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Adopting On-Line Hemodiafiltration as Standard Therapy in EMEA NephroCare Centers

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Abstract

This paper describes the historical journey that led to the adoption of on-line hemodiafiltration (HDF) as a standard therapy for the patients in the Fresenius Medical Care (FME) NephroCare dialysis network. In 1998, FME faced the tremendous challenge of consolidating a series of heterogeneous clinics under one umbrella. In 2002, the European Best Practice Guidelines (EBPG) for hemodialysis (HD) were published by the European Renal Association which FME promptly adopted within its clinic network. On the basis of this document, the strategic decision was taken to apply high-flux, biocompatible membranes throughout the entire network. To cope with the effective implementation of this step, the clinics' technical infrastructure was updated. The widespread application of high-flux therapy, together with the implementation of the required infrastructure, especially concerning water quality, opened the way to the extensive use of on-line HDF. To fully realize this ambitious goal, two further technological steps were targeted and successfully reached: introduction of the Fresenius 5008 dialysis equipment and an even stricter control of the water quality. The combined pressure from the educational activities, which brought about a preliminary cultural change, and the creation of a target based on the percentage of treatments by this technique resulted in an increasing implementation of this modality by the individual clinics. After 2004, on-line HDF continuously increased its share among the dialysis techniques prescribed in the network and currently more than 50% of patients are on this modality.

When in 1996 the dialysis division of Fresenius, then a product company, merged with National Medical Care, the leading dialysis service provider in the USA, Fresenius Medical Care (FME) was created. Thereafter, FME became a

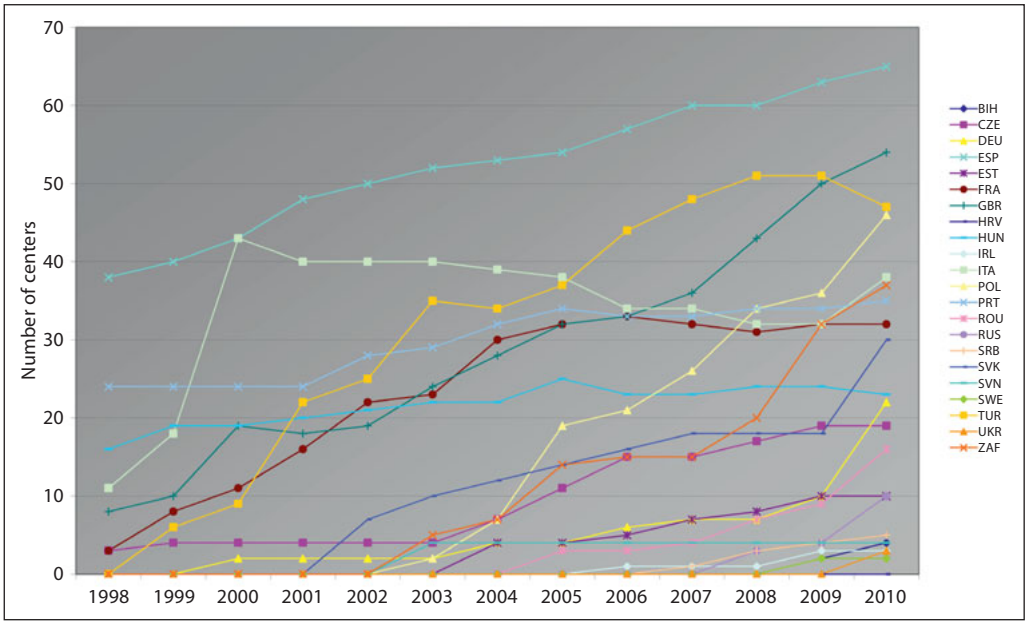

Fig. 1. Development of dialysis centers in the NephroCare EMEA Network from 1998 to 2010.

world player in the provision of dialysis services. In Europe, the new company started dialysis service activity with a group of about 100 National Medical Care clinics that were principally located in Portugal and Spain. Ever since then, FME has been expanding its presence in Europe and beyond, quickly creating a major global dialysis network through new acquisitions, construction of de novo clinics, clinic privatization and participation in public tenders [1] (fig. 1). Currently, the FME dialysis network of the region Europe, Middle East and Africa (EMEA) – nowadays represented by name NephroCare – comprises over 550 clinics in 23 countries, and treats more than 44,000 patients.

This paper describes the historical journey of FME that led to the adoption of on-line hemodiafiltration (HDF) as a standard therapy for the patients in its NephroCare network.

Setting Standards

Naturally, the move to becoming a global dialysis provider resulted in a change of focus for FME. It was obvious from the beginning of this new activity that the company's vision had to be adapted to recognize the significance of the patient in his/her central role as being the most valuable asset [1]. This meant a

fundamental change in company philosophy from a product-centric organization to a patient-centric one. This realization led to a new mission that is still valid today: ensuring all patients in all clinics of the network the delivery of dialysis treatments that result in the best clinical outcome possible, while continuously improving the patients' quality of life.

Up to the merger, the non-US based clinics were managed directly from the headquarters of National Medical Care. After the merger, FME faced the tremendous challenge of consolidating a series of heterogeneous clinics under one umbrella. The diversity between the clinics in terms of treatment modalities, quality of service and technical infrastructure soon made an organizational split between the US domestic market and the market of EMEA necessary. Most of these inter-facility differences originated from the beliefs and convictions of the original founders of the individually acquired units and from challenging constraints, mainly of economical nature, of the national and even local healthcare systems. One example is the practice of dialyzer reuse, which was still common in Portugal at the time of the merger. Consequently, a dedicated department was created in Europe to meet these challenges – Clinical Management Europe (CME).

CME started its activities in 1998 and was responsible for the coordination of all activities in the steadily growing network from a clinical point of view and for the entire EMEA region. This responsibility ranged from clinical governance to technical coordination as well as the allocation of training resources and provision of guidance from a corporate perspective. After having stopped the reuse practice in all NephroCare clinics, the next milestone was to organize the collection of patient data in each center in order to facilitate analysis of treatment modalities and evaluation of outcomes. This was initially done by manual monthly data collection via Excel sheets where information about numbers of prevalent patients, patient movements, changes of treatment, outcomes, etc. were collected and reported. The data collection would not have been possible without the tremendous support from the staff in the centers. In the following step, FME developed a specific clinical database in 1999 called EuCliD (European Clinical Database) to collage the key medical information on the treatment of dialysis patients [2]. EuCliD soon became an essential component of the Continuous Quality Improvement program of FME. It is a multi-lingual and fully codified software applying international standard coding tables (ICD 10, ISCED, national pharmaceutical data bases, etc.) and contains sensitive patient medical data while simultaneously ensuring strict data confidentiality.

In 1993, the first clinical guideline in the field of dialysis was issued by the US Renal Physicians Association [3]. The Dialysis Outcomes Quality Initiative (DOQI) guidelines followed in 1997 [4–7]. Following the American example, several European national bodies – for example, the European Dialysis and Transplantation Association (EDTA) [8], the British Renal Association [9], and the Società Italiana di Nefrologia [10] – prepared their own guidelines adapted to European or national conditions. However, it soon became obvious that the

mere availability of guidelines was not sufficient to ensure quality. Guidelines needed to be implemented and their application continuously monitored in order to guarantee that a high quality of care is delivered to the patients. In 2002, the European Best Practice Guidelines (EBPG) for hemodialysis (HD) were published by the European Renal Association [11]. Subsequently, FME decided to officially adopt this set of guidelines within its clinic network.

The implementation of Clinical Practice Guidelines was accompanied by the rolling out of supporting programs, namely the Clinical Performance Measures, the Patients' Safety Initiatives and the Continuous Quality Improvement programs. All of these initiatives in the network took advantage of the previously developed computerized monitoring system EuCliD [12]. In fact, since the beginning, EuCliD allowed the verification of the success of all quality-related activities within the FME dialysis clinics by comparison of the results with internal and external benchmarks.

Focus on High-Flux Dialysis

FME aimed, on the basis of the EBPG, to create a common strategic treatment platform targeting improved patient outcomes in terms of quality of life and survival.

Consequently, on the basis of EBPG sections III.1 and III.2, the strategic decision was taken to adopt high-flux, biocompatible membranes throughout the entire network.

EBPG III.1: *'Dialyzer membranes with the lowest degree complement and leukocyte activation should be applied. Dialyzer membranes that induce strong complement and leukocyte activation, inflammatory reactions, and/or a blunting of the response of leukocytes to stimuli should be avoided';*

EBPG III.2: *'To achieve an improved clinical outcome regarding morbidity and mortality, the use of large pore/high-flux biocompatible dialyzers should be preferred'.*

To facilitate realization of this first Quality Implementation Measure, a preparatory step was identified as necessary: updating of the clinics' technical infrastructure to cope with the effective implementation of high-flux dialysis. One of these aspects was related to the chemical and, in particular, biological quality of the dialysis water.

The network then proceeded to undertake a multitude of exertions to create and maintain a technical and organizational infrastructure that ensures that all necessary instruments and methods are properly implemented. The instruments to be adopted for these therapies were mainly based on: (a) proper control of dialysis fluid quality, achieved mainly through correct design and implementation of the water treatment system and careful quality control of the produced fluids; (b) dialysis machines equipped with the most up-to-date technology including the dialysis fluid filter, DIASAFE® Plus; and (c) use of high-

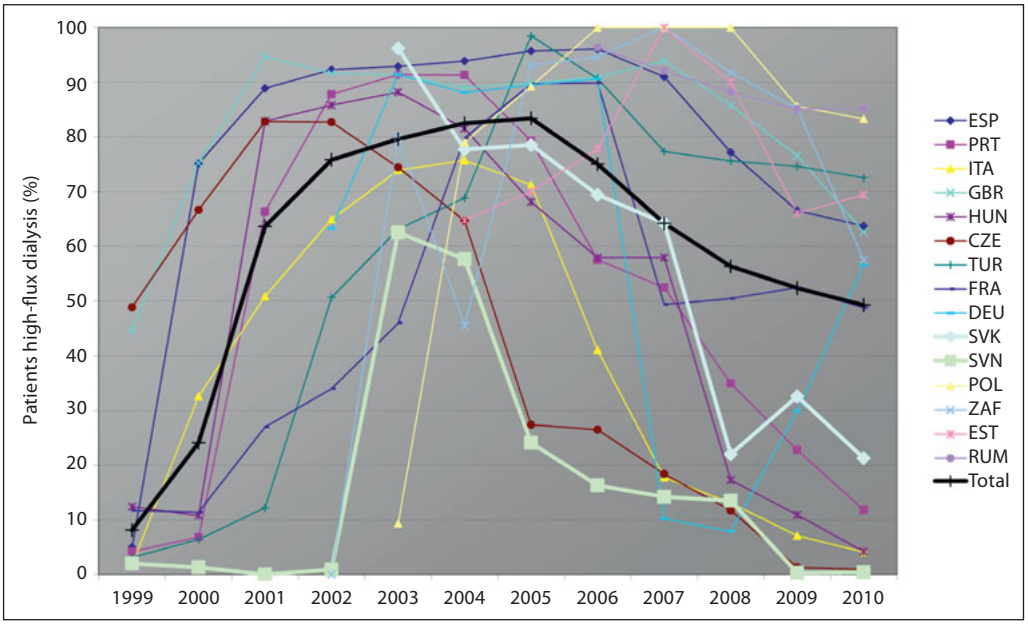

Fig. 2. Proportion of patients on high-flux dialysis in the NephroCare EMEA Network from 1999 to 2010.

flux polysulfone filters. The above aspects also required considerable efforts in terms of operator training. During these years, the company organized training sessions for all involved personnel to enable them to deal effectively with all new technical and medical issues.

The successful implementation of the EBPG was certified on the basis of the evidence collected with EuCliD [13]. As reported in figure 2, at the time of EuCliD implementation (1999), only 8.1% of patients were treated with high-flux dialysis. The public review of the draft of the EBPG on HD involving the international nephrological community (e.g. EDTA congresses, etc.) created a strong focus on the advantages of high-flux dialysis. Therefore, not surprisingly, even prior to the official issue of the guideline a spontaneous increase of the application of high-flux dialysis, wherever possible, was observed. The publication of the EBPG in 2002 boosted this development further. The preliminary promising results were validated by an internal study published by Merello Godino et al. [14] showing an improvement in the field of anemia correction, a decreased level of β_2-microglobulin and an improved lipid metabolism. By 2003, more than 80% of patients had been moved to this advantageous technology. The MPO study finally confirmed in 2009 this modality to be superior to low-flux [15]. The NephroCare network participated directly in this European trial with a number of centers in Portugal and France. At that time the major

concern in relation to the use of high porosity membranes was related to safety aspects. It has to be underlined that, even prior to the MPO publication, the NephroCare experience, which is based on millions of high-flux dialysis treatments, demonstrated the absolute safety of the technique.

Driving Change Forward

In the meantime, in parallel with the implementation of these new measures relating not only to high-flux dialyzers but also to dialysis fluid quality and dialysis machine technology, the network continued to expand the number of centers in the original group and in additional countries. What emerged was the need to combine clinical governance with the management of all other network aspects (e.g. technical) in a continuously changing environment. The new approach to patient care, which was based on simultaneous integration of the perspectives of all stakeholders (patients, employees, shareholders, community) and a holistic therapy concept, eventually merged under the NephroCare umbrella. This approach embraces the complete philosophy of care delivered to the patients ranging from dialysis products to therapies including renal pharmaceuticals (all of which are constantly being improved), as well as care from qualified, motivated clinic personnel who regularly receive further training.

The NephroCare Balanced Scorecard is the primary methodology used to reach this goal. This tool is applied to optimize patient outcome by interrelating key performance indicators addressing medical (patient) and financial aspects (shareholders) as well as internal (employees) and environmental (community) processes.

On-Line HDF as Standard Therapy

HDF combines diffusion and convection in order to facilitate the removal of high and low molecular weight solutes and has been shown to be superior to all other treatment modalities currently available. However, possible pyrogenic reactions pose a considerable threat to the patients since the risk of microbiological contamination is increased. Besides, costs are higher with increasing volumes of substitution fluid used. Therefore, the availability of high purity substitution fluid at lower cost was a clear requirement for the broad application of the modality.

In this regard, the widespread application of high-flux therapy, together with the implementation of the required infrastructure, especially concerning water quality, opened the way to the extensive use of on-line HDF therapy. This step was also recommended in sections II.2.1 and II.2.2 of the EBPG:

EBPG II.2.1: *'β2-m is representative in its kinetic behaviour of other MM and peptides of similar size, and may be used as a marker for such molecules*'.

EBPG II.2.2: *'To enhance MM removal, synthetic high-flux membranes should be used. Additional strategies, such as adding a convective component, or increasing HD time or frequency, should be used to maximize MM removal'.*

The financial constraints were largely resolved with the technique of 'on-line' fluid production resulting in the availability of unlimited volumes of ultra-pure substitution fluid at a cost close to that of dialysate for conventional HD [16, 17].

To fully realize the goal of establishing on-line HDF as a standard therapy, two further technological steps were targeted and successfully reached: introduction of the Fresenius 5008 therapy system and an even stricter control of the water quality. The latter was achieved by the creation of a company-internal guideline for dialysis fluids. The guideline was implemented in accordance with recognized international regulations (e.g. European Pharmacopoeia and ISO standards) and with the setting up of a dedicated data collection system integrated in EuCliD. In fact, FME played an important role in the review of the ISO standards: the experience collected in the network through the large number of HDF treatments already performed constituted a major contribution to this review. The result was the introduction of technically consistent regulations for the safe and sustainable implementation of on-line HDF.

However, these regulations were in themselves still not sufficient to guarantee highest treatment quality and safety: attention must also be paid to the design and organization of the dialysis center as they have a major impact on work efficiency and on the ability of the personnel to comply with essential rules, such as hygiene. Accordingly, in addition to the above-mentioned guideline on water and dialysis fluids, other internal guidelines were developed. These related to the centers' architectural design, to hygiene and nursing processes.

Moving from high-flux dialysis to on-line HDF was considered a major step also from a cultural viewpoint. To prepare the clinical staff for this major change, on-line HDF was included as an official topic in the accreditation meetings organized during the years 2005/2006 in the countries of the network. The corresponding topics discussed in these meetings referred to the required purity of water and the rationale for the use of the modality. Having as target the change from standard dialysis to on-line HDF, a detailed and open discussion on risks and benefits of this technique was hosted. The main clinical benefits expected from on-line HDF treatments include hemodynamic stability [18, 19], possibly improved quality of life [20] and a delay in the development of dialysis-related amyloidosis [21]. Survival is also expected to improve [22]. The Dialysis Outcome and Practice Patterns Study (DOPPS), a prospective survey, showed better survival of patients on high efficiency HDF [23].

The combined pressure from the educational activities, which brought about a preliminary cultural change, and the creation of a target based on the percentage of treatments by this technique resulted in an increasing implementation of the modality by the individual clinics.

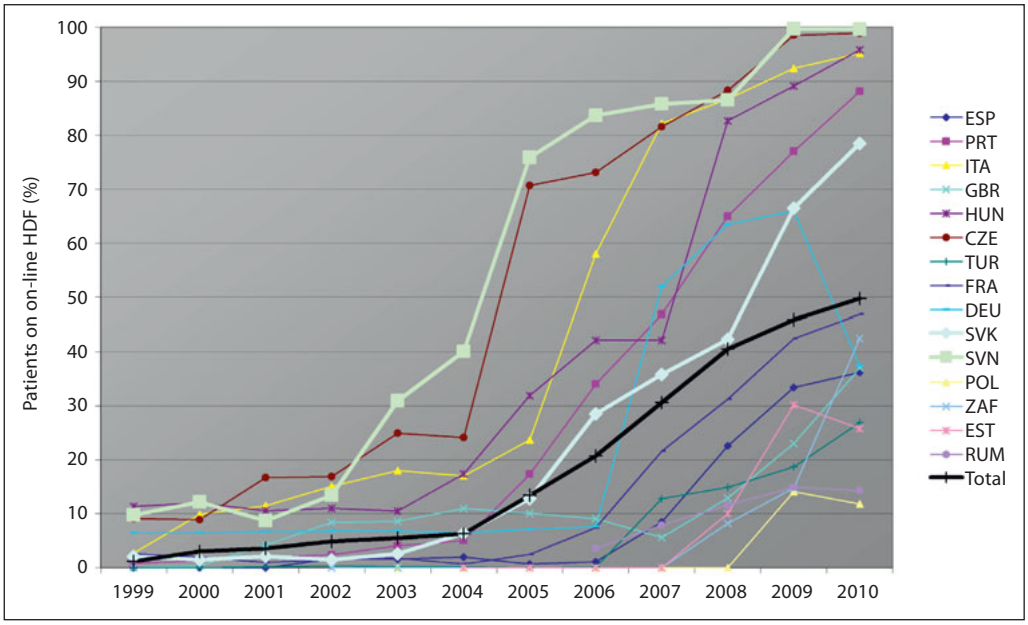

Fig. 3. Proportion of patients on on-line HDF in the NephroCare EMEA Network from 1999 to 2010.

As shown in figure 3, up to 2004, the use of on-line HDF in the NephroCare clinics was rather limited in general. After 2004, on-line HDF increased its share continuously among the dialysis techniques prescribed in the network and currently more than 50% of patients are on this modality. Conversely, the proportion of patients treated with conventional high-flux dialysis progressively decreased after 2005 (fig. 2).

With the progression of the consolidation of the network, the original EuCliD software developed in 1999 fell short of fulfilling the extended documentation requirements associated with on-line HDF. A new version aimed to collect more detailed data on each single dialysis treatment was subsequently developed and implemented in the network. The new project EuCliD 5 was initiated in 2005 and aims to support not only quality assurance, but also the day-to-day work of the clinical staff in all the clinics of the network.

At present NephroCare is addressing two new challenges in its implementation of on-line HDF as standard therapy. The first is a major revision of clinical targets defined in the NephroCare Balanced Scorecard to incorporate new and emerging medical insights. In particular, focus is moving from the per se deployment of on-line HDF to the absolute correctness in the way in which the prescription is carried out. Evidence available in the literature [23] shows that a minimum of 15 liters of reinfusion must be delivered in order to achieve the maximum benefit of on-line HDF for the patient. Consequently, this target

has to be achieved in all dialysis sessions and prescription indicators have been replaced by results-related indicators in the NephroCare Balanced Scorecard. The second major challenge is related to the global economic crisis which evolved in 2009. Focus is strong on the achievement of maximum treatment advantage also from an economic point of view. This is reflected in the latest reimbursement models being introduced in countries like Portugal or the US, namely capitation. Capitation is a prospective payment system in which the dialysis treatment providers receive a fixed, predetermined amount of money per capita (capitation) upfront to cover specified services for a defined time period [24, 25]. NephroCare's adoption of on-line HDF as standard therapy serves also to meet the expectation of generating economical savings by decreasing the contribution of pharmaceuticals to the total treatment cost.

In summary, this chapter describes the path of FME, and in particular NephroCare, over the past 13 years, which witnessed the growth from a collection of minor clinic acquisitions to a consolidated and fully integrated dialysis services network ensuring high-quality and cost-efficient treatments, such as on-line HDF, as standard therapy.

Appendix

Country Abbreviations

BIH	Bosnia and Herzegovina
CZE	Czech Republic
ESP	Spain
EST	Estonia
DEU	Germany
FRA	Spain
GBR	Great Britain
HRV	Croatia
HUN	Hungary
IRL	Ireland
ITA	Italy
POL	Poland
PRT	Portugal
ROU	Romania
RUS	Russian Federation
SRB	Serbia
SVK	Slovakia
SVN	Slovenia
SWE	Sweden
TUR	Turkey
UKR	Ukraine
ZAF	South Africa

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