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Quality of Life on Online Hemodiafiltration (HDF)

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Abstract

Online hemodiafiltration (OL-HDF) as a renal replacement therapy is gaining momentum due to the perceived added benefit from enhanced clearance of potentially harmful middle molecules. Favorable effect of OL-HDF on all-cause mortality and cardiovascular mortality and morbidity has been suggested by some clinical trials. Health-related quality of life (HRQOL) is an important component of hemodialysis patients' care. HRQOL is of interest to both health care providers and patients. Improved quality of life in hemodialysis patients has been associated with improved outcome in terms of reduced rate of hospitalization and mortality. Data on HRQOL in end-stage renal disease (ESRD) patients under OL-HDF is scarce and of marginal quality. In this review, we will try to summarize the available evidence on this subject.

Keywords: Quality of life, Health-related quality of life, Online hemodiafiltration, Hemodiafiltration, End-stage renal disease

1. Introduction

End-stage renal disease (ESRD) is characterized by significantly increase rate of mortality and morbidity. Survival of patients with end-stage renal disease is substantially decreased compared to counterparts without renal failure. It is estimated that 10–20 % of dialysis patients die annually [1]. Historically, in patients with ESRD, survival has been commonly utilized as a measure of outcome, as both health care providers and patients are most interested in prolonging life.

Quality of life (QOL) is curtailed in these patients not only due to the physical burden of the disease but also due to its effect on psychological, social interaction, rehabilitation, and employment component of patient life. Renal replacement therapy decreases morbidity related

to uremia and improves many of the uremic symptoms such as anorexia, fatigue, and pruritus that have a negative impact on the quality of daily life.

Conventional hemodialysis (HD) is reasonably effective in removing small solutes by way of diffusion across membranes. However, middle molecules which are implicated in adverse outcome are poorly removed by such mechanism. Secondary analysis of the HD trial had suggested that survival may depend on clearance of such middle molecules [2]. Convective therapy is more effective in removing larger toxic middle molecules such as β 2-microglobulin. High-volume online hemodiafiltration (OL-HDF) effectively achieves significant clearance of middle molecules. Such treatment has been shown to be beneficial in terms of lower risk of all-cause and cardiovascular mortality when compared to standard hemodialysis. Secondary analysis of initially negative clinical trials also demonstrated decreased mortality in recipients of high-volume OL-HDF [3–7].

Hemodiafiltration (HDF) combines diffusive and convective clearance of uremic solutes. It involves convection of large volume of fluid and infusing in the patient a replacement fluid that is ultrapure, sterile, and free of pyrogens. Utilization of online HDF where replacement fluid is prepared by further purifying dialysate fluid instead of manufacturer-provided solutions made it more practical and cost effective. It is believed that high-volume HDF by increasing clearance of middle molecules could potentially improve symptomatology, reduces morbidity, and may even improve survival [8]. These in turn could result in improved quality of life. Improved quality of life in hemodialysis patients has been associated with improved outcome. Analysis of data using the Kidney Disease Quality of Life Short Form (KDQOL-SFTM) obtained from 10,030 randomly selected hemodialysis patients from the USA, five European countries and Japan in the Dialysis Outcomes and Practice Patterns Study (DOPPS) demonstrated associations between HRQOL and the risk of death and hospitalization. Scores were determined for three components of HRQOL: (1) physical component summary (PCS), (2) mental component summary (MCS), and (3) kidney disease component summary (KDCS). Lower scores for the three major components of HRQOL were strongly associated with higher risk of death and hospitalization in hemodialysis patients, independent of a number of demographic and comorbid factors [9].

Information on quality of life in patients receiving renal replacement therapy in the form of OL-HDF is scarce and inconclusive. The studies often involve small sample size and uses different methods of quantifying HRQOL. In this report, we will attempt to address HRQOL in patients under OL-HDF treatment by way of defining HRQOL, describing the most common instruments used to evaluate HRQOL and presenting brief summaries of clinical studies that investigated HRQOL in individuals receiving convective therapy.

2. What is health-related quality of life (HRQOL)

The concept of HRQOL has been around for many decades. In its constitution, the World Health Organization has defined health as “a state of complete physical, mental and social

well-being and not merely the absence of disease or infirmity" [10]. Quality of life (QOL) is a broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life [11]. It is often defined differently by variable groups and professional societies. This adds to the difficulty of measuring QOL. Health constitutes an important component of QOL assessment. However, other parameters such as employment, education, housing, and family life are important contributors to the overall QOL. Cultural and religious beliefs and values also add to the complexity of assessing quality of life.

The World Health Organization defines QOL as "an individual's perception of their position in life in the context of the culture and value system where they live, and in relation to their goals, expectations, standards, and concerns" [12]. Assessment of quality of life should encompass not only the physical condition but also factors that have an impact on the individual's well-being such as social, economic, emotional, and psychological factors. Quality of life and health are closely related. Each can have a positive or a negative impact on the other depending on condition. Such a relationship is demonstrated by the notion that greater survival is associated with a higher-measured QOL [13, 14].

Assessments of HRQOL have evolved over the years to include aspects of overall quality of life that can be obviously shown to affect physical as well as mental health (MH) [15–17].

On the individual level, this includes physical and mental health perceptions and their correlates including health risks and conditions, functional status, social support, and socioeconomic status. On the community level, HRQOL includes resources, conditions, policies, and practices that influence a population's health perceptions and functional status. The construct of HRQOL enables health agencies to legitimately address broader areas of public health policy in collaboration with a wider circle of health partners, including social service agencies and community planners.

HRQOL questions about perceived physical and mental health and function have become an important component of health surveillance and are generally considered valid indicators of service needs and intervention outcomes. Self-assessed health status also proved to be a more powerful predictor of mortality and morbidity than many objective measures of health [9].

The measurement of QOL should encompass many factors that affect a subject's well-being. It should include not just the physical aspect but also the social, emotional, intellectual, and cultural components that comprise daily life. According to this foundation, we can define an aspect of QOL as being health related. This health-related quality of life (HRQOL) represents the "physical, psychological, and social domains of health that are influenced by a person's experience, beliefs, expectations, and perceptions" [18]. Each of these domains can be measured in two dimensions, objective assessments of functioning status and subjective perceptions of health as reported by the individual. The patient's subjective attitudes and expectations convert that objective assessment into the actual quality of life [10].

Within this context, health is defined as not only the absence of disease and infirmity but also the presence of physical, mental, and social well-being [11].

3. Measuring health-related quality of life

Adequate HRQOL measurement instrument should capture all the effects that disease and its treatment have on the physical, emotional, social, and mental dimensions of an individual [19]. An ideal instrument would be comprehensive, reliable, and of proven validity and would facilitate comparisons between groups of subjects with different illnesses and within the same group receiving different modes of treatment. The extracted HRQOL measures must be converted into a numerical value for proper utilization.

There is no one ideal tool of measuring HRQOL, and therefore, multiple different instruments have been developed.

Most of these instruments use a series of questions to assess quality of life indirectly. These questions are defined as “items.” Each item is then given a numerical value, based on a predetermined scale. Most researchers measure each quality-of-life domain separately, by asking specific questions pertaining to its most important components.

HRQOL instruments can be subdivided into categories based on whether the tool is global or domain specific. Three major domains comprise global HRQOL: the physical domain, the social domain, and the psychosocial or mental domain.

Many schemes have been developed to assess QOL in individuals with end-stage renal disease. Here, we will briefly describe the most common tools used in assessing HRQOL in studies involving patients under treatment by OL-HDF.

Domain	Meaning of low score	Meaning of high score	Number of questions
Physical functioning (PF)	Severe limitations in physical activity, including bathing and dressing	Performs vigorous activity without limitations	10
Role-physical (RP)	Limited ability to work because of physical health	Physical health does not limit work or other activities	4
Bodily pain (BP)	Severe limiting pain	No pain or limitations due to pain	2
General health (GH)	Perceives health as poor	Perceives health as excellent	5
Vitality (VT)	Feels tired and worn out all the time	Feels full of pep and energy all the time	4
Social functioning (SF)	Physical and emotional symptoms severely limit normal social activities	No physical or emotional limits to normal social activities	2
Role-emotional (RE)	Emotions limit daily function and work	Emotions do not interfere with daily function or work	3
Mental health (MH)	Feels nervous and depressed all the time	Feels peaceful, happy, and calm all the time	5

Ref. [25].

Table 1. Components of the Short Form-36 (SF-36).

3.1. Kidney Disease Quality of Life (KDQOL) Short Form-36 (SF-36)

The Kidney Disease Quality of Life (KDQOL) instrument is a self-report questionnaire consisting of 134 items [20]. It has the SF-36 as its generic core and is supplemented with items of relevance to the HRQOL of dialysis patients. Disease-specific items assess symptoms/problems, effects of kidney disease on daily life, burden of kidney disease, cognitive function, work status, sexual function, quality of social interaction, and sleep. Included are also items relating to social support, encouragement from dialysis staff, patient satisfaction with care, and a global rating of health. A more practical shorter version, the KDQOL-SF, was developed later in view of the length of the original one. The KDQOL-SF includes the SF-36 supplemented with 43 disease-specific items from the domains identified in the original version [21].

The KDQOL-SF is easy to administer and has been validated and used widely with hemodialysis (HD) patients. KDQOL-SF became the most widely used QOL measure for ESRD patients. It was developed in the USA for dialysis patients and has been translated into several languages, to be used in several studies involving dialysis patients [22–24].

The SF-36 Health Survey can be self-reported or obtained with the help from a health professional in patients unable to complete the survey. The SF-36 contains only 36 items, through which it evaluates eight health concepts of HRQOL. The eight health concepts are physical functioning (ten items), role limitations resulting from physical problems (four items), role limitations caused by emotional or personal problems (three items), social functioning (two items), bodily pain (BP) (two items), energy/fatigue (four items), emotional well-being (five items), and general health (GH) perceptions (five items). In addition, there is one single item that provides an indication of perceived change since 1 year. Two additional components can be calculated from the SF-36, and they are the physical component summary (PCS) and the mental component summary (MCS). A higher score is associated with a more favorable health status. Components of the SF-36 are depicted in **Table 1**.

3.2. The Kidney Disease Questionnaire (KDQ) of Laupacis et al. (Canada) [26]

In 1992, Laupacis developed this tool which is disease-specific designed for use in chronic HD patients. The KDQ consists of 26 items in five dimensions: physical symptoms (six items), fatigue (six items), depression (five items), relationships (six items), and frustration (three items). The physical symptoms dimension of the KDQ is patient specific. The six physical symptoms that are most important to each subject are identified and used to assess that dimension. Patients are asked to identify their specific physical problems, next to questions regarding frustration, depression, and well-being. Patients are asked to grade their complaints on a scale ranging from one (severe) to seven (none). The KDQ is designed for use only in patients with ESRD on HD treatment.

3.3. The Euro Quality of Life Group (EQ-5DTM) questionnaire

The EQ-5DTM measures health-related quality of life in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Scores for the five dimensions are

converted into preference weights by using country-specific value sets drawn from the general population [27].

This instrument is rather new; therefore, only few country-specific value sets are available.

3.4. The CHOICE Health Experience Questionnaire (CHEQ) [28]

This is a patient-reported measure of HRQOL developed for use in the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study [29]. The authors have defined it as “the value assigned to duration of life as modified by the impairment, functional states, perceptions, and social opportunities that are influenced by disease, injury, or policy.” This instrument was developed to evaluate the effectiveness of alternative dialysis prescriptions. It supplements SF-36 survey in measuring HRQOL for patients with ESRD. It is sensitive to differences in dialysis modality and dialysis dose. The selection of HRQOL domains to be utilized was based on literature review, analysis of focus groups, and survey of dialysis providers and patients. In order to arrange domains and items identified, a representative sample of 136 dialysis patients rated each item for frequency and distress. The survey yielded 22 HRQOL domains that included 96 items: eight generic domains in the SF-36 (health perceptions, physical, social, physical and emotional role functions, pain, mental health, and energy), eight additional generic domains (cognitive functioning, sexual functioning, sleep, work, recreation, travel, finances, and general quality of life), and six ESRD-specific domains (diet, freedom, time, body image, dialysis access, and symptoms).

4. Trials on quality of life in HDF

The results of studies on HRQOL in OL-HDF are often inconclusive. The studies used different questionnaires to assess HRQOL which probably explain some of the differences among studies.

Reference	Country	Comparison	Quality-of-life instrument used	Timing of assessment	Study result
Moura et al. [38]	Portugal	Four age quartiles (<56 years, 57–68 years, 69–75 years, >75 years old)	KDQOL-SF version 1.3 for Portuguese patients	One time at baseline	Women >56 years old had decrease in work status, patient satisfaction, and role-physical. Men had decreasing physical functioning, with increasing age. Compared to women, men generally had higher scores in all quartiles on variable combinations of physical functioning and pain, patient’s satisfaction, symptoms/problem list, work status, role-physical, emotional

Reference	Country	Comparison	Quality-of-life instrument used	Timing of assessment	Study result
					well-being, work status, energy/fatigue, and quality of social interactions
Karkar et al. [32]	Saudi Arabia	HF-HD and OL-HDF	Modified KDQOL-SF version 1.3	24 months	OL-HDF was associated with improvement in general mood, body energy, dialysis compliance, sexual performance, social activity, and patient's satisfaction
Moura et al. [43]	Portugal	Access type: AVF vs. CVC	KDQOL-SF version 1.3 for Portuguese patients	One time at baseline	Patients with CVC had a decrease in scores of physical functioning, emotional well-being, role emotional, and energy/fatigue domains when compared with those with AVF. Patients with CVC also showed a decline in cognitive function and quality-of-social interaction domains. Nondiabetic patients generally scored better than diabetic patients with similar vascular access
Mazairac et al. [37]	The Netherlands, Canada, and Norway	OL-HDF and LF-HD	KDQOL-SF-36 version 1.3	At baseline and Q 3 months for a median of 2 years	At baseline, mean PCS and MCS were similar in both groups. In both groups, multiple HRQOL domain scores declined over time. Overall health domain improved in HDF patients. A trend to a worse MCS and an improved effect of kidney disease on daily life in patients on HDF
Kantartzi et al. [33]	Greece	LF-HD vs. OL-HDF and HDF (with prepared bags)	IQOLA SF-36 Greek version	Q 3 months for 1 year	OL-HDF and HDF had better score in bodily pain and role limitations due to emotional functioning. There were no differences between the two types of hemodiafiltration
Knezevic et al. [31]	Serbia	OL-HDF vs. HF-HD and LF-HD	KDQOL-SF-36	One time at baseline	No difference in general health domain. Patients on HDF had better score in most of the domains compared with patients on HD, especially compared with low-flux HD patients. No differences between high-flux HD and low-flux HD Age, economic status, dialysis modality, and ischemic heart disease were

Reference	Country	Comparison	Quality-of-life instrument used	Timing of assessment	Study result
					associated with PCS. Age, sex, economic status, dialysis modality, and vascular access are associated with MCS
Stefánsson et al. [40]	Sweden	OL-HDF vs. LF-HD	IQOLA SF-36 (Swedish version) + local questionnaire	60 days	With the exception of a lower score for social functioning with HDF, there was no significant difference in quality of life between HD and HDF
Schiffl [34]	Germany	HF-HD vs. OL-HDF	KDQ	52 weeks	Patients in the two treatment groups had similar perceptions of their quality of life. While on OL-HDF, patients had sustained improvement in physical symptoms. No change of this dimension with the other mode of therapy
Beerenhout et al. [39]	The Netherlands	OL-HF vs. LF-HD	KDQ	At baseline, 6 and 12 months	Physical symptoms improved in the HF group after 6 and 12 months, but not in the HD group. QOL for other aspects (frustration, depression, well-being) did not change in any treatment group
Lin et al. [44]	Taiwan	OL-HDF vs. HF-HD (different combinations)	Patients' score of subjective well-being, work tolerance, and mental alertness	Weekly	Interdialytic symptomatic hypotensive episodes and interdialysis physical well-being and symptoms improved when frequency of HDF is increased to three times per week
Ward et al. [41]	Germany	OL-HDF vs. HF-HD	The Kidney Disease Questionnaire	26 and 52 weeks	Both groups had similar perceptions of their quality of life. Patients' assessment of physical symptoms improved during the course of the study independent of mode of therapy
Verzetti et al. [42]	Italy	AFB vs. BHD in patients with diabetic ESRD	Patients' score of their degree of subjective well-being	Monthly	Subjective report of well-being increased when patients switched from traditional HD to AFB

Abbreviations: AFB, acetate-free biofiltration; AVF, arteriovenous fistula; BHD, bicarbonate hemodialysis; CVC, central venous catheter; HDF, hemodiafiltration; HF, hemofiltration; HF-HD, high-flux hemodialysis; IQOLA, International Quality of Life Assessment; KDQOL, Kidney Disease Quality of Life; KDQ, Kidney Disease Questionnaire; LF-HD, low-flux hemodialysis; MCS, mental component summary; OL-HDF, online hemodiafiltration; OL-HF, online hemofiltration; PCS, physical component summary; SF-36, Short Form-36.

Table 2. Summary of studies assessing QOL in patients treated with convective therapy.

The following is the description of trials that examined HRQOL in patients under treatment of OL-HDF, hemofiltration (HF), and acetate-free biofiltration (AFB) in comparison to low-flux hemodialysis (LF-HD) or high-flux hemodialysis (HF-HD). Summary of these trials is presented in **Table 2**.

4.1. Moura et al.

Moura et al. performed an evaluation of 322 ESRD under OL-HDF from five dialysis units in north Portugal in which patients reported HRQOL utilizing the Kidney Disease Quality of Life Short Form (KDQOL-SF). Patients showed a mean (\pm SD) of 53.17 % (\pm 15.31 %) in SF-36 total score, 50.17 % (\pm 9.51 %) in the SF-36 mental component summary (MCS), and 49.75 % (\pm 9.44 %) in the SF-36 physical component summary (PCS). Red cell distribution width (RDW), female gender, and diabetes were found as significant predictors of SF-36 total score of HRQOL, which accounts for 12 % of the total explained variance. Patient satisfaction, RDW, body mass index, and gender were identified as predictors for the PCS, which accounts for 22 % of total explained variance. Furthermore, patient satisfaction and dry weight were found as predictors for MCS. These predictors accounted for 28 % of the total explained variance. The authors concluded that the coexistence of diabetes, female gender, and anemia are predictors of HRQOL in patients under OL-HDF and suggest that more attention should be given to these issues in order to improve HRQOL [30]

4.2. Knezevic et al.

Knezevic et al. examined whether hemodialysis modality and membrane flux, independent of membrane biocompatibility, make differences in quality of life in 124 patients from Serbia. The patients were divided, based on therapy, into three groups: online HDF, high-flux hemodialysis, and low-flux hemodialysis. Health-related quality of life was assessed using the Short Form-36 questionnaire combined with special questionnaire, which included demographic and clinically related questions. Health-related quality of life was better in patients on HDF compared with patients on hemodialysis, especially compared with low-flux hemodialysis patients in most of the scales and in both dimensions: physical component scale and mental component scale. There were no differences in Short Form-36 domains between high-flux hemodialysis and low-flux hemodialysis. The conclusion was that HDF has a potential positive influence on quality of life, which is sufficient to justify further research in prospective and longitudinal study design [31].

4.3. Karkar et al.

Karkar et al. investigated the effect of online HDF vs. high-flux hemodialysis (HF-HD) on a patient's health-related satisfaction level. The study involved 72 patients from Saudi Arabia on regular low-flux HD who were randomized to HF randomized to HF-HD and to HDF ($n = 36$) and followed up for 24 months. Satisfaction level was assessed using modified questionnaires of the Kidney Disease Quality of Life Short Form (KDQOL-SF) version 1.3. The HDF group achieved a higher satisfaction level than the HD group ($P < 0.0001$) with less cramps, itching, joint pain, and stiffness. There was an improvement in general mood, sexual

performance, and social activity. The investigators concluded that high-efficiency postdilution online HDF significantly improved patients' satisfaction level and quality of life [32].

4.4. Kantartzi et al.

Kantartzi et al. reported a prospective crossover study involving 24 patients. Each patient received HD, OL-HDF, and HDF with prepared bags of substitution fluid for 3 months, with the dialysis modality subsequently being altered. Quality of life was measured by the Short-Form Health Survey with 36 questions (SF-36), and subscale scores were calculated. There were statistical significant differences in QOL for the total SF-36, bodily pain score, and role limitations due to emotional functioning in favor of online HDF over low-flux HD [33].

4.5. Schifffl

Schifffl studied 76 clinically stable patients on low-flux conventional HD (LF-HD) in a prospective crossover clinical evaluation of high-flux ultrapure hemodialysis (HF-HD) and OL-HDF. They were randomized to HF-HD or OL-HDF (24 months) and switched to the alternative treatment (24 months). Online HDF had a greater clearance of urea, phosphate, and β_2 -microglobulin. Both OL-HDF and high-flux ultrapure HD significantly improved nutritional status and the response to erythropoietin. Disease-related quality of life was determined after 52 weeks of each study period using the KDQ. The KDQ determines quality of life in five dimensions: physical symptoms, fatigue, depression, relationship with others, and frustration. The patients in the two treatment groups had similar perceptions of their quality of life. However, the patients' assessment of their physical symptoms showed a sustained improvement during treatment with OL-HDF. There was no change of this dimension with the other modes of therapy ($P < 0.05$). None of the other dimensions of the Kidney Disease Questionnaire showed a change during the course of the study [34].

4.6. Mazairac et al.

Mazairac et al. analyzed data of 714 patients from the Convective Transport Study [35, 36] with a median follow-up of 2 years to assess the effect of HDF on quality of life compared with HD in patients with ESRD. Quality of life was assessed with the KDQOL-SF. There were no significant differences in changes of HRQOL over time between patients treated with HD ($n = 358$) or hemofiltration ($n = 356$) [37].

4.7. Moura et al.

Moura et al. evaluated the influence of aging on patients' perception of HRQOL in 305 ESRD patients under OL-HDF. Data about comorbidities, hematological data, iron status, dialysis adequacy, and nutritional and inflammatory markers were collected from patient's records. Quality of life was assessed by using the KDQOL-SF. Analysis of the data showed significant decrease with increasing age in some parameters evaluated by the KDQOL-SF instrument, namely, for work status, physical functioning, and role-physical (RP) [38].

4.8. Beerenhout et al.

Beerenhout et al. examined the effects of LF-HD and predilution online HF (OL-HF) on cardiovascular and nutritional parameters, interdialytic levels of uremic toxins, and quality of life. The KDQ of Laupacis [26] was used for QOL assessment. At 1 year, 27 patients were eligible for analysis (HF, 13 patients; HD, 14 patients). QOL for physical symptoms improved in the HF group (4.2 ± 1.2 – 5.0 ± 1.1), $P < 0.05$ within the HF group, but not in the HD group (4.0 ± 1 – 4.4 ± 1.4) [39].

4.9. Stefánsson et al.

Stefánsson et al. performed a prospective, randomized, and patient-blinded crossover study involving 20 patients from Sweden on chronic HD. The patients received either HD for 2 months followed by postdilution HDF for 2 months or in opposite order. Online postdilution HDF was used, and the replacement volume was standardized to 25–30 % of the total blood volume treated. The two treatments were similar with respect to dialysis-related complications, quality of life, and the biomarkers of oxidative stress and inflammation. Interviews for assessment of quality of life were double blinded. Patients answered health-related questions in two separate questionnaires. The first one was the Swedish version of the standardized quality-of-life questionnaire, SF-36. The second one was generated by the study designers and specifically concerned 12 symptoms and health-related conditions occurring during the previous 4 weeks. With the exception of a lower score for social functioning with HDF ($P < 0.05$), there was no significant difference in quality of life between HD and HDF [40].

4.10. Ward et al.

Ward et al. tested the hypothesis that HDF provides better solute removal than HF-HD in a prospective, randomized clinical trial. Twenty-four patients were randomized to online postdilution HDF, and twenty-one patients were allocated to HF-HD for a period of 12 months. Removal of both small (urea and creatinine) and large (β_2 -microglobulin and complement factor D) solutes was significantly greater for HDF than for HF-HD. Pretreatment plasma β_2 -microglobulin concentrations decreased with time ($P < 0.001$); however, the decrease was similar for both therapies. The patients' assessment of their quality of life was determined after 26 and 52 weeks of the study. A single interviewer administered the questionnaire to all patients. The patients in both groups had similar perceptions of their quality of life as assessed by the KDQ. The patients' assessment of their physical symptoms showed a significant improvement during the course of the study which was independent of the treatment modality. None of the other dimensions of the KDQ showed a change over the course of the study [41].

4.11. Verzettì et al.

Verzettì et al. performed a study to compare standard bicarbonate hemodialysis (BHD) with acetate-free biofiltration (AFB) in a group of 41 stable diabetic patients on dialysis treatment for 25 ± 22 months. Twenty-four type II and seventeen type I diabetic patients, all requiring

insulin therapy, were included and were followed up for 1 year in a 6-month crossover randomized study for both methods. The analysis was carried out on dialysis symptoms, interdialysis symptoms, and nutritional status. On a monthly basis, patients were also required to score their degree of subjective well-being. All the clinical events occurring during the study period, together with the number of hospitalizations and mortality rates, were recorded. AFB significantly reduced dialytic and extra-dialytic symptoms ($P = 0.003$ and 0.001 , respectively). Cardiovascular collapses decreased by 43 %, and other dialysis symptoms showed a similar trend (–35 %). The interdialysis symptoms decreased by 28 % and were accompanied by an increase in subjective well-being (39 %) when patients were switched from traditional HD to AFB. Acid-base control was better with AFB ($P = 0.01$), both at the beginning and during the session. In comparison to traditional HD, hypotensive episodes and other dialysis symptoms during AFB decreased by 43 % and 35 %, respectively. Interdialysis symptoms showed the same favorable trend, decreasing by 28 %. Moreover, subjective report of well-being increased by 39 % when the patients switched from traditional HD to AFB. The number of hospital admissions and the mortality rate were lower during the AFB than the BHD period. The authors concluded that AFB allows better control of some metabolic aspects, reduces intra- and extra-dialysis symptoms, and improves patient QOL [42].

4.12. Moura et al.

Moura et al. examined the effect of vascular access type (arteriovenous fistula (AVF) vs. central venous catheter (CVC)) on patients reported HRQOL in 322 ESRD under OL-HDF. Arteriovenous fistula (AVF) was used by 252 patients (78.3 %), whereas 70 patients (21.7 %) had a central venous catheter (CVC). Patients using CVC as a vascular access presented a decrease in four SF-36 domain scores, namely, physical functioning, emotional well-being, role-emotional, and energy/fatigue when compared with those using AVF as a vascular access. Additionally, these patients also showed significant decline in cognitive function and quality-of-social interaction domains. Left-arm AVF was associated with higher scores in three SF-36 domain scores, namely, physical functioning, pain, and general health. It was also associated with a higher score in ESRD target areas of symptoms/problem list and effects of kidney disease and quality-of-social interaction domains. The authors concluded that ESRD patients under OL-HDF using AVF as a vascular access had higher HRQOL scores in several domains when compared with those using CVC. Patients using AVF in the left forearm presented with higher HRQOL scores [43].

4.13. Lin et al.

Lin et al. compared OL-HDF (thrice, twice, and once per week) with different frequencies of combination high-flux HD. Interdialytic symptomatic hypotensive episodes were reduced when frequencies of online HDF were increased. Interdialysis physical well-being and symptoms similarly improved when frequency of HDF is increased to three times per week [44].

4.14. Nistor I et al.

Nistor et al. [45] conducted a systematic review of randomized controlled trials in which data for quality of life were extractable from eight trials (988 participants), including six evaluating HDF and one each evaluating HF or acetate-free biofiltration [33, 34, 36, 39–42, 44]. The authors Stated that in very low-quality evidence, data for quality of life were inconsistent. Data from the four parallel-group trials [33, 36, 39, 41] showed that there was no difference in the change in quality of life (any domain) comparing HDF with HD in one trial [36]. Both HDF and HD patients reported significant improvement in physical symptoms irrespective of treatment allocation in a second trial [41]. Hemodialysis patients had lower physical well-being scores than patients on HDF, but treatment effects on work tolerance and mental alertness were not available in a third trial [33]. Comparative data for HF and HD were not available in a fourth trial [39]. The remaining four studies were crossover design, and data for the end of the first phase of treatment were not available.

5. Summary

The available data on HRQOL in patients under OL-HDF therapy is limited and of low quality. Most parallel-group randomized clinical trials on this subject demonstrate no or limited improvement in HRQOL associated with OL-HDF. However, several crossover studies support a beneficial role of OL-HDF in enhancing quality of life in these patients. The effect of online HDF on quality of life reported by clinical studies is variable. The inconsistency of these results is probably related to different methods used to assess quality of life, sample size, duration of study, and the different characteristics of the convective therapy utilized such as blood flow rate, vascular access type and type of the dialyzer, convection volume, and frequency of online HDF. The most widely used and tested method of assessing health-related quality of life in patients undergoing online HDF replacement therapy is Kidney Disease Quality of Life Short Form-36 (KDQOL-SF-36). It is easily administrable and has been validated.

With the increased popularity of OL-HDF as a renal replacement therapy, larger better organized studies will probably become available in the future. Such studies, hopefully, will better clarify the issue.

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