## Comparative Study between Online Hemodiafiltration and Conventional Hemodialysis as Regard Nutritional and Inflammatory States in Chornic Hemodialysis Patients

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Abstract: Background: In recent years, online hemodiafiltration (OL-HDF) was introduced as an alternative to standard HD, as it was claimed that OL-HDF would be more biocompatible, would increase dialysis efficacy and reduce the inflammatory response - features that would diminish the risk of morbidity and mortality in ESRD. Methods: The study will be prospective cross section study which includes 120 end stage renal disease patients on regular hemodialysis three sessions per week, 4 hours per session, whose will be assigned to three groups for hemodialysis with online hemodiafiltration (n = 40), high-flux hemodialysis (n = 40) and low flux hemodialysis (n = 40) 40) for 24 weeks. These patients will be recruited and investigated in Maadi Military Hospital and air forces hospital. We measured CBC, ESR, CRP, Ferritin, Serum albumin, total protein, Calcium, phosphorus and PTH. Results: Comparative study between the 3 groups revealed non-significant difference as regards age, baseline weight, height, BMI, MAC and skin fold thickness (p > 0.05). Comparative study between the 3 groups revealed non-significant difference as regards follow up weight, height, BMI, MAC and skin fold thickness (p > 0.05). Comparative study between the 3 groups revealed non-significant difference as regards all baseline laboratory variables (p > 0.05). Comparative study between the 3 groups revealed; highly significant decrease in TLC, ESR, CRP and PTH in HDF group compared to HF and LF groups; with highly significant statistical difference (p = 0.004, p = 0.006, p < 0.0001, p < 0.0001 respectively). Comparative study between the 3 groups also revealed; highly significant increase in platelets and calcium in HDF group compared to HF and LF groups; with highly significant statistical difference (p = 0.01, p = 0.004 respectively). Conclusion: HDFis better than HFHDx and LFHDx in improvement of aneamia, hyperphosphatemia, hypocalcemia, and inflammation (CRP, ESR). But the difference between HDF and HFHDx is not big difference. The main disadvantages of HDF are its cost and the loss of albumin.

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Key words: Hemodiafiltration, Conventional Hemodialysis, Chornic Hemodialysis and Inflammatory States.

# 1. Introduction:

End-stage renal disease (ESRD) is a growing public health problem with increasing prevalence worldwide. It is estimated that the number of patients with ESRD registered in 2005 will increase almost 60 %, by 2020, leading to higher costs associated with health care assistance (1).

Patients with ESRD have a high mortality rate that far exceeds the mortality rate for the non-ESRD population (2).

Hemodialysis (HD), widely used during the past half century, brought forth a way to lengthen ESRD patients' lives. Nonetheless, it is poorly suited to the effective removal of larger solutes, such as b2 microglobulin.

In recent years, online hemodiafiltration (OL-HDF) was introduced as an alternative to standard HD, as it was claimed that OL-HDF would be more biocompatible, would increase dialysis efficacy and

reduce the inflammatory response – features that would diminish the risk of morbidity and mortality in ESRD (3).

In order to increase mid-to-large molecule clearance by combining diffusive and convective transport, online hemodiafiltration (HDF), using ultrapure dialysate, was introduced (3). In the past decade, evidence has accumulated regarding the superiority of post dilution HDF over hemodialysis (HD). Specifically, HDF has been associated with higher survival rates compared with low and high-flux HD (4). when using high convection volumes (5). Additionally, HDF has been reported to provide better hemodynamic stability (6). especially when using higher convective volumes a better quality of life (7). and fewer depression symptoms (8). HDF has also been reported to improve beta2-microglobulin (B2-m) phosphate and urea removal (9). Some others studies have reported better anemia correction (10). and lower

inflammation when using HDF (11). The main disadvantages of HDF are its cost and the loss of albumin (12).

### 2. Patient and Methods:

The study will be prospective cross section study which includes 120 endstage renal disease patients on regular hemodialysis three sessions per week, 4 hours per session. whose will be assigned to three groups for hemodialysis with online hemodiafiltration (n = 40), high-flux hemodialysis (n = 40) and low flux hemodialysis (n = 40) for 24 weeks.

These patients will be recruited and investigated in Maadi Military Hospital and air forces hospital.

All patients will be subjected to the following:

- Full medical history.
- physical examination.

• Anthropometric measures (mid-arm circumference, skin fold thickness, height, weight And BMI).

• Lab investigations (CBC, ESR, CRP, Ferritin, Serum albumin, total protein, Ca, phosphorus and PTH).

### **Inclusion criteria:**

All endstage renal disease patients on regular hemodialysis for at least 6 months through native A-V fistula or A-V graft.

All ESRD patients aged more than 18 years old.

**Exclusion criteria:** 

Patients with BMI<18.

Patients with active, recent infection or critical illness.

Patients less than 18 years old or elderly.

Patients with hypoalbuminemia.

Patients with advanced liver disease or advanced cardiopulmonary disease.

Patients dialyzed via catheter.

Patients on CAPD.

## **Statistical Analysis:**

Data entry, processing and statistical analysis was carried out using MedCalc ver. 15.8. Tests of significance (Chi square, ANOVA, Paired t test) were used. Data was presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. P-values less than 0.05 (5%) was considered to be statistically significant.

#### **Descriptive statistics:**

✓ Mean, Standard deviation ( $\pm$  SD) and range for parametric numerical data, while Median and Inter-quartile range (IQR) for non-parametric numerical data.

✓ Frequency and percentage of non-numerical data.

### Analytical statistics:

✓ Paired Student's t test was used to assess the statistical significance of the difference between two (paired) study group means.

✓ Chi-Square test was used to examine the relationship between two qualitative variables.

✓ ANOVA test was used to assess the statistical significance of the difference between more than two study group means.

# 3. Results:

Table (1): Comparison between the 3 groups as regards some follow up (24 weeks) laboratory data using one-way ANOVA test:

	HDF group	HF group LF group		ANOVA	
Variable	(N= 39)	(N=40)	(N=40)	test	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	F-ratio	p value
Hb (g/dL)	$10.69 \pm 1.12$	$10.78 \pm 1.22$	$9.31 \pm 1.16$	1.847	0.162
TLC $(10^{3}/\mu L)$	$4.48\pm2.45$	$5.91 \pm 1.84$	$8.77\pm3.03$	1.521	0.004**
Platelets $(10^3/\mu L)$	$242.08 \pm 75.15$	$190.28 \pm 79.51$	$220.4 \pm 69.35$	4.786	0.010**
ESR (mm/hr)	$10.15 \pm 31.24$	$31.33 \pm 31.96$	$45.68 \pm 22.14$	0.451	0.006**
CRP (mg/dL)	$18.56 \pm 14.79$	$23.48 \pm 17.61$	$46.38 \pm 25.85$	8.766	<0.0001**
Ferritin (ng/mL)	$388.13 \pm 87.46$	$377.9 \pm 350.09$	$414.64 \pm 435.54$	0.228	0.796
Ca (mg/dL)	$9.49\pm0.82$	$8.1\pm0.02$	$7.08\pm0.86$	3.260	0.004**
$PO_4 (mg/dL)$	$4.82 \pm 1.3$	$4.55 \pm 1.78$	$5.18 \pm 1.43$	1.788	0.172
PTH (pg/ml)	$416.79 \pm 566.56$	$606.35 \pm 623.54$	$862.8 \pm 557.74$	0.835	<0.0001**
Total protein (g/dL)	$7.14 \pm 0.51$	$6.96 \pm 1.69$	$7.06\pm0.5$	0.272	0.762
Albumin (g/dL)	$3.62\pm0.3$	$3.42\pm0.83$	$3.59\pm0.29$	1.049	0.354

 $\checkmark$  The patients were classified according to method of hemodialysis into 3 groups:

✓ Patients on LF (40 patients)

- ✓ Patients on HDF (39 patients)
- ✓ Patients on HF (40 patients)

Comparative study between the 3 groups revealed non-significant difference as regards age, baseline weight, height, BMI, MAC and skin fold thickness (p > 0.05).

Comparative study between the 3 groups revealed non-significant difference as regards follow up weight, height, BMI, MAC and skin fold thickness (p > 0.05).

Comparative study between the 3 groups revealed non-significant difference as regards all baseline laboratory variables (p > 0.05).

Comparative study between the 3 groups revealed; highly significant decrease in TLC, ESR, CRP and PTH in HDF group compared to HF and LF groups; with highly significant statistical difference (p = 0.004, p = 0.006, p < 0.0001, p < 0.0001 respectively).

Comparative study between the 3 groups also revealed; highly significant increase in platelets and calcium in HDF group compared to HF and LF groups; with highly significant statistical difference (p = 0.01, p = 0.004 respectively).

Comparative study between the 3 groups also revealed non-significant difference as regards the remaining follow up laboratory variables (p > 0.05).

# Paired comparative studies regarding HDF group:

We further analyzed and compared the 39 HDF patients according to the serial (pre and post-dialysis) clinical and laboratory measurements.

Comparative study between pre and post-dialysis measurements revealed non-significant difference regarding weight, height, BMI, MAC and skin fold thickness (p > 0.05).

Comparative study between the baseline and follow up laboratory measurements revealed; highly significant decrease in TLC, ESR, CRP, ferritin and PTH in follow up measurement; with highly significant statistical difference (p = 0.0002, p < 0.0001, p < 0.0001, p = 0.0466, p = 0.008 respectively).

Comparative study between the baseline and follow up laboratory measurements also revealed; significant increase in hemoglobin and calcium in follow up measurement; with significant statistical difference (p = 0.0328, p = 0.01 respectively).

Comparative study between the baseline and follow up laboratory measurements also revealed; non-significant difference as regards the remaining laboratory variables (p > 0.05).

# Paired comparative studies regarding HF group:

We further analyzed and compared the 40 HF patients according to the serial (pre and post-dialysis) clinical and laboratory measurements.

Comparative study between pre and post-dialysis measurements revealed non-significant difference regarding weight, height, BMI, MAC and skin fold thickness (p > 0.05).







Figure (6): Mean serum calcium between the 3 study groups.



Figure (7): Mean PTH between the 3 study groups.

	1 <sup>st</sup> measurement	2 <sup>nd</sup> measurement	Paired
Variables	(pre-dialysis)	(post-dialysis)	t test
	Mean ± SD	Mean $\pm$ SD	p value
Hb (g/dL)	$10.09 \pm 1.31$	$10.69 \pm 1.12$	0.0328*
TLC $(10^{3}/\mu L)$	$6.48\pm2.09$	$4.48 \pm 2.45$	0.0002**
Platelets $(10^3/\mu L)$	$229.97 \pm 56.23$	$242.08 \pm 75.15$	0.446
ESR (mm/hr)	$46.46 \pm 6.62$	$10.15 \pm 31.24$	< 0.0001**
CRP (mg/dL)	58.79 ± 16.39	$18.56 \pm 14.79$	< 0.0001**
Ferritin (ng/mL)	$436.92 \pm 122.61$	$388.13 \pm 87.46$	0.0466*
Ca (mg/dL)	$9.06 \pm 0.6$	$9.49 \pm 0.82$	0.01*
$PO_4 (mg/dL)$	$4.97 \pm 1.39$	$4.82 \pm 1.3$	0.574
PTH (pg/ml)	$702.49 \pm 261.69$	$416.79 \pm 566.56$	0.008**
Total protein (g/dL)	$6.94 \pm 0.41$	$7.14\pm0.51$	0.065
Albumin (g/dL)	$3.72 \pm 0.33$	$3.62 \pm 0.3$	0.1655

Table (2): Comparison between HDF patients as regards serial pre and post-dialysis laboratory measurements using Paired t test:

Table (3): Comparison	between HF	patients as	s regards	serial p	ore and	post-dialysis	laboratory	measurements	using
Paired t test:									

	1 <sup>st</sup> measurement	2 <sup>nd</sup> measurement	Paired
Variables	(pre-dialysis)	(post-dialysis)	t test
	Mean $\pm$ SD	Mean $\pm$ SD	p value
Hb (g/dL)	$9.72 \pm 2.46$	$10.78 \pm 1.22$	0.017*
TLC $(10^{3}/\mu L)$	$6.76 \pm 2.78$	$5.91 \pm 1.84$	0.003**
Platelets $(10^3/\mu L)$	$203.55 \pm 50.18$	$190.28 \pm 79.51$	0.375
ESR (mm/hr)	$47.4 \pm 27.08$	$31.33 \pm 31.96$	0.008**
CRP (mg/dL)	$50.55 \pm 22.13$	$23.48 \pm 17.61$	< 0.0001**
Ferritin (ng/mL)	$435 \pm 420.85$	$377.9 \pm 350.09$	0.499
Ca (mg/dL)	$8.77 \pm 0.62$	$8.1 \pm 0.02$	0.052
$PO_4 (mg/dL)$	$5.22 \pm 1.28$	$4.55 \pm 1.78$	0.056
PTH (pg/ml)	$672.6 \pm 633.44$	$606.35 \pm 623.54$	0.627
Total protein (g/dL)	$7.11 \pm 0.68$	$6.96 \pm 1.69$	0.607
Albumin (g/dL)	3.69 ±0.53	$3.42 \pm 0.83$	0.103

Comparative study between the baseline and follow up laboratory measurements revealed; highly significant decrease in TLC, ESR and CRP in follow up measurement; with highly significant statistical difference (p = 0.003, p = 0.008, p < 0.0001 respectively).

Comparative study between the baseline and follow up laboratory measurements also revealed; significant increase in hemoglobin in follow up measurement; with significant statistical difference (p = 0.017).

Comparative study between the baseline and follow up laboratory measurements also revealed; non-significant difference as regards the remaining laboratory variables (p > 0.05).

# Paired comparative studies regarding LF group:

We further analyzed and compared the 40 LF patients according to the serial (pre and post-dialysis) clinical and laboratory measurements.

Comparative study between pre and post-dialysis measurements revealed non-significant difference regarding weight, height, BMI, MAC and skin fold thickness (p > 0.05).

	1 <sup>st</sup> measurement	2 <sup>nd</sup> measurement	Paired
Variables	(pre-dialysis)	(post-dialysis)	t test
	Mean $\pm$ SD	Mean $\pm$ SD	p value
Hb (g/dL)	$10.20 \pm 1.53$	$9.31 \pm 1.16$	0.004**
TLC $(10^{3}/\mu L)$	$6.61 \pm 2.24$	$8.77 \pm 3.03$	< 0.0001**
Platelets $(10^3/\mu L)$	$228.7 \pm 72.62$	$220.4 \pm 69.35$	0.467
ESR (mm/hr)	$33.62 \pm 23.48$	$45.68 \pm 22.14$	< 0.0001**
CRP (mg/dL)	$36.4 \pm 15.56$	$46.38 \pm 25.85$	< 0.0001**
Ferritin (ng/mL)	$384.42 \pm 465.1$	$414.64 \pm 435.54$	0.479
Ca (mg/dL)	$8.77 \pm 1.04$	$7.08\pm0.86$	< 0.0001**
$PO_4 (mg/dL)$	$4.97 \pm 1.63$	$5.18 \pm 1.43$	0.377
PTH (pg/ml)	$774.65 \pm 560.75$	862.8 ± 557.74	0.027*
Total protein (g/dL)	$6.93 \pm 0.62$	$7.06 \pm 0.5$	0.145
Albumin (g/dL)	$3.64 \pm 0.39$	$3.59 \pm 0.29$	0.453

Table (4): Comparison between LF patients as regards serial pre and post-dialysis laboratory measurements using Paired t test:

Comparative study between the baseline and follow up laboratory measurements revealed; highly significant increase in TLC, ESR, CRP and PTH in follow up measurement; with highly significant statistical difference (p < 0.0001, p < 0.0001

Comparative study between the baseline and follow up laboratory measurements also revealed; highly significant decrease in hemoglobin and calcium in follow up measurement; with high significant statistical difference (p = 0.004, p < 0.0001 respectively).

Comparative study between the baseline and follow up laboratory measurements also revealed; non-significant difference as regards the remaining laboratory variables (p > 0.05).

#### 4. Discussion:

In our study there were insignificant differences in Albumin between the three groups which agree with the study done by NicolásMacías, et al.,2016(13), Oates T et al.,2011(14) and Vilar E et al., 2009(15).

In our study there were significant differences in Hb between the three groups which agree with study done by Maduell et al.,2017(16) and Locatelli et al.,2011(17).

And disagree with study done by vilar et al., 2009(15) in which there is no advantage of HDF over high-flux HD in anemia management.

In our study there were significant differences in CRP between the three groups, and this result agrees with the study done by Maduell et al.,2017(16).

And this result disagrees with the study done by Ping Jia et al.,2016(18), Oates T et al., 2011(14) and Tiranathanagul K et al., 2009(19).

### In conclusion:

HDFis better than HFHDx and LFHDx in improvement of aneamia, hyperphosphatemia, hypocalcemia, and inflammation (CRP, ESR). But the difference between HDF and HFHDx is not big difference. The main disadvantages of HDF are its cost and the loss of albumin.

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