HL Tang 鄧漢樂
SH Wong 黃思豪
KH Chu 朱國康
W Lee 李威廉
A Cheuk 卓　鷗
CMK Tang 鄧文娟
ILL Kong 江琳琳
KS Fung 馮加信
WK Tsang 曾偉基
HWH Chan 陳慧嫻
KL Tong 唐國隆

Sodium ramping reduces hypotension and symptoms during haemodialysis

血液透析過程中遞減鈉濃度以減少出現低血壓和相關症狀

Objectives. To evaluate the effectiveness of sodium ramping (profiling) in reducing hypotensive episodes and symptoms during haemodialysis.
Design. Prospective study.
Setting. Regional hospital, Hong Kong.
Patients. Thirteen patients who experienced frequent episodes of hypotension and/or symptoms such as cramps, dizziness, chest pain, nausea, vomiting, and headache during haemodialysis in the preceding 4 weeks.
Interventions. Each patient was switched from standard haemodialysis with a constant dialysate sodium concentration of 135 to 140 mmol/L to a ramped sodium haemodialysis for a period of 4 weeks. During this time the dialysate sodium concentration was ramped linearly downwards from 150 mmol/L at the beginning of dialysis to 140 mmol/L at the end of dialysis.
Main outcome measures. Intradialytic hypotensive episodes, intradialytic symptoms, nursing interventions, systolic and diastolic blood pressures, and interdialytic weight gain.
Results. A total of 248 haemodialysis sessions undertaken by 13 patients were analysed. Switching from constant sodium haemodialysis to ramped sodium haemodialysis resulted in a significant reduction in the number of intradialytic hypotensive episodes from 5.8 (standard deviation, 6.4) to 2.2 (3.3) [P<0.05], the total number of intradialytic symptoms from 7.1 (3.4) to 0.9 (1.3) [P<0.01], and nursing interventions from 11.3 (6.3) to 1.7 (3.9) [P<0.01]. Post-dialysis systolic and diastolic blood pressures were higher during ramped sodium haemodialysis compared with constant sodium haemodialysis (systolic blood pressure, 139 [standard deviation, 23] vs 133 [22] mm Hg, P<0.001; diastolic blood pressure, 77 [11] vs 74 [13] mm Hg, P<0.01), and there was a trend towards a smaller drop in blood pressure after dialysis. The interdialytic weight gain with sodium ramping haemodialysis was greater compared with constant sodium haemodialysis (3.1 [standard deviation, 1.0] vs 2.7 [1.1] kg, P<0.001).
Conclusion. Sodium ramping during haemodialysis effectively reduces hypotensive episodes and intradialytic symptoms. Post-dialysis blood pressure is better maintained. A side-effect of sodium ramping is a greater interdialytic weight gain.

目的：評估在血液透析過程中，遞減鈉濃度以減少低血壓次數和相關症狀的有效性。
設計：前瞻性研究。
安排：分區醫院，香港。
患者：13位在研究開始前的4個星期內接受血液透析的病人，他們在透析過程中頻密出現低血壓，以及／或者出現相關症狀如痙攣、眩暈、胸痛、噁心、嘔吐和頭痛。
療法：所有病人由原來施以透析液鈉濃度恆常為135-140 mmol/L的標準透析，改為連續4星期施以鈉濃度遞減的血液透析。在每次透析時，逐步按線性比例降低透析液的鈉濃度，由透析開始時的 150 mmol/L 減至透析結束時的 140 mmol/L 。
主要結果測量：透析期內出現低血壓的次數、透析期內的症狀、護理介入次數、血液收縮壓和舒張壓，以及透析期之間的增重。
結果：本研究合共分析了 13 位病人共 248 節血液透析的數據。由恆常鈉濃度血液透析轉為鈉濃度遞減血液透析後，透析期內出現低血壓的次數大幅減少，從5.8次（標準差為 6.4 次）下跌至 2.2 次（標準差為 3.3 次）[P<0.05]；透析期內的症狀總數從 7.1（標準差為 3.4）下跌至 0.9（標準差為 1.3）[P<0.01]；護理介入則從 11.3 次

Key words:
Blood pressure;
Hemodialysis solutions;
Kidney failure, chronic;
Renal dialysis;
Sodium

關鍵詞：
血壓；
血液透析溶液；
腎衰竭，慢性；
腎透析；
鈉

Hong Kong Med J 2006;12:10-4

Division of Nephrology, Department of Medicine and Geriatrics, Princess Margaret Hospital, Laichikok, Hong Kong
HL Tang, MRCP, FHKAM (Medicine)
SH Wong, MRCP, FHKAM (Medicine)
KH Chu, MRCP, FHKAM (Medicine)
W Lee, MRCP, FHKAM (Medicine)
A Cheuk, MRCP
CMK Tang, BSN
ILL Kong, BSN, MNurs
KS Fung, MRCP, FHKAM (Medicine)
WK Tsang, FRCP, FHKAM (Medicine)
HWH Chan, FRCP, FHKAM (Medicine)
KL Tong, FRCP, FHKAM (Medicine)

Correspondence to: Dr HL Tang (e-mail: pmhrenal@hotmail.com)

（標準差為 6.3 次）下跌至 1.7 次（標準差為 3.9 次）[P<0.01]。鈉濃度遞減血液透析後的兩種血壓均較恆常鈉濃度血液透析後的為高——收縮壓是 139（標準差為 23）mm Hg 比 133（標準差為 22）mm Hg（P<0.001），而舒張壓是 77（標準差為 11）mm Hg 比 74（標準差為 13）mm Hg（P<0.01）。透析期之間的增重比對方面，鈉濃度遞減血液透析的病人為 3.1（標準差為 1.0）kg，恆常鈉濃度血液透析的病人則為 2.7（標準差為 1.1）kg（P<0.001）。

結論：鈉濃度遞減血液透析能有效減少低血壓次數和透析期內的症狀，且保持較穩定的透析後血壓，但有透析期之間增重過多的副作用。

Introduction

Hypotension and dialysis disequilibrium syndrome are the two major complications that occur during haemodialysis. Hypotension is often caused by the decreased plasma volume that results from net fluid loss.[1-3] When fluid is removed from the intravascular compartment, maintenance of plasma volume is dependent on refill from the interstitium. Rate of refill is in turn dependent on the plasma osmolality and hydration of the interstitium.[1,3] If the rate of refill cannot match ultrafiltration, plasma volume falls. Dialysis disequilibrium syndrome is defined as the occurrence of muscle cramps, dizziness, nausea, vomiting, and headache during haemodialysis.[4] The theory of a 'reverse urea effect' has been proposed to explain the pathogenesis of dialysis disequilibrium syndrome.[5,6] Urea is rapidly removed from the plasma during haemodialysis. The slow removal of urea from the brain establishes a brain-to-plasma osmotic gradient. This gradient causes water influx into the brain cells, and results in cerebral oedema and acute neurological dysfunction. A high dialysate sodium concentration compensates for the fall in plasma osmolality caused by the removal of solutes during dialysis. As a result, plasma refill improves and fall in plasma volume reduces.[7] Maintaining plasma osmolality during dialysis can protect the patient from dialysis disequilibrium syndrome,[8] since it avoids water influx into the intracellular compartment.[9] Nonetheless a high dialysate sodium concentration may cause a net positive sodium balance. Sodium ramping aims to overcome this problem by varying the dialysate sodium concentration during dialysis from an initially high level (to offset the fall in plasma osmolality) to a lower level towards the end of dialysis to prevent a net sodium gain.[10]

The results of previous studies of the benefits of sodium ramping have been inconsistent.[11-17] We conducted a prospective study to evaluate the effectiveness of sodium ramping in reducing hypotensive episodes and disequilibrium symptoms during haemodialysis, and the side-effects of interdialytic weight gain and hypertension.

Methods

Patients

Patients were selected from the Haemodialysis Unit of the Princess Margaret Hospital, Hong Kong. Thirteen Chinese patients on maintenance haemodialysis who experienced frequent episodes of hypotension and/or frequent symptoms during haemodialysis treatment in the preceding 4 weeks were recruited. There were four female and nine male patients with a mean age of 49.6 (standard deviation [SD], 10.5) years. Eight patients were receiving haemodialysis 2 times a week and the remaining five were receiving haemodialysis 3 times a week. The length of dialysis treatment ranged from 4 to 5.5 hours with a mean of 4.7 (SD, 0.5) hours. Ten patients used the Gambro AK 200 haemodialysis machine (Gambro, Lund, Sweden), two patients used the Gambro AK 100 (Gambro, Lund, Sweden), and one patient used the Fresenius 4008B (Fresenius Medical Care, Bad Homburg, Germany). Dialysate sodium concentrations were 140 mmol/L in 11 patients and 135 mmol/L in two patients throughout dialysis. Hollow-fibre dialysers and bicarbonate-containing dialysate were used in all patients and the mean dialysate bicarbonate level was 30.8 (SD, 3.4) mmol/L. The mean ultrafiltration coefficient of the dialysers was 11.2 (SD, 11.7) mL/h·mm Hg.

Treatment protocol

Each patient was switched from conventional haemodialysis with a constant dialysate sodium concentration to a ramped sodium haemodialysis. The dialysate sodium concentration was ramped from 150 mmol/L at the beginning of dialysis to 140 mmol/L at the end of dialysis (linear sodium ramping) [Fig]. The linear sodium ramping setting was preprogrammed in the haemodialysis machine. Ultrafiltration was maintained at a constant rate throughout dialysis. The type of dialyser, dialysate bicarbonate concentration, and length of dialysis were unchanged during the study period. The patients were followed up for 4 weeks after conversion to sodium ramping.

Outcome measures

Supine blood pressure was recorded before and after each dialysis. Intradialytic blood pressure was monitored every 15 minutes to 1 hour depending on the haemodynamic state of the patient. Hypotensive episodes were recorded. A hypotensive episode was defined as an abrupt decrease in systolic blood pressure to lower than 100 mm Hg or diastolic blood pressure to lower than 60 mm Hg. Intradialytic symptoms including cramps, dizziness, chest pain, nausea, vomiting, and headache were also noted, along with consequent nursing interventions. An intervention was defined as any one of the following: an infusion of normal saline, a bolus injection of 5.85% hypertonic saline, reduction in blood flow rate, reduction or halting of ultrafiltration, and discontinuation of haemodialysis. The total number of hypotensive episodes, each individual symptom, and each type of nursing intervention were counted during the 4-week period of ramped sodium dialysis and the preceding 4-week period of constant sodium dialysis.

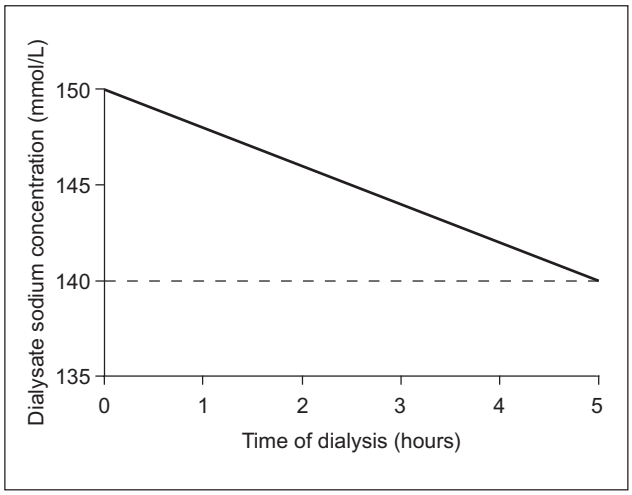

Fig. Linear sodium ramping used in this study
Dialysate sodium concentration was ramped down linearly from 150 mmol/L at the beginning of haemodialysis to 140 mmol/L at the end of dialysis

The variables for each mode of dialysis were then compared. Data obtained during the preceding 4 weeks of constant sodium dialysis served as the patients' historical control.

The interdialytic weight gain between two consecutive haemodialysis sessions and the intradialytic weight loss during a single dialysis treatment were recorded. Pre-dialysis and post-dialysis serum sodium and blood urea levels were checked during the last session of constant sodium dialysis and during the period of ramped sodium dialysis. The urea reduction ratio (URR) and single-pool Kt/V (spKt/V) of the dialysis session were calculated using the pre-dialysis and post-dialysis blood urea levels.

Statistical analysis

The non-parametric Wilcoxon signed rank test was used to compare the means of the total number of hypotensive episodes, individual intradialytic symptoms, each type of nursing intervention, pre-dialysis and post-dialysis serum sodium levels, URR, and spKt/V between the constant and ramped sodium dialysis. The paired Student's *t* test was used to compare the means of the pre-dialysis and post-dialysis systolic and diastolic blood pressures, the percentage decrease in systolic and diastolic blood pressures after dialysis, the interdialytic weight gain, and the intradialytic weight loss between the two modes of dialysis. A P value of less than 0.05 was regarded as statistically significant.

Results

A total of 248 haemodialysis sessions undertaken by 13 patients were analysed. There was a 62% reduction in intradialytic hypotensive episodes and an 87% reduction in total intradialytic symptoms after switching to ramped sodium dialysis (Table 1). All symptoms, including cramps, dizziness, chest pain, nausea, vomiting, and headache were significantly reduced. All nursing interventions required to manage these complications were also significantly fewer during ramped sodium haemodialysis (Table 2). Overall, total nursing interventions were reduced by 85%. There was no significant difference in the pre-dialysis systolic and diastolic blood pressures between constant and ramped sodium dialysis. However, the post-dialysis systolic and diastolic blood pressures were significantly higher following ramped sodium dialysis (Table 3). The percentage decrease in systolic and diastolic blood pressures after haemodialysis was smaller during sodium ramping but not statistically significant (Table 3). The interdialytic weight gain between two consecutive dialysis sessions was significantly greater with ramped sodium haemodialysis. Intradialytic weight loss was also significantly greater (Table 4).

There was no significant difference in pre-dialysis and post-dialysis serum sodium level between constant and ramped sodium dialysis (Table 5). No statistical difference in URR and spKt/V between the two types of dialysis was observed (Table 5).

Discussion

This study focused on the effect of sodium ramping on intradialytic complications and events during haemodialysis. There was a 62% reduction in hypotensive episodes, an 87% reduction in intradialytic symptoms, and an 85% reduction in nursing interventions after sodium ramping. The reduction was marked for intradialytic symptoms and nursing interventions. Certain symptoms such as chest pain, nausea, vomiting, and headache virtually disappeared after sodium profiling. Muscle cramps, previously the most common intradialytic symptom, also showed a marked reduction. The post-dialysis systolic and diastolic blood pressures were higher during ramped sodium dialysis and there was a smaller percentage decrease in both after dialysis although statistically insignificant. Nonetheless there was no increase in the pre-dialysis systolic and diastolic blood pressures. Thus, sodium profiling does not seem to result in an increase in pre-dialysis hypertension.

Sodium ramping was associated with some side-effects. Interdialytic weight gain was greater although no patient experienced any severe sequelae of fluid overload such as congestive heart failure or pulmonary oedema. The intradialytic weight loss also increased during the period of sodium ramping reflecting greater intradialytic fluid removal. There was no change in the pre-dialysis and post-dialysis serum sodium concentration or dialysis adequacy indices.

Previous studies of the benefits of sodium profiling during haemodialysis have shown inconsistent results.[11-17] Some studies showed a decrease in the incidence of intradialytic hypotension and the need for nursing interventions during profiled dialysis,[11-14] but other studies showed no such reduction.[15,16] Sadowski et al[15] demonstrated

Table 1. Hypotensive episodes and intradialytic symptoms during constant and ramped sodium haemodialysis

	Constant sodium haemodialysis, n=13*	Ramped sodium haemodialysis, n=13*	P value
Hypotensive episodes	5.8 (6.4)	2.2 (3.3)	<0.05
Cramps	4.8 (3.1)	0.6 (1.0)	<0.01
Dizziness	1.5 (1.9)	0.3 (0.6)	<0.05
Other symptoms†	0.8 (1.2)	0	<0.05
Total symptoms	7.1 (3.4)	0.9 (1.3)	<0.01

* Values are expressed as mean number of episodes (SD)
† Other symptoms include chest pain, nausea, vomiting, and headache

Table 2. Nursing interventions during constant and ramped sodium haemodialysis

	Constant sodium haemodialysis, n=13*	Ramped sodium haemodialysis, n=13*	P value
Normal saline infusion	2.2 (2.1)	0.5 (1.2)	<0.01
Hypertonic saline (5.85%)	3.8 (2.4)	0.4 (1.0)	<0.01
Reducing blood flow rate	1.8 (1.3)	0.3 (0.9)	<0.05
Reducing or stopping ultrafiltration	2.5 (2.2)	0.5 (1.2)	<0.01
Stopping haemodialysis	1.0 (1.0)	0.2 (0.4)	<0.05
Total interventions	11.3 (6.3)	1.7 (3.9)	<0.01

* Values are expressed as mean number of interventions (SD)

Table 3. Systolic and diastolic blood pressures during constant and ramped sodium haemodialysis

	Constant sodium haemodialysis, n=124*	Ramped sodium haemodialysis, n=124*	P value
Systolic blood pressure (mm Hg)			
Pre-dialysis	155 (20)	159 (25)	0.053
Post-dialysis	133 (22)	139 (23)	<0.001
% Decrease	14 (13)	11 (15)	0.069
Diastolic blood pressure (mm Hg)			
Pre-dialysis	83 (11)	85 (13)	0.056
Post-dialysis	74 (13)	77 (11)	<0.01
% Decrease	10 (15)	8 (13)	0.197

* n=number of haemodialysis treatments; values are expressed as mean (SD)

Table 4. Body weight during constant and ramped sodium haemodialysis

	Constant sodium haemodialysis, n=124*	Ramped sodium haemodialysis, n=124*	P value
Interdialytic weight gain (kg)	2.7 (1.1)	3.1 (1.0)	<0.001
Intradialytic weight loss (kg)	2.7 (1.0)	3.0 (1.0)	<0.001

* n=number of haemodialysis treatments; values are expressed as mean (SD)

Table 5. Pre-dialysis and post-dialysis serum sodium levels, and haemodialysis adequacy during constant and ramped sodium haemodialysis

	Constant sodium haemodialysis, n=7*	Ramped sodium haemodialysis, n=7*	P value
Pre-dialysis serum sodium level (mmol/L)	137 (2)	137 (3)	0.683
Post-dialysis serum sodium level (mmol/L)	137 (4)	138 (1)	0.671
Urea reduction ratio (%)	75 (7)	75 (8)	0.735
Single-pool Kt/V	1.8 (0.3)	1.8 (0.4)	0.612

* Values are expressed as mean (SD)

an improvement in cramps, headaches, and nausea; and Levin and Goldstein[17] showed an improvement in 70% of lightheadedness or cramps and 100% of headaches with sodium profiling. Nonetheless two other studies demonstrated no such benefits.[12,16] A greater interdialytic weight gain after sodium profiling was observed in some

reports,[13,14] but not others.[11,12,15-17] The techniques of sodium profiling and the dialysate sodium concentrations used in these studies were quite heterogeneous. Different ramping methods—linear, stepwise, and exponential—have been used and the dialysate sodium concentration used at the beginning of dialysis ranged widely from 145 to 160 mmol/L. It remains unclear whether different methods of sodium profiling and different dialysate sodium concentrations at the beginning of dialysis will have different effects on intradialytic morbidity. A significant elevation of serum sodium level after both linear and stepwise sodium ramping dialysis has been demonstrated.[13] This study, however, demonstrated no change in serum sodium level after ramping dialysis although there was a greater interdialytic weight gain.

Sodium ramping (from 150 to 140 mmol/L, linear) effectively reduced intradialytic hypotensive episodes and disequilibrium symptoms. Post-dialysis blood pressure was better maintained and there was a trend towards a lesser drop in blood pressure after dialysis. As to side-effect, sodium ramping resulted in a greater interdialytic weight gain. Large-scale studies to compare different types of sodium profiling (linear, stepwise, and exponential) and different dialysate sodium concentrations, and their effect on haemodynamic stability and individual intradialytic symptoms are required.

Acknowledgements

The authors would like to thank the nursing staff of the Renal Dialysis Unit of Princess Margaret Hospital for their assistance in the study.

References

1. de Vries JP. Plasma volume changes during hemodialysis. Semin Dial 1992;5:42-7.
2. Lins LE, Hedenborg G, Jacobson SH, et al. Blood pressure reduction during hemodialysis correlates to intradialytic changes in plasma volume. Clin Nephrol 1992;37:308-13.
3. de Vries JP, Kouw PM, van der Meer NJ, et al. Non-invasive monitoring of blood volume during hemodialysis: its relation with post-dialytic dry weight. Kidney lnt 1993;44:851-4.
4. Arieff AI. Dialysis disequilibrium syndrome: current concepts on pathogenesis and prevention. Kidney Int 1994;45:629-35.
5. Silver SM, DeSimone JA Jr, Smith DA, Sterns RH. Dialysis disequilibrium syndrome (DDS) in the rat: role of the "reverse urea effect". Kidney Int 1992;42:161-6.
6. Silver SM, Sterns RH, Halperin ML. Brain swelling after dialysis: old urea or new osmoles? Am J Kidney Dis 1996;28:1-13.
7. van Kuijk WH, Wirtz JJ, Grave W, et al. Vascular reactivity during combined ultrafiltration-haemodialysis: influence of dialysate sodium. Nephrol Dial Transplant 1996;11:323-8.
8. Rodrigo F, Shideman J, McHugh R, Buselmeier T, Kjellstrand C. Osmolality changes during hemodialysis. Natural history, clinical correlations, and influence of dialysate glucose and intravenous mannitol. Ann Intern Med 1977;86:554-61.
9. Van Stone JC, Bauer J, Carey J. The effect of dialysate sodium concentration on body fluid distribution during hemodialysis. Trans Am Soc Artif Intern Organs 1980;26: 383-6.
10. Parsons DS, Harris DC. A review of dialysis profiling. Nephrology 1998;4:303-11.
11. Acchiardo SR, Hayden AJ. Is Na+ modeling necessary in high flux dialysis? ASAIO Trans 1991;37:M135-7.
12. Jenson BM, Dobbe SA, Squillace DP, McCarthy JT. Clinical benefits of high and variable sodium concentration dialysate in hemodialysis patients. ANNA J 1994;21:115-21.
13. Sang GL, Kovithavongs C, Ulan R, Kjellstrand CM. Sodium ramping in hemodialysis: a study of beneficial and adverse effects. Am J Kidney Dis 1997;29:669-77.
14. Oliver MJ, Edwards LJ, Churchill DN. Impact of sodium and ultrafiltration profiling on hemodialysis-related symptoms. J Am Soc Nephrol 2001;12:151-6.
15. Sadowski RH, Allred EN, Jabs K. Sodium modeling ameliorates intradialytic and interdialytic symptoms in young hemodialysis patients. J Am Soc Nephrol 1993;4:1192-8.
16. Parsons DS, Yuill E, Llapitan M, Harris DCH. Sodium modelling and profiled ultrafiltration in conventional haemodialysis. Nephrology 1997;3:177-82.
17. Levin A, Goldstein MB. The benefits and side effects of ramped hypertonic sodium dialysis. J Am Soc Nephrol 1996;7:242-6.