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Original Article

Online Hemodiafiltration Versus High-Flux Hemodialysis in Pediatric Patients.

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Abstract

Introduction Online haemodiafiltration (OL-HDF is associated with increased convective clearance compared to HD, even with a high flux membrane. The aim of this study was to compare the effect of OL-HDF and high-flux HD (HF-HD) on anemia, metabolic bone disease markers and dialysis efficiency.

Methods
In this prospective study, 16 children, on hemodialysis for at least three months, were shifted from HF-HD to OL-HDF for a period of 3 months on each modality. The mean age of patients was 10.31 ± 3.28 years, and the mean duration on HD was 57.50 ± 38.24 months. Blood pressure, hemoglobin (Hb), Calcium, phosphorus and Parathyroid hormone were measured after 3 months of HF-HD and again after 3 months of OL-HDF.

Results
In our study, dialysis efficiency expressed by Kt/V was significantly improved by OL-HDF (2.07±0.47) as compared to HF-HD (1.75±0.46); p value of 0.006. Significantly lower levels of Phosphorus and Parathyroid hormone (PTH) on HF-HD compared to OL-HDF were observed (4.25 ±1.3 to 4.92 ±1.9 mg/dl on OL-HDF, p value 0.04; and 404±476 to 749±79 g/dl, p value 0.001, respectively). The levels of Hb, hematocrit (HCT) and ferritin, Erythropoietin dose requirements were not significantly differnet. Systolic blood pressure values showed significant reduction on HF-HD (111.4 ±12.3 and 114.4 ±10.9 mmHg respectively, p value 0.013).

Conclusions
Over a period of three months, oHDF was not associated with better anemia management and nutrition when compared to HF-HD, while HDF proved to be more beneficial in dialysis efficiency. HF-HD was more effective in controlling BP and metabolic bone disease.

Keywords
Anemia, dialysis efficiency, high-flux haemodialysis, metabolic bone disease, online haemodiafiltration, outcome, pediatric.

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Introduction

Theoretically, online hemodiafiltration (OL-HDF is associated with increased convective clearance compared to HD, even with a high flux membrane, however clinical results are deficient especially in children. Our goal was to examine and compare the outcomes of both modalities.

HDF is a hybrid therapy combining within the same dialysis module the two main solute transport mechanisms: Diffusion – as in HD - where the rate of diffusion of molecules is inversely proportional to the square root of the molecular weight , in which larger molecules have a relatively low speed of diffusion and therefore a relatively slow clearance by HD, and Convection which depends on the solvent drag where molecules- irrespective of their molecular weight- are transported across the membrane by bulk fluid flow, hence increasing the removal of those middle and large sized molecules that are poorly cleared by diffusion therapies **[1]**. Dialyzer membrane in HD is one of the main determinants of dialysis effectiveness. HD using high-flux dialyzers has the ability to remove more middle molecular weight uremic toxins such as β2-microglobulin than low-flux HD, because of their higher porosity **[2]**.

Patients and Methods

This study was conducted in the hemodialysis (HD) unit of the Pediatric Nephrology Unit at Abu el Rish Children's hospital, Cairo University during the period from February to August 2010. The study protocol conformed to the ethical guidelines of the 1975 Helsinki declaration and was approved by the local ethical committee of the Pediatric Department, Faculty of Medicine, and Cairo University. Sixteen children 4-16 years of age on regular HD for at least three months were recruited. Inclusion criteria included patients on regular hemodialysis for at least three months prior to the study, while patients who received blood transfusions or were admitted to the hospital in the 30 day period prior to the study, or those with irregular attendance of hemodialysis were excluded. Informed consent was obtained from all participants. All the patients were treated with the dialyzer polysulfone FX-40 or 50 (Fresenius Medical Care, Bad Hamburg, Germany) and Fresenius 4008/5008 dialysis systems (Fresenius Medical Care), receiving either standard high-flux HD and ultrapure bicarbonate-based dialysis fluid or online HDF treatment in postdilution mode and ultra-pure bicarbonate-based dialysis fluid. The substitution flow rate in HDF was set at 20-25% of the blood flow rate. A control of transmembrane pressure was assessed by the Fresenius 4008/5008 machines. Duration of dialysis session was 4 hours for both standard HD and HDF. Median dialysis vintage was 6.2 (0.5–35) years. The delivered dialysis dose was assessed by calculating the equilibrated urea Kt/V ratio (K, body urea clearance, T, time of dialysis and V, urea distribution volume) by machine derived online clearance monitoring (OCM) **[3].**

All patients were subjected to thorough history taking, clinical examination and follow up throughout the study period. All patients received recombinant human Erythropoietin (rhEPO). rhEPO doses were adjusted as needed to maintain Hb in the range of 11 to 12 g/dl.

All 16 patients were put on HF-HD for 3 months, then shifted to OL-HDF for 3 months. Patients were subjected to complete physical assessment including anthropometric and BP measurements. For the sake of comparison between patients, we divided the weight and height by the median weight and height for age and sex respectively. Laboratory tests included CBC, serum urea and creatinine by Beckman synchrony automated clinical system Cx5, albumin, Ca, P, Parathyroid hormone (PTH), Na, K, alkaline phosphatase levels (ALP), KT/V and iron indices. All tests were done at the end of a period of 3 months of HF-HD and repeated 3 months after initiation of OL-HDF.

Nominal data were expressed as frequency and percentage. Numerical data were expressed as median and range for non-parametric data mean and standard deviation for parametric data. Comparisons had been done using chi-square tests for nominal and student t-tests for parametric data. Associations had been studied using Pearson's correlations. P values less than 0.05 were considered significant. Data were subjected to computer assisted statistical analysis using SPSS package version 16.0.

Results

Females represented 75% (N=12), with a female to male ratio 3:1. The mean age of the patients was 10.31 ± 3.281 yrs. (range 4 to 16 years). The mean weight of patients was 19.781 ± 6.1724 kg (range 10.4-32.3 kg) and the mean height was 111.75 ± 15.71 cm (range 80-135 cm). Weight was 53.95 ± 13.72 % (range 27.5 to 76.6 %) and height was 79.54 ± 6.21 % of normal (range 64.9 to 87 %). Patients 'mean body surface area was 0.81 ± 0.18 m^2 (range 0.48-1.11 m^2). The mean body mass index was 18.01 ± 1.89 (range 15.2-22.2).

Congenital anomalies of the kidney and urinary tract (CAKUT) constituted the majority of causes of ESRD among our patients (7 patients, 43.9%); 25% (4 patients) had end stage renal disease (ESRD) of undetermined etiology, other causes included chronic tubulointerstitial nephritis (2 patients, 12.5%) and glomerulopathies (6.3% of cases). There was no statistically significant difference in our study group as regards the dose of rhEPO requirements (mean 379.75± 240.63 IU/Kg/week) on both dialysis modalities. (Table1) showing comparison between mean blood pressure values (in mmHg) on high-flux (Table 2) showing different laboratory parameters OL- HDF and HF HD

Table 1: Comparison between mean blood pressure values (in mmHg) on high-flux HD & online HDF.

		HDF		High-flux HD		p value*
		Mean	SD	Mean	SD	
SBP (mmHg)	**Pre**	124.69	15.86	118.75	14.09	**0.03***
	after 3 months	114.50	10.98	111.44	12.36	**0.01***
DBP(mmHg)	**Pre**	82.81	10.16	77.75	9.55	**0.01***
	after 3 months	72.19	6.57	77.13	8.37	0.32
MBP(mmHg)	**Pre**	96.77	11.68	91.42	10.79	0.86
	after 3 months	86.29	7.79	108.7	8.96	0.62
P- Values < 0.05 are considered significant.						

Table 2: Different laboratory parameters OL- HDF and HF HD.

	HDF		High-flux HD		P- Value*
	Mean	SD	Mean	SD	
Anemia Parameters					
Hb (g/dl)	9.33	1.77	9.7	1.6	0.52
HCT (%)	28.73	5.64	31.65	6.51	0.16
Ferritin (ng/ml)	553	306.63	827.38	662.35	0.06
Bone function parameters					
Ca (mg/dl)	8.83	1.03	7.92	0.87	**0.02***
P (mg/dl)	4.92	1.90	4.25	1.39	**0.04***
CaxP	45.19	19.13	33.21	10.54	**0.003***
ALP (IU/L)	836.44	788.66	705	962	0.21
PTH (pg/ml)	749	788.66	404	476	**0.001***
Dialysis Adequacy parameters					
Urea (mg/dl)	78.56	31.63	64.4	14.325	**0.02***
Creatinine (mg/dl)	9.819	4.87	8.38	3.79	0.21
KT/V	2.08	0.47	1.75	0.46	**0.006**
Electrolytes					
Na (mmol/L)	134.69	2.87	134	2.22	0.48
K (mmol/L)	4.98	1.26	4.58	0.81	0.15
Nutrition Parameters					
Albumin (g/dl)	3.52	0.34	3.35	0.48	0.22
OL-HDF online hemodiafiltration, HF-HD high flux hemodialysis P- Values < 0.05 are considered significant.					

Discussion

Anemia is a major metabolic derangement in CKD, it is commonly hypo-proliferative, normochromic and normocytic and indistinguishable from anemia of chronic disease [4]. CKD patients have lower plasma levels of erythropoietin and less erythropoiesis than other patients with similar degree of anemia, suggesting inadequate production of erythropoietin by the diseased kidney as the primary mechanism of renal anemia [5]. Comparing HF-HD to OLHDF regarding the control of anemia and the dosage of erythropoietin in our study group, showed no significant difference in the levels of Hb, HCT and ferritin in both groups. No significant difference in the doses of rhEpo required to achieve adequate control of anemia (defined in our study as Hb in the range of 11 to 12 g/dl) in patients on HDF compared to high-flux HD was found either. Other studies comparing HDF with HD did not find a significant difference in terms of EPO responsiveness [6] or hemoglobin level [7]. Vaslaki et al. however found a higher Hct level at a comparable EPO dose in adult patients, who converted from HD to HDF [8].

Uremic syndrome results from malfunctioning of various organ systems due to retention of compounds, which under normal conditions, would be excreted into the urine and/or metabolized by the kidneys. If these compounds are biologically active, they are called uremic toxins [7]. Dialysis efficiency expressed by Kt/V was significantly improved by HDF as compared to HF HD. Whether this is secondary to the higher convection volumes required for HDF alone is not clear. Many studies argue for an advantage of HDF over HF -HD in improving Kt/V [9, 10], on the other hand other studies show no difference between the two renal replacement modalities [6, 7].

There was a statistically insignificant reduction in post dialysis sNa during the OLHDF and the HFHD (134.69 +/- 2.869 and 134 +/- 2.221, respectively, P =0.484). This agreed with Hwang et al who reported that pre and post-dialysis sNa were not significantly different between OL HDF and HFHD [11]. On the other hand, Jean et al. found that compared to HF-HD, OL-HDF has a greater serum lowering effect for Na, which might explain the ability of OL-HDF to stabilize both pre and post-dialysis SBP [12]. Although we could not reproduce the same results regarding serum Na, we found statistically significant difference in SBP among our study group (114.50 ±10.9 on OL-HDF vs 111.4 ±12.3 on HF-HD, P =0.013) but not in DBP. In addition, increased removal of higher molecular weight uremic toxins like β2-microglobulin, leptin and advanced glycation end products [AGE]) influence long-term dialysis-related vascular disease.

HDF has been reported to remove P more efficiently than HF-HD [8, 1], however our study showed statistically significant higher levels of P on HDF.

In the majority of studies comparing OL-HDF to HF-HD, Ca and PTH levels did not differ significantly, whereas our results showed higher levels of Ca and PTH on HDF [6, 10]. Similar studies on adult patients show contradicting results. Rius et al. showed that PTH levels are reduced after a session with low volume HDF, but increase after high volume HDF, possibly secondary to negative calcium balance [13]. Jean et al did not observe any differences in P levels in HDF compared to HF-HD patients [14], while Lornoy et al. reported P mass removal to be enhanced by 15-20% after shifting to HDF [15] also Francisco et al reported lower P level at the end of his study in HDF patients compared to HFHD (3.4=/-0.8 versus 4.5 +/- 1.6 mg/dl, P<0.05) [16]. In one large study by Penne et al, predialysis P levels in HDF were reduced by 6% and the percentage of patients reaching phosphate treatment targets increased from 64% to 74% after 6 months of HDF, however this is not a uniform finding, and may depend on membrane characteristics [17]. Movilli et al. reported significant reduction of serum P (from 5.1 +/-1.0 to 4.0 +/- 0.7, P<0.0001) and PTH concentrations (from 307 +/-167 to 194 +/-98, P<.0001) while there was no significant change Ca and phosphate binder dose on post-dilutional HDF [10].

It is not possible to make a significant conclusion from our assessment of bone parameters in both modalities, since the duration of both treatment modalities was short (3 months) compared to the previously mentioned studies. We found no studies on comparable age groups to guide the judgment of our results, and no data to estimate the duration on each modality needed to affect the different studied parameters.

We found no significant difference in albumin levels in HDF patients compared to HD patients 3.519 +/-0.3391 versus 3.350 +/-0.48 +/-0.219 (P= 0.219). Wizemann et al, reported no significant difference in HDF compared to HD patients [19]. As regard the nutritional marker in this study represented by the albumin if we considered the large dialyzer surface area, the membrane porosity and the high amount of convective transport in HDF, an increased loss of valuable amino acids, peptides and proteins, e.g. albumin can be expected. On the other side removal of certain middle molecules like leptin improves appetite and consequently malnutrition. We found that there was no difference in plasma albumin between both study groups. Also Locatelli et al did not demonstrate an influence of dialysis membrane or convection on any of the variables related to the nutritional status (body weight, serum albumin etc.) [20]. Several other studies did not prove a significant difference between serum albumin levels in patients treated with HD versus patients treated with HDF [6, 7].

Albumin level reduction with HDF was reported by several authors [21, 22], but without having a clear clinical impact. Combarnous et al. studied albumin removal with predilutional HDF, most likely due to an interaction with the polymer surface of the dialysis membrane. Albumin loss during HDF seemed to have no acute impact on plasma albumin [23].

Our study has several limitations: First, the design of our study was not a randomized, controlled study but rather was a analytical non-randomized study. Limitations also include the small size of the study group and the length of the study. Reasons behind this is the high turnover of patients in our unit, as most children are prepared for transplantation as soon as possible, and the economic burden of maintaining children on HDF. We recommend further studying the comparison of both modalities over longer periods, and stratification of patients according to comorbidities, e.g. hypertension.

Conclusions

We found no advantages of HDF over high-flux HD with respect to anemia management, metabolic bone disease and nutrition, however HDF proved to be more beneficial in dialysis efficiency and control of SBP.

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Declaration

Ethics approval and consent to participate

This study protocol and the consents were approved and deemed sufficient by Ethical Committee of Pediatric Department, Faculty of Medicine, Cairo University. And informed written consent was obtained in every case from their legal guardians.

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