution fluid for HDF or haemofiltration is the only viable way to maintain these methods. Regarding the technical aspects, on-line production
incorporated into the machine reduces the complexity of HDF machines and facilitates the task for the nursing staff; access to i.v. quality fluid will permit in the near future compensation of hypovolaemia and hypotension directly from on-line substitution fluid, either manually or automatically (feedback loop for volaemia control); daily home haemodialysis, an emerging RRT modality, should benefit from an on-line system permitting a totally automated machine ensuring the rinsing, priming and reconditioning of the dialyser.

From a legal perspective, taking into account the availability and reliability of today’s ultrafilters and microfilters, cold sterilization should be acknowledged by the Pharmacopoeia as a safe procedure for the instantaneous production of sterile non-pyrogenic i.v. solutions that should not be stored. The validation of cold sterilization procedures should be facilitated by the fact that hidden infusion of dialysis fluid is also an obligatory phenomenon due to back-filtration during high-flux haemodialysis with highly permeable membranes [41]. Finally, the safety and reliability of the method should be validated on a large scale through a permanent survey using an on-line HDF vigilance registry.

Conclusions

On-line high-flux HDF offers, at the present time, the most effective RRT for ESRF patients [53,54]. High-flux HDF allows delivery of a high ‘dialysis dose’ in a relatively short treatment time based on the conventional urea marker. By enhancing the contribution of convective fluxes, HDF also enlarges the spectrum of uraemic toxins cleared. HDF has the lowest haemoreactivity profile of any RRT option. On-line production of substitution fluid reduces the cost of treatment and simplifies the technical aspects of the method. In addition, by giving access to an unlimited amount of high quality i.v. fluid, the on-line HDF concept opens up new therapeutic perspectives including more automation. Such specific properties should place the on-line HDF in a leading position among the ESRF therapeutic options to enhance the overall efficacy of RRT and to improve the global care of ESRF patients [55].

References