Hong Kong Journal of Nephrology
2001;3(1):21-26.

ORIGINAL ARTICLE

On-line hemodiafiltration and high-flux hemodialysis: comparison of efficiency and cost analysis

Hon-Lok TANG, Wai-Kay TSANG, Ka-Shun FUNG, Candic TANG, Hilda Wai-Han CHAN, Kwok-Lung TONG
Division of Nephrology, Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong.

Abstract

With on-line hemodiafiltration (HDF), low molecular weight substances are predominantly cleared by diffusion while middle molecules such as ß$_2$-microglobulin (ß$_2$M), an amyloidogenic factor, are removed mainly by convection. The objectives of this study are to evaluate the cost-effectiveness and safety of on-line HDF with dialyzer reuse, and to compare HDF and high-flux hemodialysis (HD) with respect to ß$_2$M removal, urea kinetics (Kt/V) and symptom relief in those patients having dialysis-related amyloidosis. Ten chronic HD patients were put on post-dilution HDF for a period of 14.2 ±7.1 months. The AK 100 ULTRA system was used for on-line preparation of substitution fluid. These patients were then switched over to high-flux HD for a period of 4.6 ±3 months. Dialyzers were reused up to 30 times to reduce the cost of HDF. All the patients were hemodynamically stable during both HDF and high-flux HD treatments. No febrile reactions were reported. The percentage reduction of ß$_2$M during HDF was significantly higher when compared with high-flux HD (75 ±4% vs 51 ±7%, p < 0.001). After 14.2 ±7.1 months of HDF, the patients had significant reduction of both the pre-dialysis ß$_2$M level (47.4 ±7.9 µg/mL vs 28.2 ±4.9 µg/mL, p < 0.01) and post-dialysis ß$_2$M level (11.4 ±2.8 µg/mL vs 6.8 ±1.0 µg/mL, p < 0.01). eKt/V achieved by HDF was significantly higher than that achieved by high-flux HD (1.94 ±0.26 vs 1.75 ±0.23, p < 0.01). Those patients with dialysis arthropathy and carpal tunnel syndrome had decreased joint pain and hand numbness respectively after putting on HDF but symptoms recurred while on high-flux HD. There were no statistical significant differences in the percentage reduction of ß$_2$M, ß$_2$M clearance, urea clearance and eKt/V with dialyzer reuse, and no adverse patient reactions had been recorded.

Conclusions: On-line HDF has been proven to be a safe and reliable treatment. The clearance of ß$_2$M and urea are significantly increased by HDF when compared with high-flux HD, and the increase in clearance of ß$_2$M is sustained throughout the HDF treatment period. Symptoms of dialysis-related amyloidosis are improved by HDF. Dialyzer reuse, which reduces the cost of HDF by 30%, is feasible and safe.

Key words: ß$_2$-microglobulin (ß$_2$M), Hemodiafiltration (HDF), High-flux hemodialysis (HD), Kt/V

中文摘要

當進行在線血液透析濾過（HDF）時，低分子量物質主要由擴散來清除，而中分子量物質如ß$_2$-微球蛋白（ß$_2$M），一種導致澱粉樣變性的因數，則主要通過對流來清除。本研究的目的是評價重複使用透析器的HDF治療的安全性及其費用──療效關系，並且比較HDF和高流量血液透析（HD）對有透析誘導的澱粉樣變性骨關節病的病人的ß$_2$M清除、尿素清除指數（Kt/V）和症狀緩解的效果。十個長期血液透析（HD）病人先用後稀釋法HDF治療14.2 ± 7.1月。置換液用AK 100 ULTRA系統來準備。這些病人然後再使用高流量HD治療4.6 ± 3月。透析器重復使用最多達30次以便減少HDF的費用。所有的

Correspondence: *Dr. Hon-Lok TANG, Department of Medicine and Geriatrics, Princess Margaret Hospital, 2-10 Princess Margaret Hospital Road, Lai Chi Kok, Kowloon, Hong Kong. Fax: (852) 2741 0752, E-mail: tongkl@ha.org.hk*

病人在HDF和高流量HD治療期間血液動態學指標處於穩定狀態。沒有發熱反應。$ß_2M$下降的百分率在用HDF治療比高流量HD治療顯著要高（75 ± 4% 對 51 ± 7% ， $p < 0.001$）。HDF治療14.2 ± 7.1月後，病人的透析前$ß_2M$（47.4 ± 7.9微克 / 毫升對28.2 ± 4.9微克 / 毫升， $p < 0.01$）和透析後$ß_2M$（11.4 ± 2.8微克 / 毫升對6.8 ± 1.0微克 / 毫升， $p < 0.01$）水平均有明顯下降。HDF治療後的eKt/V比高流量HD顯著高（1.94 ± 0.26對1.75 ± 0.23 ， $p < 0.01$）。HDF治療後有透析性關節病和腕骨綜合症的病人的關節痛和手麻木明顯減輕，而轉為高流量HD後以上症狀再次出現。透析器的重複使用對$ß_2M$下降百分率、$ß_2M$清除、尿素清除和eKt/V變化沒有統計學差異，病人無不適投訴。

結論：HDF被証實是一種安全可靠的治療方法。與高流量HD相比，HDF顯著地增加$ß_2M$和尿素的清除，並且在HDF治療過程中$ß_2M$的高清除率持續存在。透析有關的澱粉樣變性導致的症狀在HDF治療過程減輕。透析器重複使用使得費用降低30%並且是可行的和安全的。

INTRODUCTION

Hemodiafiltration (HDF) as a blood purification method is a combination of hemodialysis (HD) and hemofiltration. HD is a transport process by which a solute passively diffuses down its concentration gradient from one fluid compartment to another. Hemofiltration refers to use of a hydrostatic pressure gradient to induce the convection of plasma water across the membrane of the hemofilter. The frictional force between water and solutes, which is called solvent drag, results in the convective transport of solutes in the same direction as water. HDF therefore removes toxins by convection in addition to diffusion. The rate of solute transport by diffusion decreases more rapidly with increasing size of molecules than that by convection (1). Theoretically, middle molecules such as $ß_2$-microglobulin ($ß_2M$) are therefore better removed by convection.

The AK 100 ULTRA (Gambro, Lund, Sweden) is a system for HD, hemofiltration and HDF using on-line prepared bicarbonate dialysate and substitution solution. After being prepared from reverse osmosis water, the fluid is pre-filtered through a U8000 ultrafilter (2.2 m^2 polyamide, Gambro, Lund, Sweden) before entering the machine. A (acidic)- and B (bicarbonate)-concentrates are then added to the fluid. To ensure a high level of microbiological quality, the bicarbonate solution is prepared from a dry powder, BiCart® (Gambro, Lund, Sweden). This prepared fluid is filtered through a second U8000 ultrafilter and is used as sterile dialysate in HD and HDF treatments. The substitution fluid required for hemofiltration and HDF treatments is filtered through a third, final U2000 ultrafilter (0.2 m^2 polyamide, Gambro, Lund, Sweden) before being infused into the patient's blood line. To ensure a high microbiological quality of the fluid, the machine is filled with peracetic acid when not in use during nights and weekends. The two U8000 ultrafilters are included in the disinfection loop and replaced every 2 weeks. The final U2000 filter is disposable together with the infusion line.

The primary aim of the study was to evaluate the cost-effectiveness and safety of the AK 100 ULTRA system for on-line preparation of substitution fluid and HDF treatment with dialyzer reuse. The secondary aim was to compare HDF and high-flux HD with respect to $ß_2M$ removal, urea kinetics (Kt/V) and symptom relief in those patients having dialysis-related amyloidosis.

PATIENTS AND METHODS

A prospective cross-over study was performed on 10 chronic HD patients (5 females and 5 males) with a mean duration of HD of 10.1 ±6.1 years. Six of them had been put on continuous ambulatory peritoneal dialysis for a mean duration of 11.6 ±17.3 months before conversion to chronic HD. Their mean age was 40.2 ±7.8. Four of the patients had proven dialysis-related amyloidosis by magnetic resonance imaging. Three of them had involvement of the shoulder joints and one had involvement of both the shoulder and wrist joints. All of them were symptomatic with arthralgia over the involved joints. Three of these four patients also had documented carpal tunnel syndrome secondary to dialysis-related amyloidosis. All of them had release operations performed but symptom of hand numbness recurred after operation. These four patients with dialysis-related amyloidosis had been receiving chronic HD for a mean duration of 15 ±2.6 years.

The 10 patients were put on post-dilution HDF using the AK 100 ULTRA on-line system for a period of 14.2 ±7.1 months. The mean blood flow rate was 249 ±13 mL/minute and the mean infusion volume of substitution fluid was 18.9 ±1.3 L per HDF treatment. They were then switched over to high-flux HD for a period of 4.6 ±3 months with a mean blood flow rate of 241 ±24 mL/minute. The same dialysis machine was used during the high-flux HD period. There was no significant difference in the mean blood flow rate between the two modes of dialysis treatment ($p = 0.134$). All the patients were receiving dialysis twice weekly with duration of 5 hours

per session for both modes of treatment. All the treatments were performed with high-flux dialyzer (F60S, Fresenius Medical Care, Bad Homburg, Germany), made of synthetic membrane, polysulfone, with a surface area of 1.3 m^2. The prescribed substitution fluid composition (in mmol/L) was: sodium 135 to140, potassium 2, calcium 1.75, magnesium 0.5, chloride 109.5, bicarbonate 30 to 35, acetate 3. The temperature of the substitution fluid was kept at 37 ^oC during all the dialysis treatments. The dialysate flow rate was set at 500 mL/minute. The treatment time, number of treatments per week, type of dialyzer and dialysate flow rate were kept unchanged during the whole study period.

Blood pressure, heart rate, body temperature and body weight were recorded before and after treatment. Pre-dialysis blood samples were collected monthly for analysis of blood chemistries. Blood samples for assay of $ß_2M$ and urea levels were obtained pre-dialysis and 30 minutes post-dialysis at monthly interval. The percentage reduction of $ß_2M$ was calculated from the pre- and post-dialysis levels. The pre-dialysis and post-dialysis $ß_2M$ levels before and after the HDF period, and after the high-flux HD period were recorded. Equilibrated Kt/V (eKt/V) was computed from the pre and post-dialysis urea levels using the Daugirdas second generation equation (2):

$$eKt/V = - \ln (Ct/Co - 0.008\ t) + (4 - 3.5\ Ct/Co) \times UF/W$$

Co = pre-dialysis urea level, mmol/L
Ct = equilibrated post-dialysis urea level, mmol/L
t = time of dialysis, hour
UF = ultrafiltration volume, L
W = post-dialysis body weight, kg

The equilibrated post-dialysis urea level was sampled at 30 minutes after the end of dialysis. Symptoms of dialysis arthropathy (joint pain) and carpal tunnel syndrome (hand numbness) were evaluated before the commencement of HDF, at the end of HDF treatment period and at the end of high-flux HD period by using questionnaires.

During the period of high-flux HD, the polysulfone dialyzers were reused up to 30 times to reduce the cost of the dialysis treatment. The percentage reduction of $ß_2M$, $ß_2M$ clearance, urea clearance and eKt/V during the first use of dialyzer were compared with that during the thirtieth use of dialyzer. The $ß_2M$ clearance and urea clearance were computed as the blood flow rate times the percentage reduction across the dialyzer in the plasma solute ($ß_2M$ or urea) concentration (3). The percentage reduction of $ß_2M$ or urea level across the dialyzer was obtained by sampling the dialyzer inlet and dialyzer outlet blood levels. The blood flow rate was maintained the same during the first use and the thirtieth use of dialyzer. The disinfectant used for dialyzer reprocessing was Renalin® PA Cold Sterilant (Minntech Renal Systems, Minneapolis, U.S.A.) which contains 20% of hydrogen peroxide, 4% of peracetic acid and 76% of inert ingredients. The Renatron® Automated Dialyzer Reprocessing System (Minntech Renal Systems, Minneapolis, U.S.A.) was used for reprocessing of dialyzer.

Fluid samples for microbiological evaluation were collected every 2 weeks from two different positions of the AK 100 ULTRA system: position 1: after the first U8000 ultrafilter; position 2: after the second U8000 ultrafilter at the infusion port. Fluid samples were cultivated on Tryptone Glucose Extract Agar for 7 days at 22 ^oC.

The paired Student's *t*-test was used to compare the mean percentage reduction of $ß_2M$ and eKt/V between HDF and high-flux HD, and the mean body temperature before and after HDF/high-flux HD treatment. The non-parametric Wilcoxon Signed Ranks test was used to compare the mean pre-dialysis and post-dialysis $ß_2M$ level before and after the HDF treatment period, and after the high-flux HD period. The test was also used to compare the mean percentage reduction of $ß_2M$, $ß_2M$ clearance, urea clearance and eKt/V between the first use and thirtieth use of the dialyzer.

RESULTS

The hemodynamic parameters: blood pressure, heart rate and body temperature were all stable during both the HDF period (Table 1) and the high-flux HD period (Table 2). There were no hypotensive episodes or febrile reactions during both periods. There was no significant difference in body temperature before and after the dialysis session during both the HDF period ($p = 0.684$) and the high-flux HD period ($p = 0.362$) (Table 1,2). Changes in body weight were in the expected ranges for a session of dialysis treatment. All the patients tolerated

Table 1. Patient parameters, HDF period (Mean ±SD, n = 30).

	SBP (mmHg)	DBP (mmHg)	Heart Rate (beats/min)	Body temperature (^oC)	BW (kg)
Pre-treatment	158 ±12	87 ±12	78 ±15	36.4 ±0.3	49.3 ±6.3
Post-treatment	149 ±21	84 ±12	77 ±14	36.5 ±0.3	46.6 ±6.3

Table 2. Patient parameters, high-flux HD period (Mean ±SD, n = 30).

	SBP (mmHg)	DBP (mmHg)	Heart Rate beats/min	Body temperature (^oC)	BW (kg)
Pre-treatment	139 ±21	76 ±13	75 ±13	36.5 ±0.3	49.4 ±6.4
Post-treatment	143 ±20	81 ±13	77 ±14	36.5 ±0.4	46.8 ±6.5

Table 3. $ß_2M$ % reduction and urea kinetics (eKt/V) (Mean ±SD, n = 30).

	HDF	High-flux HD	*p* value
$ß_2M$ % reduction	75 ±4	51 ±7	< 0.001
eKt/V	1.94 ±0.26	1.75 ±0.23	< 0.01

both types of treatment well. All the blood chemistries remained stable during the study period.

The percentage reduction of $ß_2M$ during HDF and high-flux HD are shown in table 3. The percentage reduction of $ß_2M$ during HDF was significantly higher when compared with high-flux HD (75 ±4% vs 51 ±7%, $p < 0.001$). After 14.2 ±7.1 months of HDF, the pre-dialysis $ß_2M$ level was significantly reduced (47.4 ±7.9 μg/mL vs 28.2 ±4.9 μg/mL, $p < 0.01$) (Table 4). The post-dialysis level was also significantly decreased (11.4 ±2.8 μg/mL vs 6.8 ±1 μg/mL, $p < 0.01$) (Table 4). However, after switching over to high-flux HD for a period of 4.6 ±3 months, the pre-dialysis $ß_2M$ level increased back to 33.3 ±4 μg/mL ($p < 0.05$) and the post-dialysis level increased back to 11.3 ±2.5 μg/mL ($p < 0.01$) (Table 5). With regard to urea kinetics, the eKt/V achieved by HDF was significantly higher than that achieved by high-flux HD (1.94 ±0.26 vs 1.75 ±0.23, $p < 0.01$) (Table 3).

All the four patients with dialysis arthropathy had decreased joint pain after being on HDF for 20 ±5.8 months but symptoms recurred when switching to high-flux HD. Three of these patients also had a recurrence of carpal tunnel syndrome after release operation. All of them had improvement in hand numbness while on HDF but symptoms relapsed after conversion to high-flux HD.

With dialyzer reuse, there were no significant differences in percentage reduction of $ß_2M$, $ß_2M$ clearance, urea clearance and eKt/V during the first use and the thirtieth use of dialyzer (Table 6). No adverse patient reactions had been reported during dialyzer reuse. By reusing the polysulfone dialyzer 30 times, the cost of HDF can be reduced by 30%. Table 7 shows the reduction of the costs of HDF and high-flux HD with reuse of polysulfone dialyzer three, six and 30 times.

Microbiological analysis of the substitution fluid from two different positions of the system revealed that only five out of 55 fluid samples from position 1 had positive culture. Positive culture was expressed as number of colony forming unit (CFU) per 1000 mL substitution fluid. Amount the five positive cultures, the maximum value was only 3 CFU/1000 mL. No positive culture was found in 57 fluid samples from position 2. The high quality of the substitution fluid was also reflected by the absence of febrile reactions or adverse events during HDF treatment in all the patients.

DISCUSSIONS

In Hong Kong, similar to most Asian countries, the organ donation rate is low. More than 1000 end-stage renal failure patients were on the waiting list for renal transplant. Many of these patients stayed on dialysis for many years. From the data of the Hong Kong Renal Registry, as of 31 March 1999, there were 3066 patients on dialysis. Among these 3066 dialysis patients, 13% were receiving chronic HD (4). These patients were prone to develop long-term complications of chronic HD. Dialysis-related amyloidosis is one of these long-term

Table 4. Pre-dialysis and post-dialysis $ß_2M$ levels after 14.2 ±7.1 months of HDF (Mean ±SD, n = 10).

	At the start of HDF period	At the end of HDF period	*p* value
Pre-dialysis $ß_2M$ level, μg/mL	47.4 ±7.9	28.2 ±4.9	< 0.01
Post-dialysis $ß_2M$ level, μg/mL	11.4 ±2.8	6.8 ±1.0	< 0.01

Table 5. Pre-dialysis and post-dialysis $ß_2M$ levels after 4.6 ±3.0 months of high-flux HD (Mean ±SD, n = 10).

	At the end of HDF period	At the end of high-flux HD period	*p* value
Pre-dialysis $ß_2M$ level, μg/mL	28.2 ±4.9	33.3 ±4.0	< 0.05
Post-dialysis $ß_2M$ level, μg/mL	6.8 ±1.0	11.3 ±2.5	< 0.01

Table 6. Reuse of dialyzer (Mean ±SD, n = 10).

	First use of dialyzer	30th use of dialyzer	*p* value
$ß_2$M % reduction	54 ±6	53 ±5	0.445
$ß_2$M clearance (mL/min)	49 ±15	47 ±9	0.959
Urea clearanc (mL/min)	211 ±18	208 ±18	0.721
eKt/V	1.80 ±0.17	1.72 ±0.28	0.445

Table 7. Reduction of cost of HDF by reusing dialyzer.

	Cost of one session dialysis treatment (HK$)		
Number of dialyzer reuse	**HDF**	**High-flux HD**	**Conventional HD**
Single use	780	724	388
3 times	626	570	
6 times	581	525	
30 times	545	489	
	(30% cost reduction)		

complications. A prospective postmortem study has detected joint amyloid deposition in 21% of patients requiring HD for less than 2 years, 50% at 4 to 7 years, 90% at 7 to 13 years, and 100% at more than 13 years (5). For clinical symptomatic disease, the prevalence was 0% at 5 years but increased to approximately 50% at 12 years, and was almost 100% at 20 years (6). $ß_2$M has been shown to be the major component of amyloid deposits in dialysis-related amyloidosis (7) and plays an important role in the pathogenesis of dialysis-related amyloidosis (8-11).

HDF, which removes toxins by convection in addition to diffusion, has been shown to remove $ß_2$M more efficiently then HD (12-14). In this regard, our study has demonstrated a better removal of $ß_2$M by HDF when compared with high-flux HD. In addition, we also demonstrated a sustained reduction of $ß_2$M throughout the HDF treatment period as evidenced by the decline in both the pre-dialysis and post-dialysis levels after the HDF treatment period. This reduction of $ß_2$M during the HDF period was attenuated after switching over to high-flux HD. HDF also resulted in better clearance of small molecules such as urea when compared with high-flux HD as shown by a significantly higher eKt/V achieved by HDF than that achieved by high-flux HD. Kim et al had demonstrated a significant improvement in shoulder pain secondary to dialysis-related amyloidosis when $ß_2$M were efficiently removed during post-dilution HDF (13). For those patients with symptomatic dialysis-related amyloidosis, our study has shown that HDF was superior to high-flux HD in alleviating the joint pain of dialysis arthropathy and hand numbness of carpal tunnel syndrome. On-line HDF was well tolerated by all the patients in the study as reflected by their stable hemodynamic parameters and the absence of febrile reactions during treatment.

Today only a limited number of patients in Hong Kong are treated with HDF, mainly because of the cost of the substitution solution and dialysis consumables. The on-line production of substitution solution is a major breakthrough in the reduction of cost. However, the expensive high-flux dialyzers and bacterial ultrafilters are the other factors that hinder the development of a large-scale HDF program. In Hong Kong, only less than 2% of the HD patients were put on HDF. Reuse of dialyzers can reduce the cost of dialysis while achieving an acceptable quality of both small molecule and middle molecule clearance. We have found no significant differences in the percentage reduction of $ß_2$M, $ß_2$M clearance, urea clearance and eKt/V with dialyzer reuse. The reduction of consumable cost of on-line HDF is around 30% by reusing dialyzer up to 30 times.

CONCLUSIONS

HDF with on-line preparation of bicarbonate dialysate and substitution solution by the AK 100 ULTRA system has been proven to be a safe and reliable treatment in patients with end-stage renal disease. Reuse of dialyzer increases the cost-effectiveness of on-line HDF. No adverse patient reactions have been recorded during HDF treatment and dialyzer reuse. The substitution fluid has been shown to be of excellent microbiological quality. HDF has a definite advantage over high-flux HD in terms of $ß_2$M removal and urea kinetics (Kt/V). It is more efficient than high-flux HD in alleviating the symptoms of dialysis arthropathy and carpal tunnel syndrome in chronic HD patients with established dialysis-related amyloidosis.

Acknowledgment

The authors would like to thank the Gambro (China) Limited for the partial sponsorship of this study.

REFERENCES

1. Renkin EM. Filtration, diffusion, and molecular sieving through porous cellulose membranes. J Gen Physiol 1954;38:225-243.
2. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: An analysis of error. J Am Soc Nephrol 1993;4:1205-1213.
3. Daugirdas JT, Van Stone JC. Hemodialysis: Physiologic principles and urea kinetic modeling. In: Daugirdas JT, Blake PG, Ing TS, eds. Handbook of Dialysis. Philadelphia: Lippincott Williams & Wilkins; 2001;15-45.
4. Lui SF, Ho YW, Chau KF, Leung CB, Choy BY. Hong Kong Renal Registry 1995-1999. Hong Kong J Nephrol 1999;1:53-60.
5. Jadoul M, Garbar C, Noel H, Sennesael J, Vanholder R, Bernaert P, Rorive G, Hanique G, van Ypersele de Strihou C. Histologic prevalence of beta2-microglobulin amyloidosis in hemodialysis: a prospective post-mortem study. Kidney Int 1997;51:1928-1932.
6. Koch KM. Dialysis-related amyloidosis. Kidney Int 1992;41:1416-1429.
7. Gejyo F, Odani S, Yamada T, Honma N, Saito H, Suzuki Y, Nakagawa Y, Kobayashi H, Maruyama Y, Hirasawa Y. $ß_2$-Microglobulin: a new form of amyloid protein associated with chronic hemodialysis. Kidney Int 1986;30:385-390.
8. Miyata T, Ingai R, Iida Y, Sato M, Yamarh N, Oda O, Maeda K, Seo H. Involvement of $ß_2$-microglobulin modified with advanced glycation end products in the pathogenesis of hemodialysis-associated amyloidosis: Induction of human monocyte chemotaxis and macrophage secretion of tumour necrosis factor alpha and interleukin-1. J Clin Invest 1994;93:521-528.
9. Iida Y, Miyata T, Inagi R, Sugiama S, Maeda K. $ß_2$-microglobulin modified with advanced glycation end products induces interleukin-6 from human macrophages: Role in the pathogenesis of hemodialysis-associated amyloidosis. Biophy Res Commun 1994; 201:1235-1241.
10. Miyata T, Iida Y, Ueda Y, Shinzato T, Seo H, Monnier VM, Maeda K, Wada Y. Monocyte/macrophage response to $ß_2$-microglobulin modified with advanced glycation end products. Kidney Int 1996; 49:538-550.
11. Miyata T. New aspects in the pathogenesis of dialysis-related amyloidosis: Pathophysiology of advanced glycation end products in renal failure. Nippon Jinzo Gakkai Shi 1996;38:191-197.
12. Shinzato T, Kobayakawa H, Maeda K. Comparison of various treatment modes in terms of beta 2-microglobulin removal: Hemodialysis, hemofiltration, and push/pull HDF. Artif Organs 1989; 13:66-70.
13. Kim ST, Yamamoto C, Asabe H, Sato T, Takamiya T. On-line haemodiafiltration: Effective removal of high molecular weight toxins and improvement in clinical manifestations of chronic haemodialysis patients. Nephrology 1996;2:S183-S186.
14. Lornoy W, Becaus I, Billiouw JM, Sierens L, van Malderen P. Remarkable removal of beta-2-microglobulin by on-line hemodiafiltration. Am J Nephrol 1998;18:105-108.