Chapter 8
Online Hemodiafiltration by Fresenius Medical Care

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Abstract Hemodiafiltration has been identified by Fresenius Medical Care (FMC) as a vital need to improve care and outcome of chronic kidney disease patients. By enhancing the removal of middle molecular uremic toxins and improving hemodynamic and global tolerance of dialysis sessions, HDF was recognized as an efficient dialysis modality and a mean to improve patient treatment perception and reduce disease burden. By providing fluid substitution online, HDF appeared the only economically and technically long-term viable solution. Online HDF therapy has been a major R&D focus for FMC over the last decades leading to the development of several online HDF machines with different features.

Keywords AutoSub Plus • Disinfection • High volume HDF • Online hemodiafiltration • Predilution • Postdilution • Substitution fluid • Transmembrane pressure

Introduction

Hemodiafiltration has been identified by Fresenius Medical Care (FMC) as a vital need to improve care and outcome of chronic kidney disease patients [1]. By enhancing the removal of middle molecular uremic toxins and improving hemodynamic

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and global tolerance of dialysis sessions, HDF was recognized as an efficient dialysis modality and a mean to improve patient treatment perception and reduce disease burden. By providing fluid substitution online, HDF appeared the only economically and technically long-term viable solution [2]. Online HDF therapy has been a major R&D focus for FMC over the last decades leading to the development of several online HDF machines with different features [3], see Fig. 8.1.

Water Treatment System Required

The water treatment system for hemodialysis and hemodiafiltration shall be designed on knowledge of the feed water characteristics. This system should ensure a water quality at the dialysis machine inlet complying to applicable national standards, as well as the international ISO 13959 standard (Water for haemodialysis and related therapies). Concentrates must meet the requirements of ISO 13958 (Concentrates for haemodialysis and related therapies), and the produced dialysis fluid those of the ISO 11663 standard (Quality of dialysis fluid for haemodialysis and related therapies).

Fig. 8.1 HDF machine

Short Description and Outline of the HDF Machine

Touch screen is ensuring a user-friendly interface and displaying useful information (technical, therapeutical) user specific; a hydraulic circuit designed to produce electrolytic dialysis and substitution fluids in compliance with technical requirements and medical prescription; blood and hydraulic (dialysate and infusion) circuits activated by adjustable pumps and secured by appropriate sensors. In addition, the dialysate circuit includes a volumetric balance chamber.

State of the art HDF technology benefits from a hydraulic branch delivering online prepared substitution fluid. Drawn from fresh dialysis fluid by utilization of a specially designed ultrafilter, substitution fluid is filter-sterilized and depyrogenated. Since the substitution is a fraction of the dialysate fluid pathway, the patients' fluid balance is assured in hydraulics using a volumetric balance chamber, which was a standard in Fresenius dialysis machines from the beginning. All fluid pathways are tested against fluid leakages before and disinfected after the treatment. Technical features of the 5008 dialysis machine are summarized in Table 8.1.

HDF Prescription Modality (Manual/Automatic)

Considering that blood flow, treatment time and weight loss are set according to medical treatment, HDF prescription may be performed in manual or automatic mode [4]. In *manual mode*, the user deselects the "AutoSub plus" function (5008 machines) and sets the substitution pump to the desired flow. In *automatic mode*, the user selects the substitution mode (post, pre or mixed) depending on the HDF machine type, and the monitor will run automatically the session targeting to adjust substitution volume while keeping transmembrane pressure in a safe range. The substitution flow rate is adjusted automatically in consideration of blood viscosity, membrane size and fiber geometry, see snapshot of screen in Fig. 8.2. The Fresenius 5008 dialysis machine, equipped with 'AutoSub plus' allows to maximize HDF substitution volumes without treatment discontinuation by hemoconcentration-related alarms [5]. A dialyzer stress test by permanent analysis of static and dynamic pressures using extracorporeal and hydraulic sensors optimizes infusion rate for each patient individually.

Consequently, high volume HDF is feasible in routine clinical practice [6]. By running HDF machine in 'AutoSub plus' mode, filtration fraction can be increased up to 30–35 % and total substitution volume by 13–20 % in post dilution mode [7].

HDF Modalities

Post and predilution modalities can be run indifferently on the same HDF machine equipped with two pumps (for blood flow, and for substitution flow). Mixed-dilution modality requires a specific three pumps HDF machine (for blood flow, postdilution

Table 8.1 Technical features of the 5008 online HDF machine

Technical features	5008 online HDF (Fresenius)
Blood pump flow range (ml/min)	30–600 ml/min
Dialysate flow (ml/min)	0; 100–1000 ml/min
Dialysate flow selection mode	Manual; eco-flow; auto flow
Emergency button	Yes
Substitution mode: manual/automatic	Manual or automatic (AutoSub plus)
Settable parameter(s) in volume control mode	Substitution rate (ml/min); target substitution volume (L)
Substitution fluid flow range	0–200 ml/min (0–1.2 L/h)
Electrolyte concentration adjustment	Pre-selected concentrates of Na and HCO3 in mmol/L
Substitution fluid delivery options	Predilution, postdilution, mixed dilution
Online priming, rinsing, IV bolus	Yes
Stationary ultrafilters	Yes, 2, Diasafe and online filter
Additional ultrafilter	No
Integrity pressure test ultrafilter	Yes
Blood access monitoring	Yes
Online clearance monitoring	Yes (OCM)
Blood volume monitoring (BVM)	Yes, optional
Blood temperature monitoring	Yes, optional
Other monitoring options	Yes, BVM, BTM, OCM
Alarm and information signals	Yes, blood circuit leakage, pressure alarms, dialysate composition, pressure test failure
IT connectivity	Yes,
Data transfer via patient card	TDMS
Standard safety features	Yes, complying to international standards
Advanced safety features	Yes, early detection of bleeding by dynamic pressure monitoring (DPM), leakage sensors on hydraulic circuit; optional: vascular access monitoring dislodgement (VAM)
Touchscreen operation and ergonomic design	Yes
Special features	Feedback controlled BVM/BTM

and predilution). Management of flow pumps is ensured by pressure sensors (prefilter, venous, hydraulic), integrated microprocessors and proprietary software that track continuously substitution flow and TMP and react in adjusting pre and postdilution flows to keep TMP in safe range [8].

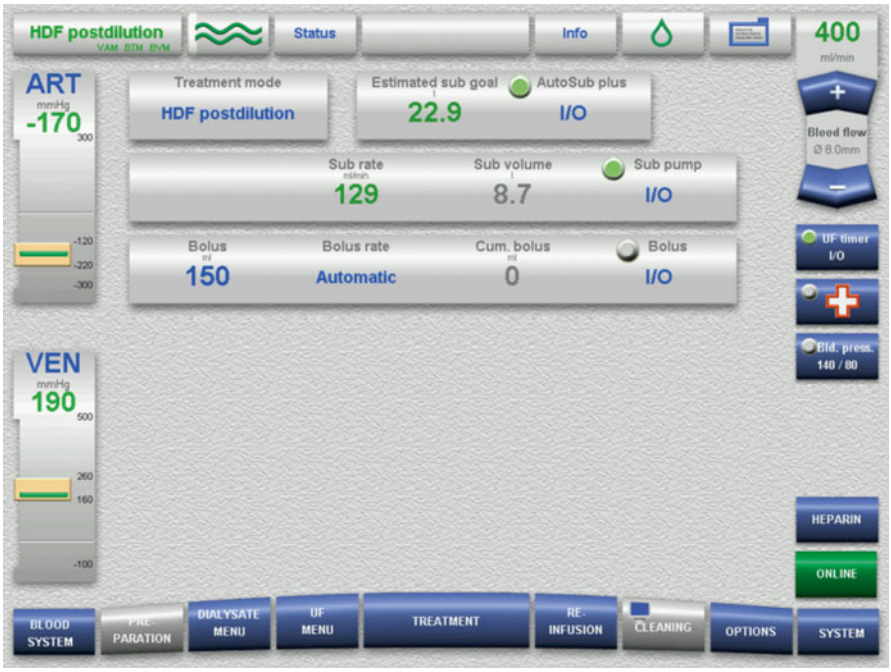

Fig. 8.2 Snapshot of screen I

Specificities of Disposables Required

Hemodiafilters are typically not captive of the blood tubing set. All high-flux hemodialyzers, validated for online-HDF, can be used on FMC machines. It is mandatory to assess clinically the currently used hemodiafilter to ensure that performance (ultrafiltration and solutes clearance) and albumin loss are in the targeted range and conform to manufacturer description. Fresenius FX/F hemodiafilters have been tested and validated for this application [5, 9–11].

Specifically designed and featured with membrane characteristics that ensure sterile filtration of dialysis and substitution fluids, are proprietary and captive of HDF machines. Two such ultrafilters are inherent to the HDF machine, the first (Diasafe) is placed on the inlet dialysis fluid circuit and the second (Online Filter) is placed on the substitution circuit. The Diasafe filter is flushed regularly during the treatment. The Online filter operates in cross-flow mode. The membranes' integrity, qualified for 100 consecutive treatments, is assessed by a pressure holding test prior to dialysis [4].

Additional Therapeutic Options

Several additional technical features are basic or optional part of Fresenius HDF machines.

- Blood temperature monitoring (BTM) (option) may be used for controlling thermal balance of dialysis patient (isothermic, cooling) and reducing hemodynamic instability (reducing intradialytic hypotensive episodes), and can be used to measure blood access recirculation [4].
- Blood volume monitoring (BVM) (option) is used to assess blood volume reduction induced by ultrafiltration. BVM relies on an ultrasound sensor coupled to the arterial blood tubing set that measures hematocrit associated blood density changes. This measurement of relative blood volume changes during HDF provides a tool to estimate blood volume refilling capacity and a patient threshold limit for ultrafiltration [12].

Additional Monitoring Options

- To determine ionic dialysance after modulation of electrolyte concentration, online clearance measurement (OCM) is intermittently applied and the clearance or dose is displayed throughout the session, see Fig. 8.3. OCM provides

Fig. 8.3 Snapshot of screen 2

quite reliable values reflecting urea clearance, and is used as surrogate of dialysis dose delivered. It has been validated in online HDF with large substitution volumes [12].
- Feedback controlled BVM may facilitate treatment of hypotensive prone patients. The relative blood volume change is tracked during the session, and based on threshold limit set by the user, the algorithm of the HDF machine reacts in adjustment of ultrafiltration according to the refilling capacity of the patient [13].

Cleaning and Disinfection

Several disinfection procedures have been validated and released for Fresenius HDF dialysis machines, e.g. Citrosteril™ heat disinfection or Puristeril™ cold disinfection.

Risk Management System

Safety Features

HDF machines are equipped with all safety devices required by standards to ensure maximum safety to patients and staff. The online substitution supply system in FMC Online HDF dialysis machines benefits from a redundant safety setup. In the unlikely case of a leaking ultrafilter during treatment the concomitant filter still ensures sterility.

Display of Settings and Connection to Hospital Information System

The Fresenius Therapy and Data Management System (TDMS) consist of a set of applications linked to the dialysis machine network providing pre-setting of therapeutic parameter and treatment documentation. Data management associated with the HDF therapy is supported by TDMS.

Cost Assessment

Cost of HDF treatment relies on three main components: (1) Online HDF machine and technical feature options; (2) Disposable tubing sets and sterilizing ultrafilters; (3) Microbiological monitoring of water and dialysis fluid [14]. Points 1 and 2 will not be disclosed here since they are country specific and market related. Point 3 is

certainly the more sensitive one. In Fresenius HDF machine, blood tubing and substitution tubing lines are presented as single use disposable and proprietary sets. No additional and final sterilizing filter is required on the substitution line. The two sterilizing ultrafilters have to be replaced after 100 treatments or every 3 months. This cost benefit has been recently confirmed in an independent study showing that extra cost per treatment session was the lowest (−1.29 €) among assessed HDF therapies [15].

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