Comparative crossover controlled study using polysulphone and Vitamin E coated dialyzers

Mohamed S. Al-Jondeby, RN, Iolani T. Cabaguing, RN, Amelita A. Pajarillo, RN, Fahd A. Hawas, MBBS, Facharzt, Dujanah H. Mousa, MBBS, FRCP, Mohamed H. Al-Sulaiman, MBBS, Faissal A. Shaheen, MBBS, FRCP, Abdulla A. Al-Khader, MBA, FRCP.

ABSTRACT

Objective: There is relatively little clinical experience reported on the use of the vitamin E coated dialyzer (CL-EE12, Terumo). This study compares its efficacy and intradialytic symptoms with a polysulphone dialyzer in 2 groups of patients in a controlled crossover trial design.

Methods: This study was carried out at the Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia, during the time period January to March 2002. In group A, 34 patients were dialyzed for 4 weeks with vitamin E dialyzer then switched over to Fresenius 60 (F60) for 4 weeks. In group B, 41 patients were dialyzed with F60 for 4 weeks then switched to vitamin E coated dilayzers for 4 weeks. The following parameters were measured weekly, hemoglobin level, urea reduction ratio (URR), urea clearance ratio (Kt/V), pre and post dialysis diastolic blood pressure (DBP) and systolic blood pressure (SBP), interdialytic weight gain. The patients were observed for interdialytic hypotension or symptoms.

Results: No significant findings were found in any of the parameters except more dialyzer clotting was observed with vitamin E dialyzer than in F60 dialyzers (1.6% of dialysis sessions versus 0.1% P<0.03). The interdialytic weight gain tended to be less in the vitamin E group but did not reach statistically significant difference. The Kt/V and URR were slightly higher when using the vitamin E dialyzer only in the second and third weeks. hypotensive episodes (P<.007) less leg cramp (P<.31) and less itching (P<.02) in the vitamin E coated treated group within group B.

Conclusion: There were only minor differences noted between the 2 dialyzers in the parameters measured

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Vitamin E coated dialyzers are new hollow fiber dialyzers employing synthetic co-polymers coated with vitamin E. Vitamin E has been used as a scavenger and a coating molecule to increase the biocompatibility of the filter. Recent studies have shown that it causes less production of cytokines[1] and oxygen free radicals.[2] In another study vitamin E dialyzers were shown to cause less intradialytic symptoms[3] and to cause less clotting during dialysis.[4] Fresenius 60 is a polysulphone high flux dialyzer. It is the most widely used dialyzer of high flux type worldwide and has been shown to cause less proinflammatory reactions[5] It has been reported that this dialyzer has ability in inhibiting complement activation and produced a transient decrease in leukocytes and antithrombogenic action. These properties have been confirmed in clinical use.[6,7] Hydraulic and flow dynamic characteristics of vitamin E bonded dialyzers have been shown to be satisfactory. There is evidence to support the role of vitamin E membranes in combating lipid peroxidation.[8] Significant improvement has occurred in the field of dialysis delivery in recent years. However, major concerns have

From the Department Nephrology, Armed Forces Hospital, Riyadh 11159, *Kingdom of Saudi Arabia*.

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Address correspondence and reprint request to: Dr. Abdullah A. Al-Khader, Director of Nephrology, Armed Forces Hospital, PO Box 7897, Riyadh 11159, *Kingdom of Saudi Arabia*. Tel. +966 (1) 4791000 Extn. 5486. Fax. +966 (1) 4791000 Extn. 3837. E-mail: aaalkhader@hotmail.com

emerged concerning long-term derangements in patients on hemodialysis (HD) and possible blood-membrane interactions. These may contribute to intradialytic symptoms occurrence. In this study we compare polysulphone high flux dialyzer F60 and vitamin E coated dialyzer (CL-EE12, Terumo, Japan) concentrating specially on intradialytic symptoms and adequacy of dialysis.

Methods. This study was carried out Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia, during the time period January to March 2002. In Group A, 34 patients have been dialyzed for 4 weeks using vitamin E (CL-EE12 Terumo) dialyzer surface area 1.2 meters and after a one week 'washout' period, the same patients were dialyzed for 4 weeks using F60 of surface area 1.3sq. meters. During both periods the patients were kept on the same diet, same period and frequency of dialysis (all were receiving three times weekly dialysis except 2 patients on twice weekly dialysis), the same dry weight and the same blood pressure (BP) medications if any (8% of the patients were receiving antihypertensive medications). In Group B, 41 (different patients) were dialyzed for 4 weeks using F60 and after one week washout period the same group of patients were dialyzed for 4 weeks using vitamin E dialyzer. Again, they were kept on the same diet, frequency and duration of dialysis (all were receiving thrice weekly dialysis except 2 patients on twice weekly dialysis), the same dry weight and antihypertensive medications (23% were on antihypertensive medications). In Group A, the mean age was 61.5 years (range 26-90); there were 20 males and 14 females. The mean duration on dialysis was 62.1 month. In Group B, the mean age was 52 (range 22-76); there were 22 males and 19 females. The mean duration on dialysis was 63.2 months (**Table 1 & 2**). At the beginning of the study period and weekly thereafter the following parameters were measured; hemoglobin level, predialysis systolic blood pressure (SBP) and diastolic blood pressure (DBP), post dialysis SBP and DBP, intradialytic weight gain, urea clearance ratio (Kt/V), any event of hypotension (defined as drop in BP requiring saline infusion), urea reduction ratio (URR), incidence of clotting of dialyzer (by inspection), incidence of any symptoms reported by the patient, during dialysis.

Statistics. For comparing parametric means, paired Student t test was used and for non-parametric variables, Chi square test was used. The 2 periods of study in group A were compared, and 2 periods of study in group B were compared.

Results. ***Intradialytic weight gain.*** There was no difference in interdialytic mean weight gain seen at any of the weeks.

Predialysis systolic blood pressure and diastolic blood pressure. No difference was noted between the group treated with the vitamin E coated dialyzer and the group treated with F60 in all the 4 weeks of observation.

Table 1 - Clinical details of patients.

Variables	Group A	Group B
Mean age (years)	61.52	51.97
Range	26-90	22-76
Mean session length (hrs)	3.47	3.46
Mean frequency	2.911	2.92
Mean dialysis duration (months)	62.11	63.17
n of patients on anti hypertension	8 (23.5)	13 (31.7)
n of patient on twice a week dialysis	3 (8.8)	3 (7.3)
n of patients on 3 times a week dialysis	31 (91)	38 (93)

Table 2 - Comparison of Fresenius 60 (F60) and Vitamin E dialyzers (EE12) in the 4 week study. (Combining group A and group B).

Parameters	(EE12) Mean ± SD	(F60)	p.value
1st week			
Weight gain	2.17 ± 1.2	2.14 ± 1.2	0.44
Pre dx B.p/s	153 ± 27	151 ± 25	0.35
Pre dx Bp/d	78 ± 15	79 ± 14	0.29
Post Bp/s	135 ± 23	138 ± 24	0.28
Post Bp/d	71 ± 15	72 ± 12	0.43
Hgb	11.8 ± 1.46	11.8 ± 1.4	0.39
Kt/V	1.37 ± 0.2	1.36 ± 0.34	0.41
URR	68 ± 6	67 ± 8.7	0.71
2nd week			
Weight gain	2.22 ± 1.1	2.26 ± 1.22	0.39
Pre dx B.p/s	151 ± 27	155 ± 26	0.15
Pre dx B.p/d	79 ± 15	80 ± 13	0.29
Post Bp/s	142 ± 27	144 ± 24	0.34
Post Bp/d	74 ± 13	74 ± 12	0.47
Hgb	11.79 ± 1.46	11.78 ± 1.35	0.48
Kt/V	1.46 ± 0.32	1.36 ± 0.28	0.03
URR	70 ± 7.21	67 ± 7.7	0.02
3rd week			
Weight gain	2.4 ± 1.27	2.37 ± 1.24	0.31
Pre dx B.p/s	156 ± 30	154 ± 28	0.39
Pre dx B.p/d	80 ± 15	81 ± 13	0.46
Post Bp/s	139 ± 29	137 ± 21	0.32
Post Bp/d	72 ± 14	73 ± 12	0.47
Hgb	11.9 ± 1.5	11.77 ± 1.44	0.27
Kt/V	1.42 ± 0.25	1.33 ± 0.28	0.022
URR	69.25 ± 6.74	66 ± 7.67	0.027
4th week			
Weight gain	2.45 ± 1.24	2.28 ± 1.27	0.27
Pre dx B.p/s	156 ± 24.82	152 ± 28.91	0.23
Pre dx B.p/d	81.6 ± 15.61	82 ± 15.82	0.44
Post Bp/s	140 ± 21.80	139 ± 27.98	0.38
Post Bp/d	75 ± 12.05	73 ± 12.65	0.20
Hgb	11.80 ± 1.45	12.02 ± 1.32	0.16
Kt/V	1.6 ± 0.26	1.39 ± 0.24	0.19
URR	67.25 ± 7.45	68.49 ± 6.74	0.14

Vitamin E dialyzers - EE12, dx B.p/s - dialysis systolic blood pressure
dx B.p/d - dialysis diastolic blood pressure

Table 3 - Intradialytic symptoms.

Symptoms	Group A (EE12)	Group A (F60)	p value	Group B (F60)	Group B (EE12)	p value
n of dialysis session	388	388		482	476	
No clotting	379	387		482	471	
Clotting	9	1	0.02	0	5	0.03
Hypotension	11 (32.3)	4 (11.8)	NS	14 (34.1)	3 (7.3)	0.007
Headache	1	0	NS	1	0	NS
Leg cramps	0	0	NS	5	0	0.031
Chest pain	1	0	NS	1	0	NS
Abdominal pain	0	1	NS	1	0	NS
Itching	0	0	NS	7	0	0.02
Vomiting	0	1	NS	0	0	NS

EE12 - Vitmain E dialyzers, F60 - Fresenius

Post dialysis systolic blood pressure and diastolic blood pressure. There was no difference seen between the 2 study periods.

Hemoglobin. No statistical difference was seen here during any of the weeks.

Urea clearance ratio. Urea clearance ratio was similar in the 2 dialyzers except at the end of the second and third weeks when it was higher in the vitamin E treated group (1.46 versus 1,36 ($p<0.3$) and 1.4 versus 1.33 ($p< .02$).

Urea reduction ratio. Again, the mean URR was significantly higher with EE12 compared to F60 only in the second and third weeks (70 versus 67 ($p<.02$) and 69.2 versus 66 ($p<.027$).

Other parameters measured (Table 3). The hypotensive episodes noted were significantly more with F60 than EE12 in Group B only (P.007)). There were more incidences of cramps with F60 in Group B only (P .031) and itching (P.02) (although this happened in only one patient). No difference was noted in the incidence of headaches, chest pain, abdominal pain or vomiting.

Discussion. Previous clinical studies have shown less clotting with the requirement of lesser doses of heparin and erythropoietin (EPO);[4] and fewer incidences of acute intra-dialytic symptoms with the use of vitamin-E modified dialyzers. The many symptoms encountered on dialysis are not only causing for discomfort for the patient but may reduce efficiency of dialysis though non-compliance and hypotensive episodes. The causes are multifactorial but have been thought to be due to the incompatibility of the membrane used and its structure. Polysulphone membranes are synthetic membranes with a significant degree of compatibility and efficiency and have been shown to improve morbidity and mortality rates.[9] They have also been shown to reduce inflammatory reaction, which may have short and long term adverse sequalae.[9] Vitamins E dialyzers are new dialyzers, which have been shown to be biocompatible. Reports have shown that it reduces cytokines and frees oxygen radical production.[10] Recent reports have also shown them to reduce less clotting, less intradialytic symptoms[3] and improve Hb level with significant reduction in erythropoietin dose.[4] Our study showed no significant difference in the dialysis adequacy (in terms of Kt/V or URR) between the 2 dialyzers, although the vitamin E coated dialyzer was slightly superior at the end of the second and third weeks. We have not seen previous reports documenting this transient advantage of vitamin E coated dialyzers. It would have been interesting to see whether this is related to differences, over the 4 weeks period, of free oxygen radicals or cytokines production. It would also have been useful to have carried out sensitive clotting studies over the 4 weeks to see whether changes in these can explain this transient advantage. We found the hemoglobin levels not to be different, unlike other reports,[4] which showed improvement with vitamin E dialyzers. However, even in their report this did not reach significant levels.

Interestingly, the hypotensive episodes are significantly less with vitamin E dialyzers throughout the study and this may be related to less production of vasodilator substances with the use of this dialyzer. Similarly, the interdialytic weight gain showed a tendency to be less with this dialyzer, which may be related to less thirst stimulation by less production of thirst initiating substances. If these findings are confirmed, it may be that vitamin E dialyzers have a definite place in patients with recurrent hypotensive

episodes during dialysis and in those with excessive interdialytic weight gain. However, we should point out that we have not measured cytokine levels; complement activation or other mediators that may well have a bearing on these findings. There are, however, plenty of reports, which confirm that there is, reduced free oxygen radicals and cytokine production.[8] There was no difference in terms of pre or post dialysis diastolic or systolic BP. Although it was reported that there is a tendency for less clotting with vitamin E, dialyzer[4] this did not reach significant level when compared to F60[4] and we did not find this. We found the occurrence of clotting was less with F60 although it was still low with the vitamin E dialyzer (1.6% of all dialysis sessions). Generally, however, our findings show that there are no significant differences between the 2 dialyzers at 4 weeks.

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Title: The use of biocompatible membrane (an 69) dialyzers in chronic hemodialysis patients: a preliminary report

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Abstract

Biocompatible membranes produce less biological reactions during hemodialysis than cuprophane. However, there is still some controversy whether the use of biocompatible membrane results in less morbidity in chronic stable dialysis patients. We performed a prospective study of seven such patients who were on regular dialysis for at least two years. For the first year of the study the patients remained on cuprophane dialysis and for the subsequent year they were switched on to the biocompatible membrane, polyacrylonitrile (an 69). Otherwise, the dialysis technique was identical in both periods. Clinical, radiological and laboratory parameters including b2-microglobulin levels were observed in the two phases of the study. During dialysis with the an 69 membrane a better tolerance of the hemodialysis treatment and less intradialytic hypotensive episodes were found compared to the cuprophane period. Also bone and joints symptomatology and admission days were less, while the hemoglobin level was higher resulting in lesser blood transfusion requirement in the an 69 period. However, the radiological bone abnormalities and the serum b2-microglobulin concentrations remained unchanged. The use of biocompatible membranes is associated with a lower rate of adverse hemodialysis incidents, admission days and blood transfusions. These benefits counterbalance the higher cost of these dialyzers.