ORIGINAL RESEARCH

Effectiveness and Safety of HAEMOMASTER System in Hemodialysis Patients

Zhuojia Xu, MD; Guoyu Liang, MM; Yue Wang, MM; Kai Wang, BM

ABSTRACT

Objective • HAEMOMASTER system developed by NIKKISO is a feedback control technology that combines blood volume monitoring, which is now increasingly used in many dialysis centers. We investigated the effectiveness and safety of five slopes provided by HAEMOMASTER system.
Methods • Patients undergoing hemodialysis with the support of a blood volume monitor (BVM) were enrolled. The NIKKISO DBB-05 Hemodialysis machine had automatically recorded real-time data such as BV and BP. Data from the patients' previous 10 dialysis sessions were collected into the HAEMOMASTER system for data fitting and the calculated target ΔBV. Patients received dialysis treatment with five slopes of the HEAMOMASTER system. We record the actual ΔBV and reverse events of every slope. Relative index to ΔBV of different slopes and sub-analysis was conducted by two-variable Spearman correlation analysis.
Results • One hundred participants entered, and 78 completed the study. Slope1 and Slope2 had a lower incidence of adverse reactions (5.3% and 3.8%) and higher correlation coefficients (0.827 and 0.831, $P < .001$), which means they can reflect dialysis physiology better. HEAMOMASTER system helps the hemodialysis physician develop an optimal individual hemodialysis plan for the patient, reduce adverse effects such as hypotension ,obvious sweating, palpitation, fatigue, and the hemodialysis process is interrupted or the ultrafiltration volume being adjusted.
Conclusion • We evaluated the safety and effectiveness of the HAEMOMASTER System in hemodialysis patients. This study serves as a roadmap for the development and widespread use of the HAEMOMASTER system and a resource for the creation of novel biofeedback control strategies. The HAEMOMASTER system has good clinical application prospects in hemodialysis patients and can be used to develop individualized ultrafiltration schemes for patients and improve the comfort and safety of hemodialysis. Slope1 and Slope2 of HAEMOMASTER are more suitable for the majority of patients with a better fit to the actual physiological conditions and lower incidence of adverse events. (*Altern Ther Health Med.* [E-pub ahead of print.])

Zhuojia Xu, MD; Associate chief physician; **Guoyu Liang, MM;** Attending doctor; **Yue Wang, MM;** Attending doctor; **Kai Wang, BM;** Chief physician; Department of Nephrology, Civil Aviation General Hospital, Beijing, China.

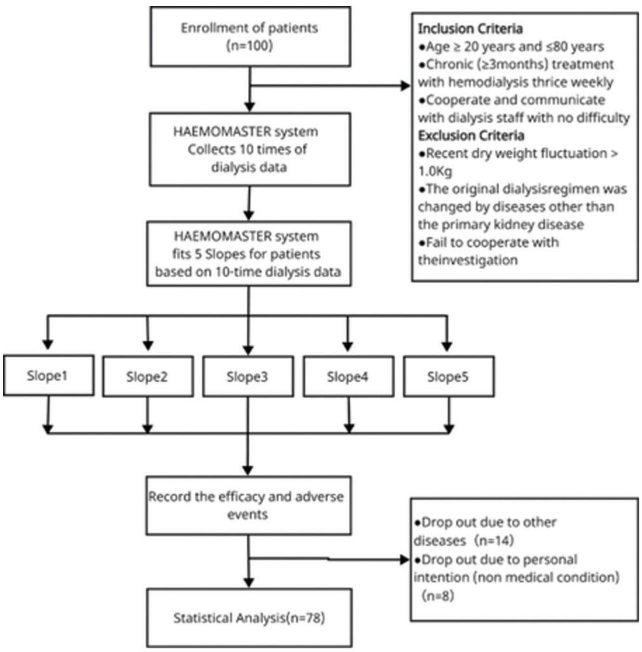
Corresponding author: Zhuojia Xu, MD
E-mail: xuzhuojia_CAGH@163.com

INTRODUCTION

Many end-stage kidney disease patients require hemodialysis treatment. Most hemodialysis patients suffer from fluid retention between hemodialysis sessions. Ultrafiltration dehydration allows for a gradual decrease in blood volume to remove excess water retained between hemodialysis sessions. Online blood volume monitoring (BVM) is a non-invasive, painless, easy-to-use, safe, and effective method for monitoring hemodialysis.[1-6] It has the advantages of real-time dynamic and accurate assessment of blood volume changes, high resistance to interference. It can reflect the volume and hemodynamic status of patients on hemodialysis.[1,6-9] Previous studies[9-20] have shown that online BVM can provide real-time information on the relative blood volume (RBV) of hemodialysis patients, which can be useful for improving the stability of hemodynamics and ensuring the safety of dialysis.[1,7,12,20-22] However, existing hemodialysis methods measure RBV values only 1-2 times, which is insufficient for real-time monitoring, and multiple measurements are needed to develop appropriate individualized RBV thresholds.[7,8,10,23]

NIKKISO has recently developed the HAEMOMASTER system based on the Blood Volume Control Tool, which combines RBV feedback control technology with dynamic BVM. HAEMOMASTER provides the hemodialysis

Figure 1. Study flow chart



physician with several sets of slopes to choose from after data analysis and modeling by collecting the patient‘s RBV and blood pressure over several dialysis sessions. Subsequent dialysis will automatically monitor RBV and feedback control ultrafiltration according to the selected slopes. This system helps the hemodialysis physician develop an optimal individual hemodialysis plan for the patient, reduce adverse effects such as hypotension, and improve the efficiency and comfort of hemodialysis ultrafiltration.

The HAEMOMASTER system uesd in the real-world dialysis practice have not been reported. This system is expected to be implemented at more hemodialysis centers in the future. However, studies on the clinical effectiveness of different slopes in this system have not been known. In this study, we included 100 hemodialysis patients with five slopes of the HAEMOMASTER system to observe the adverse effects and clinical outcomes and obtain clinical data on the effectiveness and safety of the HAEMOMASTER system.

MATERIALS AND METHODS

Participants

All patients were enrolled in the dialysis center of Civil Aviation General Hospital, Beijing, China. Study inclusion criteria were as follows: adults (age≥18 years and≤80 years), chronic (≥3 months) treatment with hemodialysis thrice weekly, and patients could cooperate and communicate with dialysis staff with no difficulty. The main exclusion criteria were recent(≤2 weeks) dry weight fluctuation> 1.0 Kg; the original dialysis regimen was changed, affected by diseases other than the original kidney disease(e.g. heart disease, pulmonary infection, opertaions), and failure to cooperate with the investigation. The blood pump speed during hemodialysis for all patients ranges from 200 to 250ml/min.

Study design

This study was a non-interventional, prospective, observative study. We recruited 100 dialysis patients for inclusion in the study and registered patients‘ baseline data, including routine blood tests, biochemistry, and dry weight, which were reviewed every two months. The NIKKISO DBB-05 Hemodialysis machine had automatically recorded real-time dates . Data from the patients‘ previous 10 hemodialysis sessions were collected into the HAEMOMASTER system to provide a reference for data fitting. Taking the HAEMOMASTER system automatically fitted decline factor as a quantitative (ΔBV change per 1L of dehydration, range -8%-1%) and ΔBV standard line (slope1-5) as a variable, the patients were subjected to BVM bio-feedback ultrafiltration using the fitted protocol during hemodialysis. In contrast, adverse events during hemodialysis were recorded. Adverse reactions include symptoms like obvious sweating, palpitation, fatigue, blood pressure below 100/60mmHg, and the hemodialysis process is interrupted or the ultrafiltration volume being adjusted. Each slope was tested 3 times per patient. We analyzed the incidence of adverse event rates of every slope and changes in the physiological condition of patients during hemodialysis.

HAEMOMASTER system

The HAEMOMASTER system is a new BV feedback control system developed by Nikkiso. General function of the option HAEMOMASTER : During treatment there is a continuous record of the light reflection at the extra-corporal blood circuit performed by optical measurement. The result of that measurement is automatically converted and displayed on the DBB-05 as "relative Blood-Volume course". For displaying and analysis the recorded BVM-Parameter can be transferred (Download) from DBB-05 to the PC. Based on the Downloaded Parameters the BVC simply integrates that BVM-Data and displays those values as graphical lines and calculated parameters.

The basic workflow of the HEMOMASTER system is shown in Figure 2. It realizes blood volume management through BVM, BV-UFC, and BV-COC and assists physicians in determining the patient‘s dry weight. The BVM dual-channel blood volume measurement monitors the patient‘s relative blood volume changes in real-time, which can be applied to predict and avoid the occurrence of hemodialysis hypotension, and assists hemodialysis physicians in determining the patient‘s hemodialysis progress and adjusting the hemodialysis plan.

Statistical Analyses

Continuous variables were expressed as mean ± SD and categorical variables in number and relative frequencies for baseline characteristics. Relative index to ΔBV of different slopes and sub-analysis was conducted by two-variable Spearman correlation analysis. No formal sample size estimation was done because the study was exploratory and served as a clinical follow-up study after the system was used on a large scale.

Figure 2. Basic workflow of HAEMOMASTER system.

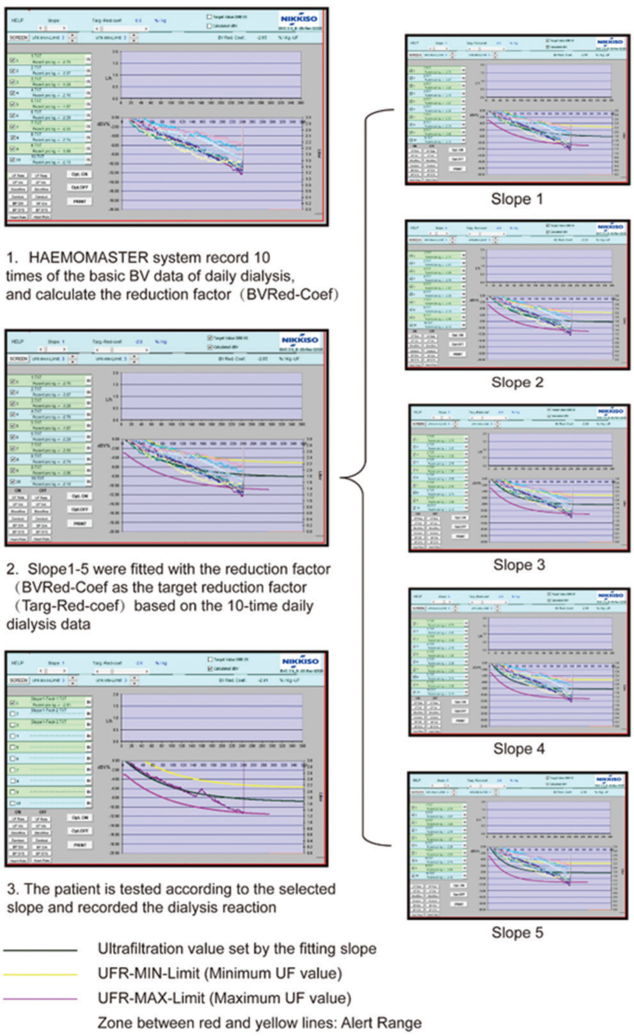


Table 1. Baseline patient characteristics

Patient Characteristics (n = 78)	Value
Mean age [years]	62.7±12.8
Female (%)	38.4%
Body mass index [kg/m²]	23.6±3.8
HCT [%]	33.4±3.2
Total protein [g/L]	64.9±5.1
Albumin [g/L]	37.1±2.7
Cause of ESRD, [n, %]	
Valvular heart disease	1(1.3%)
Polycystic kidney disease	3(3.8%)
Hypertensive nephropathy	20(25.6%)
Chronic glomerulonephritis	16(20.5%)
Diabetic nephropathy	31(39.7%)
Vasculitis	1(1.3%)
Drug	2(2.6%)
Peliosis	1(1.3%)
Other	3(3.8%)

Abbreviation: ESRD, end-stage renal disease

Table 2. Relative index to BV and AER of different slopes of HAEMOMASTER

	r	*P* value	AER
Slope1	0.827[0.722, 0.893]	<.001	5.3%
Slope2	0.831[0.712, 0.911]	<.001	3.8%
Slope3	0.782[0.694, 0.890]	<.001	10.5%
Slope4	0.739[0.585, 0.858]	<.001	6.7%
Slope5	0.768[0.601, 0.871]	<.001	5.0%

Note: $P < .05$

Abbreviation: AER, adverse event rate

All statistical analyses were performed using statistical Package for Social Science (SPSS) software version 22.0 (IBM Corporation, Armonk, NY, USA). P values were generated from an exploratory post hoc analysis. $P < .05$ was considered a statistically significant difference.

RESULTS

Baseline characteristics

One hundred chronic, stable hemodialysis patients treated three times per week from the dialysis center of Civil Aviation General Hospital (Beijing, China) were recruited to participate in this study. The baseline patient characteristics were concluded in Table 1. The mean age was 62.7 ± 12.8 years (range 31 to 90 years), and 50 patients were older than 60 years. 30(38.4%) were women. The majority (68%) of participants were normal weight (body mass index < 25 kg/m^2), and 7.6% had a body mass index > 30 kg/m^2. All patients studied were Asian Yellow; no African, Hispanic, or Caucasian patients were included in the study. 14 patients dropped out due to other diseases and need to change hemodialysis protocol. 8 patients dropped out due to personal intention (non-medical condition). Each participant received regular, high-flux dialysis three times each week.

Relative index to ΔBV and AER of different slopes

Firstly, we counted the correlation between the actual ΔBV (the actual value when patients are applied to different slopes) and the target ΔBV (calculated by HAEMOMASTER system)when all participants (n = 78) applied the HAEMOMASTER system with different slope controls and the incidence of adverse reactions. The statistical results are shown in Table 2. Among the five Slopes, Slope1 and Slope2 had a lower incidence of adverse reactions, 5.3% and 3.8%, respectively. In contrast, the incidence of adverse reactions in the other three Slopes was more than 5%. Moreover, the correlation coefficients r for Slope1 and Slope2 were 0.827 and 0.831, respectively, with $P < .001$, while the r for the other three Slopes were less than 0.8.

We divided the patients into three subgroups according to their primary disease and two subgroups according to gender and performed subgroup analysis separately. The sub-analysis of primary disease and gender is shown in Table 3 and Table 4. Different Slopes were suitable for patients with different primary diseases. Participants with the primary disease of diabetic nephropathy were more suitable for the Slope1 curve with the most moderate decreasing trend of ΔBV, and the incidence of adverse reactions was the lowest for Slope1, 3.4%, while the correlation factor r was the highest, 0.836, with $P < .001$. While participants with the primary disease of chronic glomerulonephritis and hypertensive nephropathy were more suitable for Slope2, the incidence of adverse reactions was lower, 6.3% and 0.0%, respectively, and the correlation factor r was higher, 0.787 and 0.880, respectively, with $P < .001$.

For male dialysis patients, Slope2 was a better choice with a correlation factor r of 0.865 and a $P < .001$. The

Table 3. Sub-group analysis in the cause of ESRD

	Diabetic nephropathy [n = 31]			Chronic glomerulonephritis [n = 16]			Hypertensive nephropathy [n = 20]		
	r	*P* value	AER	r	*P* value	AER	r	*P* value	AER
Slope1	0.836 [0.626, 0.957]	<.001	3.4%	0.833 [0.560, 0.952]	<.001	20.0%	0.865 [0.657, 0.956]	<.001	0.0%
Slope2	0.792 [0.524, 0.935]	<.001	6.5%	0.787 [0.451, 0.938]	<.001	6.3%	0.880 [0.655, 0.970]	<.001	0.0%
Slope3	0.797 [0.574, 0.922]	<.001	6.7%	0.552 [-0.009, 0.904]	<.001	12.5%	0.765 [0.349, 0.947]	<.001	10.0%
Slope4	0.702 [0.353, 0.913]	<.001	3.4%	0.554 [-0.033, 0.949]	<.001	6.7%	0.811 [0.480, 0.956]	<.001	5.0%
Slope5	0.803 [0.506, 0.929]	<.001	4.3%	0.522 [-0.100, 0.914]	<.001	7.7%	0.768 [0.308, 0.956]	<.001	6.7%

Note: $P < .05$

Abbreviation: AER, adverse event rate

Table 4. Sub-group analysis of gender

	Male(n = 48)			Female(n = 30)		
	r	*P* value	AER	r	*P* value	AER
Slope1	0.786 [0.581, 0.906]	<.001	4.3%	0.868 [0.729, 0.946]	<.001	6.9%
Slope2	0.865 [0.709, 0.942]	<.001	0.0%	0.784 [0.593, 0.906]	<.001	10.0%
Slope3	0.755 [0.511, 0.920]	<.001	4.2%	0.698 [0.343, 0.890]	<.001	21.4%
Slope4	0.729 [0.536, 0.864]	<.001	4.2%	0.767 [0.523, 0.921]	<.001	11.1%
Slope5	0.785 [0.561, 0.899]	<.001	5.9%	0.750 [0.481, 0.909]	<.001	3.8%

Note: $P < .05$

Abbreviation: AER, adverse event rate

incidence of adverse reactions was also low, at 0%. Female patients were more suitable for Slope1 because the r of Slope2-5 was less than 0.8, and the incidence of adverse events was higher, while the correlation factor r of Slope1 was 0.868 ($P < .001$).

DISCUSSION

The HAEMOMASTER system combines dynamic BVM technology with feedback control technology.[7,20,21,23-29] It collects the RBV and blood pressure of the patient over several dialysis sessions, and its data modeling system fits and analyzes the patient‘s hemodialysis physiological data to form several slopes.[17,21,30] However, which slope could reduce the occurrence of adverse events and improve the efficiency of hemodialysis is still unknown.

This prospective observational study included 78 patients for whom the HAEMOMASTER system was applied for hemodialysis and recorded their dialysis efficacy and adverse events. We found that the feedback control of hemodialysis ultrafiltration volume by the HAEMOMASTER system generally reflected the actual physiological conditions of the patients during hemodialysis.

Among the Slopes 1-5 provided by the HAEMOMASTER system, the feedback control of Slope 1 and Slope 2 is more suitable for the majority of patients because of their better fit to the actual physiological conditions and lower incidence of adverse events. In contrast, Slope3-5 had a slightly lower actual clinical fit and a slightly higher incidence of adverse events than Slope1-2. The Slope1-2, compared with the Slop3-5, showed a more moderate decrease in ΔBV during 100-120 minutes of dialysis than the Slop3-5 curve, which means a less ultrafiltration volume. This result suggests that the HAEMOMASTER system mathematical modeling parameters can be appropriately adjusted concerning the current Slope1-2 to develop more fitting curves suitable for clinical applications.

In addition, we also observed a variety of clinical manifestations and adverse effects in patients with different primary diseases applied to different slopes. Patients with diabetic nephropathy as a primary disease were more suitable for Slope1 with the most moderate decreasing trend of ΔBV. In contrast, hemodialysis patients with chronic glomerulonephritis and hypertensive nephropathy were more suitable for Slope2. This may be related to the fact that patients with diabetic nephropathy have poor overall vascular permeability, poor tolerance to rapid ΔBV decline, and are more likely to cause hypotension.

In terms of gender, male patients were more suitable for Slope2, and female patients were more suitable for Slope1. Male patients may be more able to adjust to rapid and extensive changes in BV than women since they are generally larger than females. The above results suggest that in clinical practice, hemodialysis physicians can choose a more optimal scheme for patients concerning their primary medical conditions and gender characteristics. The present study also observed that the patient's BMI and body surface area were correlated with the degree of ΔBV decline. This also suggests that the degree of ΔBV decline tolerated by patients can be predicted in clinical applications based on the above conditions of patients, which can provide a reference for the choice of a suitable slope.

There are also several important limitations. First, the patients in this study are all yellow Asian. Second, it was conducted only in one dialysis center, and the number of patients included was limited. Further study with multiple dialysis centers to include more participants of different ethnicities is needed in the future.

CONCLUSION

We evaluated the safety and effectiveness of the HAEMOMASTER System in hemodialysis patients. This study serves as a roadmap for the development and widespread use of the HAEMOMASTER system and a resource for the creation of novel biofeedback control strategies. The HAEMOMASTER system has good clinical application prospects in hemodialysis patients and can be used to develop „individualized“ ultrafiltration schemes for patients and improve the comfort and safety of hemodialysis. Slopes 1 and 2 are more suited for the majority of patients since they meet actual physiological conditions better and have a reduced incidence of negative outcomes. The hemodialysis physician could choose the best slope for patients according to the patient‘s baseline characteristics and primary disease. This study guides the improvement and large-scale application of this system, a reference for the development of new biofeedback control techniques, and reference data for units applying the HAEMOMASTER system.

STATEMENT OF ETHICS

This study protocol was reviewed and approved by the competent ethics committee of Civil Aviation General Hospital, approval number No.2020-10-16. The Declaration of Helsinki conducted the study, and the protocol was approved by Institutional Review Boards within each participating country. All patients were informed orally and in writing of the study's purpose, conduct, and risks and were only enrolled after signing the informed consent form.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

FUNDING SOURCES

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AUTHOR CONTRIBUTIONS

Zhuojia Xu contributed to the conception of the study, performed the data analyses, and wrote the manuscript. Dongdong Wang, Guoyu Liang and Yue Wang performed the experiment. Kai Wang contributed to the conception of the study.

DATA AVAILABILITY STATEMENT

All datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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