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Comparative Analysis of Therapeutic Effect Between Theranova® Dialyzer and High Flux Dialyzer Using OMICS

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Background
The survival rate of patients receiving hemodialysis treatment is low and a lot of efforts are needed to improve the prognosis. Recently, the novel medium cut-off (MCO) membrane, Theranova®, was developed and it is known to be able to remove the large middle molecular uremic toxin more effectively compared with conventional high flux dialyzer. This study was performed to analyze therapeutic effect of Theranova® compared with high flux dialyzer using metabolomics and proteomics.

Methods
This study was prospective pre-post intervention and dialysis schedule and time is implemented equally in each group. We conducted hemodialysis using Polyflux 170H® (high flux dialyzer) for four weeks and take the sample during mid-weekday of the fifth week (1st HF period). In the next week, we performed hemodialysis in the same way for four weeks using Theranova® and take the samples in the same way at 5th week (Theranova® period). lastly, In the next week, we performed hemodialysis using Polyflux 170H® and take the samples at 5th week (2nd HF period). Additionally, fetuin-A (51-67kDa), fibroblast growth factor-23 (FGF-23, 22.5kDa) and alpha1-microglobulin (A1M, 27kDa) were measured using ELISA and compared between two dialyzers.

Results
Large middle molecules such as A1M and FGF-23 were more effectively removed by Theranova® compared with HF (reduction ratio compared with 1st HF dialyzer: A1M, 41.4% vs. 3.2%, $p < 0.001$; FGF-23, 50.4% vs. 20.3%, $p < 0.001$). Fetuin-A is relatively large molecule and its removal was not increased by Theranova®. Pre-HD AIM concentration was decreased in Theranova® period and its effect was persistent to 2nd HF period. However, pre-HD FGF-23 and fetuin-A concentrations were not different among three groups. In metabolomic analysis, OPLS-DA result showed that metabolome characteristics can classify 1st HF and Theranova® group and its major contributor

metabolites were glycerol, phenylalanine, creatine phosphate, lactate, and histidine using pre-HD serum samples. The serum levels of pre-HD glycerol and creatine phosphate were decreased in Theranova® period compared to those in 1st HF period and its effect was persistent to 2nd HF period. There were no differences of creatine or creatinine concentration during study period. Serum phosphorus level was similar during study period (1st HF vs. Theranova® vs 2nd HF, 5.1 ± 1.4 vs 5.2 ± 1.2 vs 5.3 ± 1.8, respectively; *P* = 0.824). Kt/V_{urea} was not significantly different between study period (1st HF vs Theranova® vs 2nd HF, 1.86 ± 0.34 vs 1.92 ± 0.35 vs 1.85 ± 0.34, respectively; *P* = 0.222). The serum level of pre-HD phenylalanine was increased in Theranova® period compared to that in 1st HD period and its effect was persistent to 2nd HF period. In proteomic analysis, PLS-DA result showed that proteome characteristics can classify 1st HF vs. Theranova® group and its major contributor proteins were FETUB, C4A, RBP4, C4B and FN1 using pre-HD plasma samples. The plasma level of pre-HD FN1 in 1st HF period was higher than that in Theranova® period. On the contrary, The plasma level of pre-HD C4B and RBP4 in Theranova® period were higher than those in 1st HF period.

Conclusions

First, theranova® dialyzer has an excellent performance in removal of large middle molecule compared with high flux dialyzer. Second, in metabolomics analysis, glycerol, phenylalanine, creatine phosphate, lactate, and histidine significantly changed by theranova® compared to high flux dialyzer. Third, FN1, C4B and RBP4 were proteins that could define the character of Theranova® based on proteomic analysis results.

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study design