What is the most suitable biomarker for evaluation of characteristics and benefits of HDF?

Kenji Sakurai[1], Takeshi Saito[1], Fumi Yamauchi[1], Ayumi Suzuki[1], Hiromi Hosoya[1], Naoko Maruyama[1], Yoshitaka Kurihara[1], Daisuke Ishii [2]

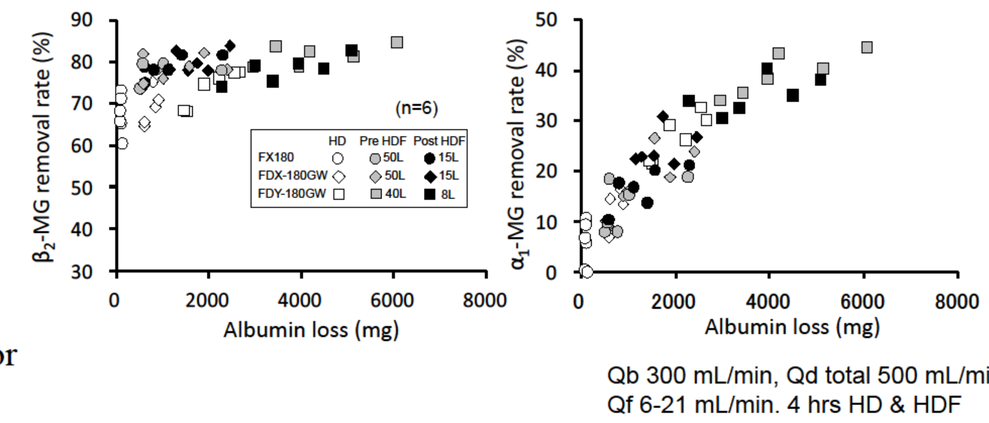
[1]Hashimoto Clinic, Kanagawa, Japan, [2] Kitasato University Hospital, Kanagawa, Japan

Introduction and aims

Hemodiafiltration (HDF) can effectively remove uremic toxins, ranging from small molecule to large molecule substances, by using a combination of diffusion and convection.

β_2-Microglobulin (β_2-MG) has a molecular weight (MW) of 11.8 kDa and is very efficiently removed mainly by diffusion with the super-high flux dialyzers or high flux dialyzers currently available in Japan. α_1-Microglobulin (α_1-MG) has a MW of 33 kDa, and its removal is achieved only by convection (right).

In the present study we investigated whether α_1-MG was the most suitable biomarker for evaluating the characteristics and benefits of HDF based on actual cases. We also evaluated the solute removal performance of three latest hemodiafilters by pre-dilution on-line HDF, and assessed the importance of α_1-MG as a biomarker.



Relation between removal rate of β_2-MG and α_1-MG and the amount of albumin loss. (Sakurai et al., EDTA, 2011)

Methods

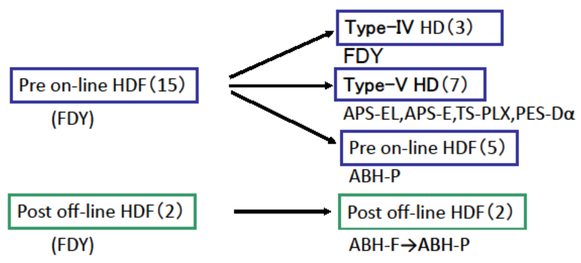
1) We changed the dialysis conditions to conform to the Japanese National Health Insurance conditions in 17 cases that had stabilized by HDF with a super high-flux dialyzer. In 10 of the cases we switched to hemodialysis (HD) with a super high-flux dialyzer, and in other 7 cases we switched to HDF with an approved hemodiafilter. The results one month after changing the dialysis conditions showed that the symptoms had worsened in 13 of the 17 cases. We changed the dialysis conditions again in the 13 cases in which the symptoms had worsened.

In 8 of the cases we changed to HDF with the super high-flux dialyzer that had been used before, and in the other 5 cases we changed to HD with a higher performance super high-flux dialyzer. The results one month after the changes showed that patient quality of life (QOL) had returned to its previous state. We then investigated the fluctuations in dialysis efficiency associated with these changes in symptoms based on small molecule substances (UN, Creat, P) and low molecular weight proteins (LMWPs: β_2-MG and α_1-MG).

2) We performed pre-dilution on-line HDF (4-hour/session) with three different types of hemodiafilters, i.e., TDF-20H, ABH-21P, and MXF-21U hemodiafilters, in 7 stable dialysis patients. We set the blood flow rate at 250 ml/min, the dialysate flow rate at 500 ml/min, and fluid replacement volume per session at 50 L. We assessed removal performance based on small molecule substances and LMWPs (β_2-MG; prolactin, α_1-MG, MW of prolactin:23 kDa).

Results

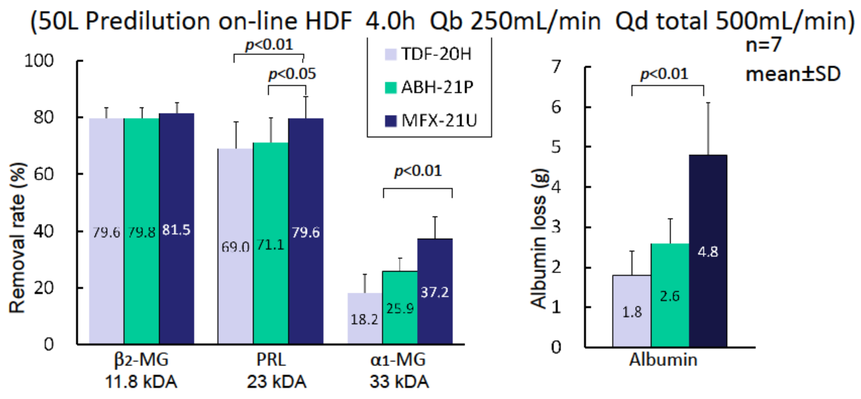
1) All 17 patients were in good conditions with HDF before switching treatment methods



After one month, general conditions in 13 out of 17 pts got worse

		Before		After	
	Kt/V	1.57	→	1.64	
Removal rate	β2-MG	78.5%	→	75.7%	····· - 3 point
	α1-MG	35.8%	→	25.5%	····· - 10 point

2) Comparison of removal performance of three hemodiafilters



2) Under the conditions that were set, the β_2-MG RR was a favorable 80% with all three types of hemodiafilters (amounts removed: TDF, 186 mg; ABH, 169 mg; MFX, 190 mg). However, there were significant differences in the α_1-MG RR: TDF, 18.2% (amount removed, 93 mg; ABH, 25.9% (amount removed: 126 mg); MFX, 37.2% (amount removed: 179 mg).

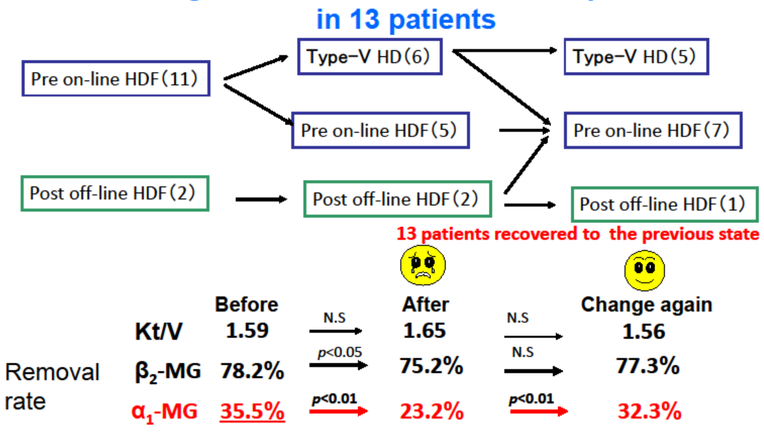
Patients symptoms after switching treatment methods

Dialysis Vintage of 13 pts : 21.0±10.1yrs

case	itchiness	bone /joint pain	decrease activity	Irritability	RLS
1	○	○	○	○	○
2			○		○
3	○		○	○	○
4			○		
5		○	○		
6		○			
7		○			
8	○	○	○		○
9		○	○		
10		○			
11		○			
12		○			
13	○	○			

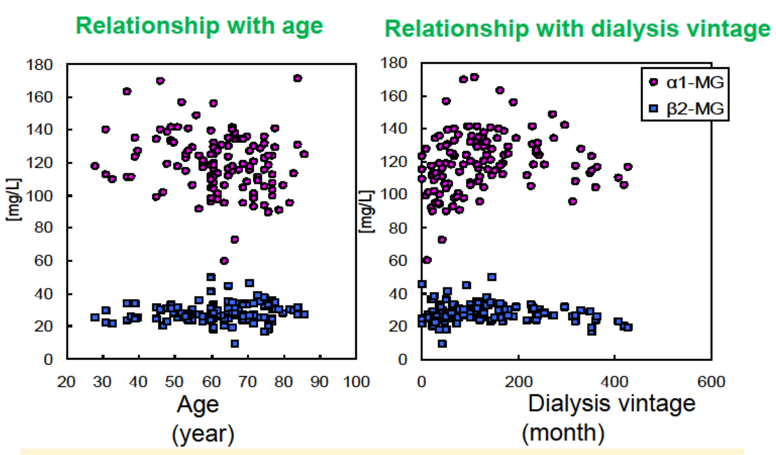
Bone/joint pain (+) group : Dialysis Vintage of 24.3±9.0 yrs

The changes in treatment and removal performance in 13 patients



1) Before the change in dialysis method in the 17 cases, the β_2-MG and α_1-MG removal rates were 78.5% and 35.8%, respectively. In the 13 cases in which the symptoms changed from "stable," to "worse," and then to "improved" α_1-MG removal rate (RR) changed significantly from 35.5%, to 23.2%, and then to 32.3% in tandem with the changes in symptoms, but the Kt/V values (1.59 → 1.65 → 1.56) and β_2-MG RRs (78.2% → 75.2% → 77.3%) fluctuated within only narrow ranges.

Relationshipof β2-MG and α1-MG (pre-dialysis values) with age and dialysis vintage



β2-MG: 27.8 ± 2.7 mg/L, α1-MG: 119.0 ± 17.9 mg/L (n=122 mean ± SD)

normal control (our clinic staff n=31); α1-MG:12.5±2.3mg/L β2-MG: 1.4±0.3 mg/L

Discussion

On-line HDF was officially approved for coverage by National Health Insurance in Japan in 2010, and four conditions for performing it were listed. The reason for changing the dialysis conditions in this study was to conform to those conditions.
There was a close correlation between the changes in symptoms and the changes in α_1-MG RR, and it appeared that the symptoms had worsened as a result of inadequate removal of uremic toxins having molecular weights around 30 kDa, and that the symptoms had improved because the removal efficiency of uremic toxins with molecular weights of around 30 kDa had increased. It was impossible to find out this trend only by the assessment of the β_2-MG removal efficiency alone.
The results of the evaluation of the removal efficiency of the three types of hemodiafilters showed that the differences among the removal performance of the hemodiafilters became more marked as the molecular weights increased from β_2-MG, to prolactin, and to α_1-MG. If the performance of these hemodiafilters were evaluated on the basis of β_2-MG alone, the results for all three types of hemodiafilters would be the same.

Conclusions

α_1-MG should be used as the biomarker for evaluation of the solute removal efficiency of HDF. When α_1-MG is used as the biomarker, it becomes possible to set suitable conditions, and the characteristics and benefits of HDF are fully utilized.

DOI: 10.3252/pso.eu.50era.2013