



Hemodialysis Headache

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Outline

- Introduction of hemodialysis headache
 - Epidemiology
- Review of clinical researches
- Potential pathophysiology
- Prospective: to investigate hemodialysis headache in Taiwan



Introduction

- End-stage renal disease in Taiwan^{1,2}
 - Incidence: 331/million
 - Ranked first in the world (2002~2005)
 - Prevalence: 1322/million
 - Ranked second in the world (2002~2005)
 - More than 90% ESRD patients received hemodialysis (HD)

1. Nephro Dial Transplant, 2008

2. Acta Nephrologica, 2007



Introduction

- Complications of hemodialysis (HD)
 - Acute: agitation, delirium, muscle cramps, convulsions, headache, irritability
 - Chronic: Wernicke's encephalopathy, dementia, amyloid neuropathy, etc
- Headache: one of the most frequently encountered neurological symptoms during HD



Epidemiology

1. Headache 1972.
2. Cephalalgia 1988.

- Frequency: reported to be 70%¹
- International Headache Society (IHS) criteria²:
 - Headache with onset during HD
 - Terminates within 24 hours after HD
 - Occurs during at least half of HD and at least thrice
 - Can be prevented by changing dialysis parameter
- Revised in 2004

Table 1.—Diagnostic Criteria of Dialysis Headache

A—At least three attacks of acute headache fulfilling criteria C and D

B—The patients on hemodialysis

C—Headache develops during at least half of hemodialysis sessions

D—Headache resolves within 72 hours after each hemodialysis session and/or ceases altogether after successful transplantation



Haemodialysis-related headache

B Göksan, F Karaali-Savrun, S Ertan & M Savrun¹

Department of Neurology and ¹Psychiatry, Cerrahpasa School of Medicine, Istanbul University, Istanbul, Turkey

Cephalalgia

Göksan B, Karaali-Savrun F, Ertan S & Savrun M. Haemodialysis-related headache. Cephalalgia 2004; 24:284–287. London. ISSN 0333-1024

- Study design: cross-sectional Study
- Subjects:
 - ESRD patients, HD > 6 months
- Setting: single hospital
- Questionnaire (validation? Measurement bias?)



Table 1 Demographic and clinical characteristics of the study population

	With DH (%)	Without DH (%)	Total
No. of patients	30 (48)	33 (52)	63
Sex, F/M	18/12 (60/36)	12/21 (40/64)	30/33
Age, years, mean \pm SD	43 \pm 10.2	43.5 \pm 10.3	44 \pm 10
Duration of HD history, years, mean \pm SD	5 \pm 3.9	4.9 \pm 3.7	5 \pm 3.8
Type of dialysis solution, acetate/bicarbonate	16/14 (46/50)	19/14 (54/50)	35/28

DH, Dialysis headache; HD, haemodialysis; SD, standard deviation.

- Dialysis headache: more frequent in women



Table 2 The difference in pre- and post-treatment values of urea, Na⁺, K⁺ and creatinine in patients

Parameter	Predialysis – post-dialysis value		P
	Patients with DH	Patients without DH	
Urea, mg/dl	111.69 ± 19.1	98.5 ± 15.7	<0.05
Na ⁺ , mEq/l	3.14 ± 2.53	2.1 ± 2.5	>0.05
K ⁺ , mEq/l	1.78 ± 1.18	1.6 ± 1.1	>0.05
Creatinine, mg/dl	6.3 ± 1.16	6.0 ± 1.0	>0.05

DH, Dialysis headache.

Table 3 Pre-and post-dialysis values of systolic and diastolic blood pressure in patients

Blood pressure (mmHg)	Predialysis values			Post-dialysis values		
	DH (+)	DH (-)	P	DH (+)	DH (-)	P
Diastolic	88.5 ± 7.7	78.8 ± 15.3	<0.01	78.5 ± 10.2	75 ± 12.6	>0.2
Systolic	142.8 ± 17.2	133 ± 28.3	<0.001	127 ± 17.6	118.4 ± 21.2	>0.05

DH, Dialysis headache.



Table 4 Features of the dialysis headache

Features of DH		Frequency, % (n)
Intensity	Moderate	73 (22)
	Severe	27 (8)
	Throbbing	87 (26)
Quality	Dull	13 (4)
	Fronto-temporal	50 (15)
Location	Occipital	27 (8)
	Diffuse	23 (7)
Duration	<4 h	63 (19)
	>4 h	37 (11)



Summary

- HD-related headache:
 - Prevalent among patients receiving HD
 - Female preponderance
 - Beginning after some hours of therapy
 - Moderate intensity
 - Throbbing character
 - Related to
 - Difference of pre- and post-treatment urea level
 - Pre-treatment blood pressure



Questions...

- Hemodialysis vs. headache
- Impotency vs. hypertension in men
- Pre-existing headache?
 - Headache patients were prone to HD?
 - Headache worsen by HD?
- *de novo* headache after initiating HD?
 - Related to HD procedure itself
- Case selection, exclusion criteria?



Headache and Hemodialysis: A Prospective Study

Ana L. Antoniazzi, MD; Marcelo E. Bigal, MD, PhD; Carlos A. Bordini, MD, PhD;
Stewart J. Tepper, MD; José G. Speciali, MD, PhD

- Study design: cross-sectional or “prospective”?
- Setting: 3 HD institution
- Subjects: ESRD patients (Jan, 1998~Dec, 1999)
 - Exclusion: HD<6 mo; dementia; inability to communicate
- Interviewed by one of the authors (A.L.A.)

- Randomly evaluated 123 patients from a total 741 of potential subjects
- Ever experienced headache: n=83 (70.7%)

*Now still experiencing headache: n=63 (51.2%)

*HA during sessions: n=50

*HA between sessions: n=13

Table 1.—Time Elapsed Between the Beginning of the Dialysis Session and the Onset of Headache

Time, h	No. (%) of Patients
<1	1 (2)
1-1.9	5 (10)
2-2.9	13 (26)
3-4	31 (62)
Total	50 (100)

Table 2.—Distribution of Headache Diagnoses in Patients From Group 1 (Those With Headaches Predating Initiation of Hemodialysis)

IHS Code	Diagnosis	No. (%) of Patients (n = 59)
1.1	Migraine without aura	18 (30.5)
1.1+2.2	Migraine without aura + chronic tension-type headache	5 (8.5)
1.2	Migraine with aura	3 (5.1)
1.7	Migrainous disorder	3 (5.1)
2.1	Episodic tension-type headache	11 (18.6)
6.8.1	Acute pressor response to exogenous agent	1 (1.7)
6.8.0.1	Arterial hypertension with migrainous features	7 (11.9)
6.8.0.2	Arterial hypertension with tension-type headache features	2 (3.3)
6.8.0.9 (1.7)	Arterial hypertension fulfilling all but one criteria for migraine	4 (6.8)
6.8.0.9 (2.3)	Arterial hypertension fulfilling all but one criteria for tension-type headache	1 (1.7)
8.1.4.2	Alcohol-induced headache with migrainous features	1 (1.7)
13	Headache not classifiable	3 (5.1)

Table 3.—Classification of Headaches Occurring During Hemodialysis Sessions or During Intervals Between Sessions

IHS code	Diagnosis	During Sessions No. (%) of Patients (n = 50)	Between Sessions No. (%) of Patients (n = 13)
1.1	Migraine without aura	2 (4)	2 (15.4)
1.2	Migraine with aura	1 (2)	1 (7.7)
1.7	Migrainous disorder	4 (8)	3 (23.1)
2.1	Episodic tension-type headache	7 (14)	5 (38.5)
2.3	Headache of the tension-type not fulfilling all criteria	0	1 (7.7)
10.5.0.1	Dialysis headache with migrainous features	19 (38)	0
10.5.0.2	Dialysis headache with tension-type headache features	13 (26)	0
10.5.0.9 (1.7)	Dialysis headache fulfilling all but one criteria for migraine	1 (2)	0
10.5.0.9 (2.3)	Dialysis headache fulfilling all but one criteria for tension-type headache	1 (2)	0
13	Headache not classifiable	2 (4)	1 (7.7)



Headache after regular HD

- Headache not fulfilled criteria of dialysis headache
- Headache fulfilled criteria for dialysis headache, but with antecedent primary headache
- Headache fulfilled criteria for dialysis headache, but without antecedent primary headache
 - i.e. “true” and “pure” dialysis headache



Controversies...

1. *N Engl J Med*, 1976

- Raskin and Fishman reported¹:
 - Patients with migraine could experience clinically identical headache during or following HD
 - And 20% of patients without previous headache could experience them in association with dialysis
 - The pain is bilateral and throbbing

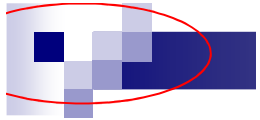


Controversy...

1. *Neurol Clin*, 1996

2. *Kidney Int*, 1982

- These headache may disappear following renal transplant, and return if rejection occurs¹
- Some authors argue²
 - HD headache should not be classified as a distinct diagnostic entity
 - HD itself is simply a nonspecific stress factor that induces headache



Research Submission

Is Low Blood Magnesium Level Associated With Hemodialysis Headache?

Basak Karakurum Goksel, MD; Dilek Torun, MD; Sibel Karaca, MD; Mehmet Karatas, MD;
Meliha Tan, MD; Nurzen Sezgin, MD; Sibel Benli, MD; Siren Sezer, MD; Nurhan Ozdemir, MD

- Study design: observational, comparative
- Subjects: ESRD patients with regular HD
 - Exclusion: history of primary headache; having focal neurologic abnormalities; malnutrition; chronic diarrhea; need TPN; alcoholism
- Questioned about quality of headache
- Patients without headache as control



Table 2.—Demographic Features of the HDH Group and the Control Group

	HDH Group (n = 75)	Control Group (n = 80)	<i>P</i> Value
Age (years)	44.9 ± 16.9	49.6 ± 16.2	>.05
Male/female	35/40	30/50	>.05
Duration of HD (months)	47.7 ± 42	41.3 ± 32	>.05

HD = hemodialysis; HDH = hemodialysis headache.

Table 3.—Comparison of Pre- and Postdialysis Findings in the HDH Group and Control Group

	HDH (n = 75)	Control Group (n = 80)	P Value
Predialysis BUN (mg/dL)	79.9 ± 20.4	82 ± 20	.53
Postdialysis BUN (mg/dL)	33.5 ± 12.4	36.4 ± 12	.14
Predialysis sodium (mEq/L)	140.1 ± 3.8	137.8 ± 5.32	.003
Postdialysis sodium (mEq/L)	140.9 ± 4.05	139.6 ± 4.9	.06
Predialysis magnesium (mg/dL)	2.83 ± 0.7	3.10 ± 0.99	.05
Postdialysis magnesium (mg/dL)	2.34 ± 0.53	2.62 ± 0.76	.02
Ultrafiltration (L)	3.36 ± 1.33	3.14 ± 1.29	.33
Urea reduction rate (%)	0.42 ± 0.08	0.45 ± 0.11	.08
Predialysis SBP (mmHg)	130.7 ± 20.3	132.5 ± 29	.74
Postdialysis SBP (mmHg)	124.5 ± 19.7	125.1 ± 22.1	.88
Predialysis DBP (mmHg)	79 ± 11.9	79.3 ± 12.9	.89
Postdialysis DBP (mmHg)	74.4 ± 14.2	78.1 ± 12.6	.14
Predialysis weight (kg)	65.6 ± 12.1	69.1 ± 13.8	.11
Postdialysis weight (kg)	62.3 ± 11.6	66.0 ± 13.4	.08
Phosphorous (mg/dL)	5.87 ± 1.62	5.84 ± 2.1	.06
Calcium (mg/dL)	9.06 ± 1.12	8.9 ± 0.97	.41
Albumin (g/dL)	4.01 ± 0.35	3.95 ± 0.2	.24
Parathormon (pg/mL)	411 ± 539	377.6 ± 365	.93

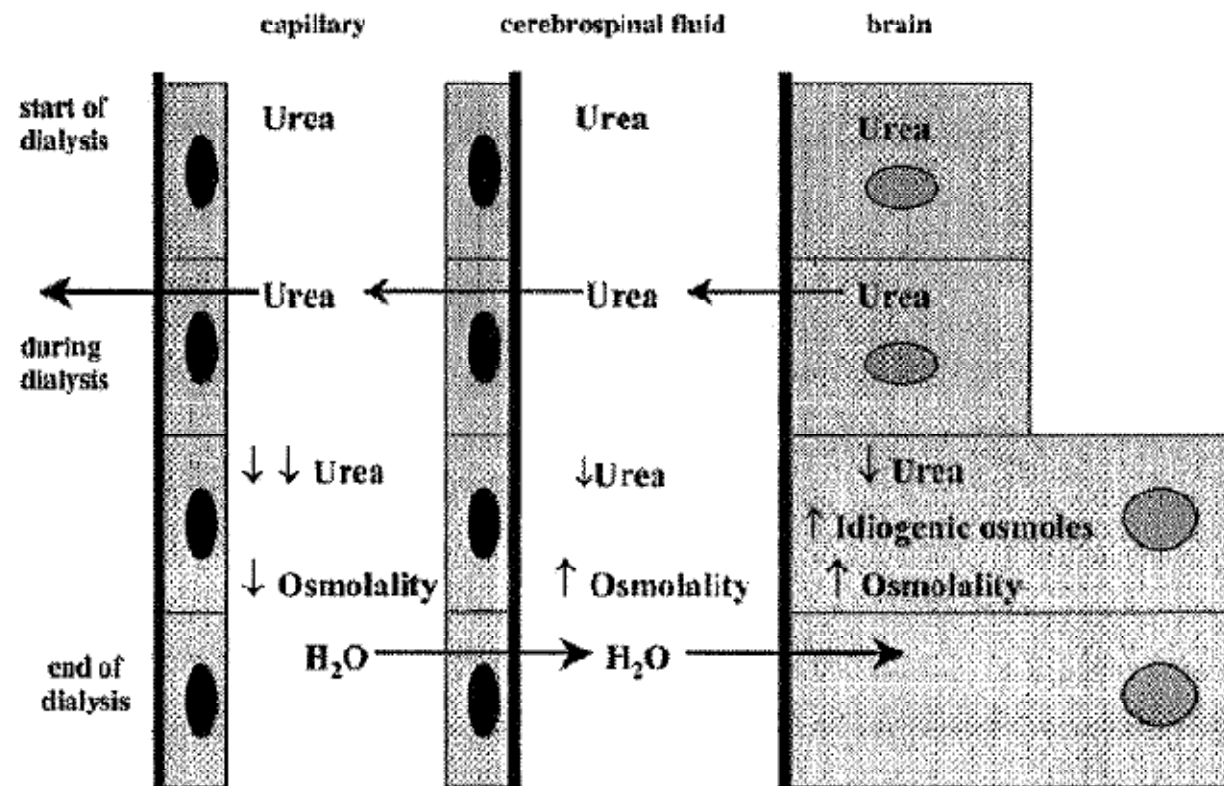
BUN = blood urea nitrogen; SBP = systolic blood pressure; DBP = diastolic blood pressure; HDH = hemodialysis headache.



Potential Pathophysiology

- Abrupt decrease of blood urea level
- Not cause a similar concomitant decrease in the brain due to blood-brain barrier
- Osmotic gradient develops
- Water shifts into the brain
 - Results in an increased intracranial pressure
 - “reverse urea effect”
- Others
 - Hypotension, Mg level

Fig 4. Pathogenesis of dialysis disequilibrium syndrome caused by increased removal of plasma urea, with slower removal from CSF and brain tissue, thus setting up an osmotic gradient with passage of water from the relatively hypotonic plasma to the relatively hypertonic brain, causing brain edema.



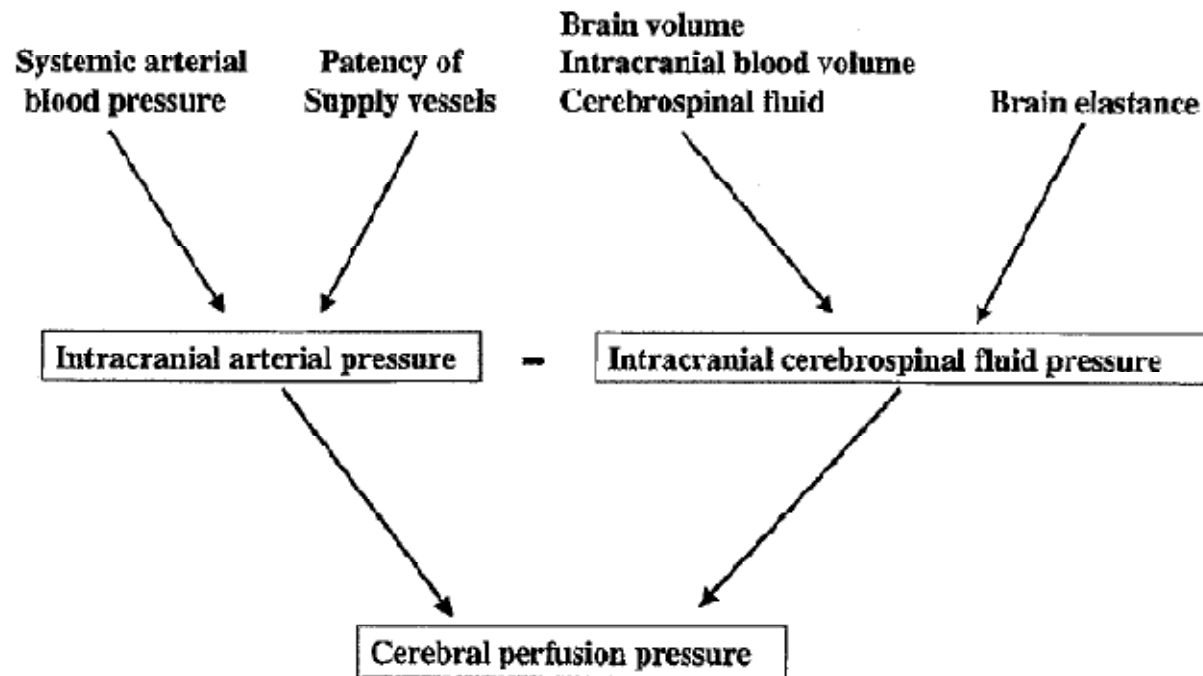


Fig 2. CPP is the difference between intracranial arterial pressure, usually measured as systemic MAP measured at the level of the carotid siphon and either intracranial CSF pressure or internal jugular venous pressure.

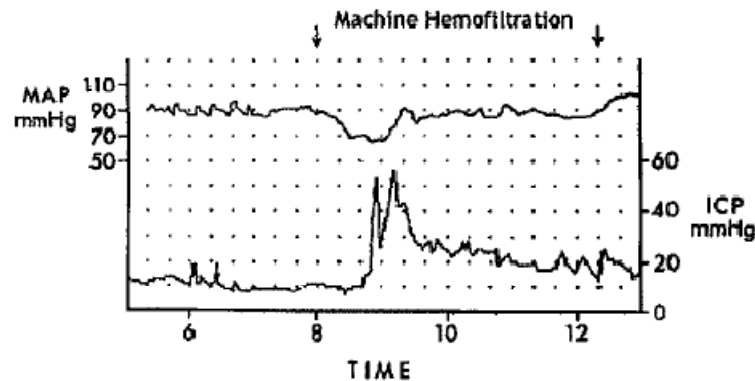


Fig 6. Chart recording of MAP and mean ICP during an intermittent machine hemofiltration treatment (17 L exchange) in a patient with cerebral edema secondary to fulminant hepatic failure.



Hemodialysis headache

M. Milinkovic¹, J. Zidverc-Trajkovic², N. Sternic², J. Trbojevic-Stankovic³, I. Maric⁴, M. Milic⁴, B. Andric⁵, P. Nikic⁵, P. Jovanovic⁶, P. Rosic⁶ and B. Stojimirovic¹

¹Institute of Urology and Nephrology, ²Institute of Neurology, Clinical Center of Serbia, ³Clinical Center Dr. D. Misovic Belgrade, ⁴Center for Endemic Nephropathy Lazarevac, ⁵Hospital Center, and ⁶Center for Hemodialysis Obrenovac, Serbia





Method and study design

- Cross-sectional or “prospective”
- Four HD centers in Serbia
- Subjects: HD patients, not mentioned inclusion and exclusion criteria
- Interviewed by a neurologist
 - Total 318 patients included
 - Hemodialysis headache: 21 (6.6%)



Table 1. Clinical characteristics of HD patients with and without HDH.

Cl. parameter (mean \pm SD)		With HDH	Without HDH	p
Sex	Women n (%)	6	113	0.386
	Men n (%)	15	184	
Age (years) mean \pm SD		55.19 \pm 15.5	60.24 \pm 12.48	0.979
Duration of HD (month) mean \pm SD		49.43 \pm 39.56	55.63 \pm 53.2	0.475
Primary renal disease	Vascular disease	9	77	0.157
	Parenchyme disease	9	132	
	Unknown etiology	3	88	

Table 2. Basic biochemical parameters of HD patients with and without HDH.

Bioch. parameter (mean \pm SD)		With HDH	Without HDH	p
s-urea nitrogen (mmol/l)		28.21 \pm 8.44	29.09 \pm 8.1	0.649
s-creatinine (μ mol/l)		841.76 \pm 239.35	889.97 \pm 244.39	0.383
Sodium, (mmol/l)		140.05 \pm 3.38	141.34 \pm 3.83	0.141
Potassium, (mmol/l)		5.37 \pm 0.74	5.33 \pm 0.88	0.844
s-Calcium, (mmol/l)		2.31 \pm 0.21	2.34 \pm 0.24	0.479
s-Phosphates, (mmol/l)		2.27 \pm 0.84	1.83 \pm 0.53	0.010
Ca \times P, (mmol ² /l ²)		5.22 \pm 1.9	4.26 \pm 1.26	0.033
s-glucose		6.48 \pm 0.48	7.06 \pm 0.31	0.010
s-albumin		43.4 \pm 3.61	42.95 \pm 0.68	0.035
Hb mean \pm SD		92.71 \pm 15.61	93.69 \pm 15.55	0.784
Systolic BP		152 \pm 26.1	140.67 \pm 22.930	0.035
Diastolic BP		87.8 \pm 19.5	88.53 \pm 24.64	0.393
Kt/V	< 1.19	13	118	0.201
	\geq 1.2	8	131	

s = serum, BP = blood pressure

Table 3. Hemodialysis headache features.

Characteristics	Number of patients n (%)
Sex-male	16 (76)
Only during HD [*]	15 (71)
Beginning in the 3rd hour of HD [*]	11 (52)
Duration less than 4 hours	16 (76)
Localization in the anterior parts of the head	11 (52)
Bilateral presentation	17 (81)
Intensity of pain (VAS ^{**} ≥ 8)	11 (52)
Quality of pain – non-pulsating	14 (67)
Without associated symptoms	14 (67)
Personal history positive for primary headache	0 (0)

*hemodialysis, **verbal-analogous scal



Table 4. Correlations between HDH and biochemical parameters.

Statistics	HDH	Glycemia	Albumin	Calcium (Ca)	Phosphates (PO4)	Ca × PO4	TA syst.	TA diastol.
Point-biserial correlation (r_{pb})	1.00	0.02	0.07	-0.04	0.14*	0.18*	0.10	-0.05
p		0.78	0.32	0.57	0.02	0.00	0.09	0.36

*Biserial correlation r_b

$$r_b = \frac{r_{pb} \sqrt{P_1 P_2}}{y}$$

for phosphates equals **0.27**, and for calcium-phosphates product equals **0.35**. HDH = hemodialysis headache.

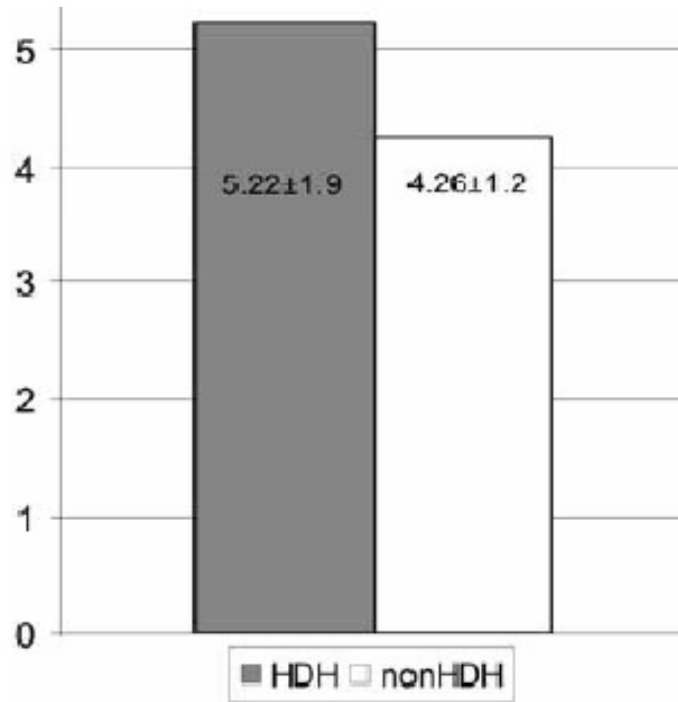


Figure 1. Calcium-phosphate product in mmol^2/l^2 ($p = 0.33$).

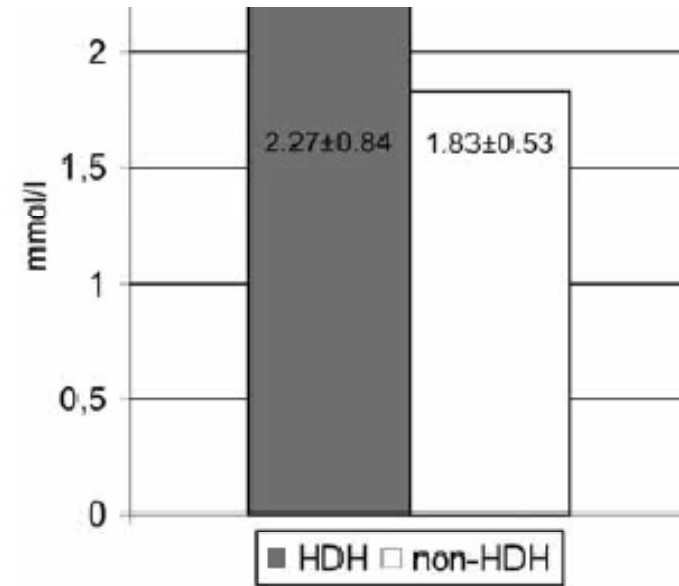
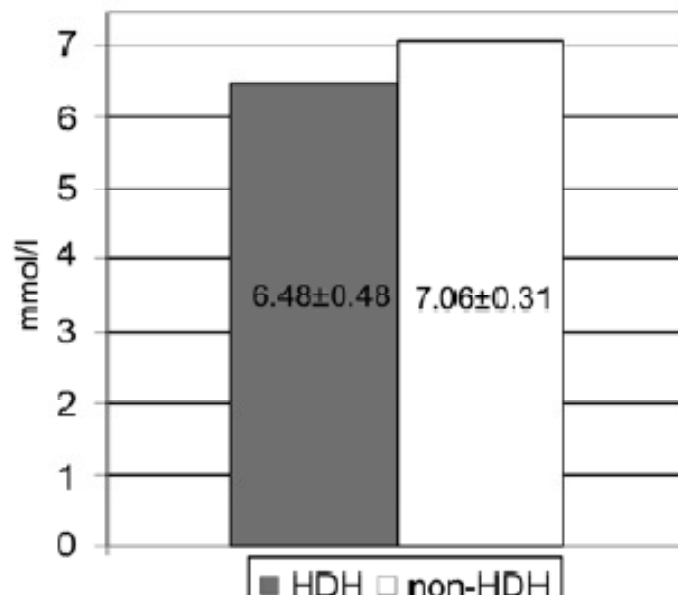


Figure 2. Serum phosphates ($p = 0.01$).

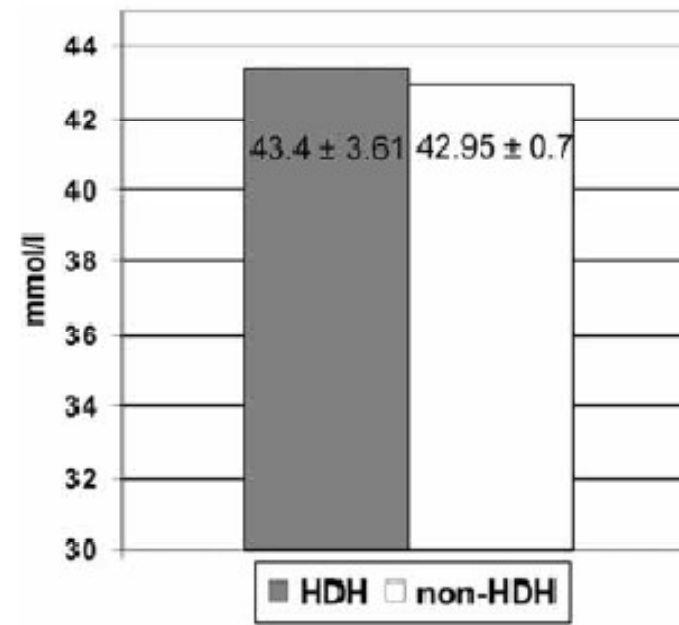


Figure 4. Serum albumin ($p = 0.035$).

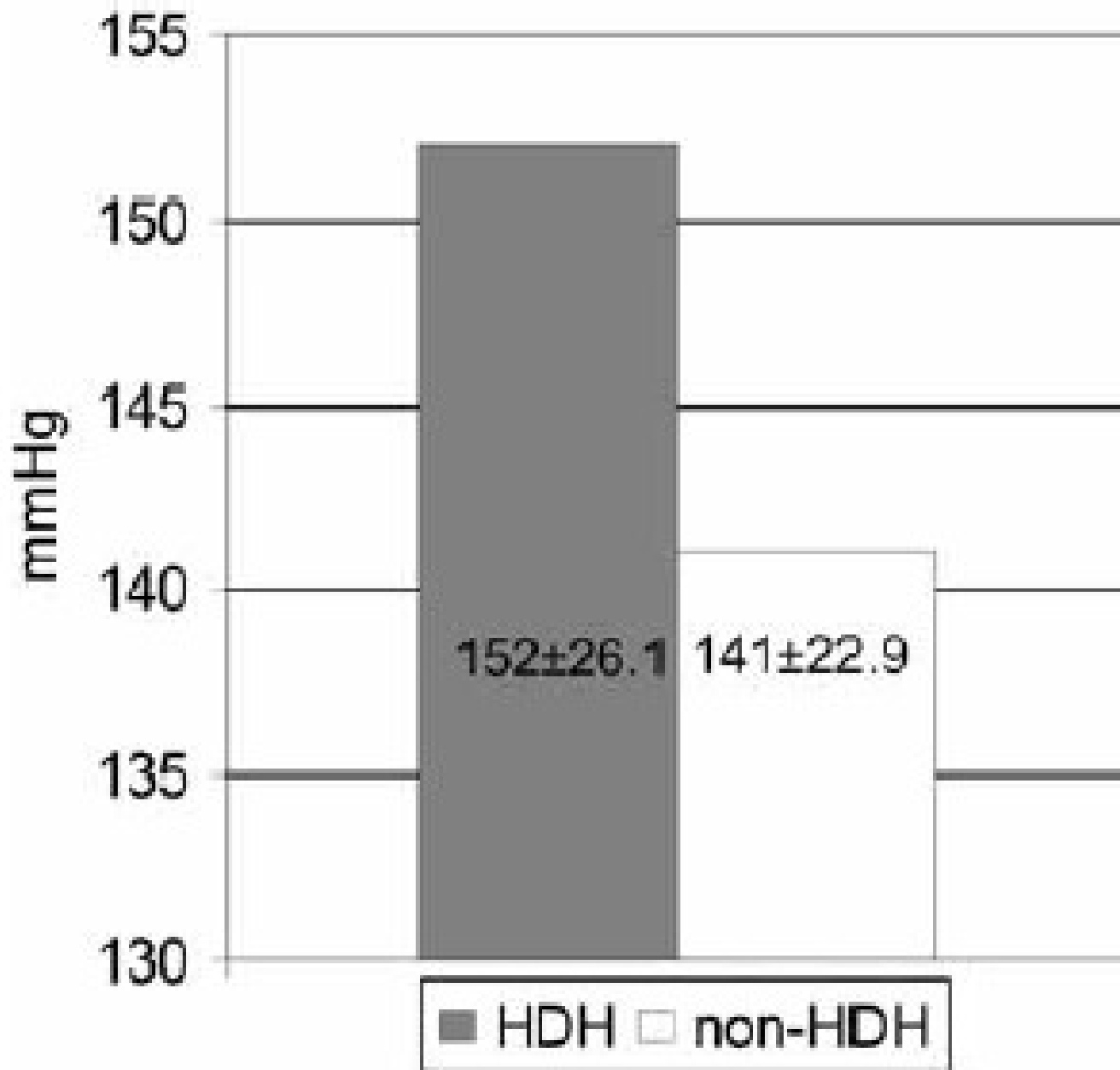


Figure 5. Systolic TA.



Conclusion

- Headache is common in patients undergoing HD
- Living chronically with an uncomfortable and tedious procedure in order to remain alive
- Also too often suffer the additional discomfort of recurrent headache



Perspective

- The prevalence of HD is high in Taiwan
- Further study of HD headache in Taiwan is warranted

01-Apr-2010

Dear Dr. Tseng:

It is a pleasure to inform you that your manuscript entitled "Comparative Outcomes between Hemo- and Peritoneal Dialysis Patients with Acute Intracerebral Hemorrhage" has been accepted by the American Journal of Nephrology and will appear on the web as a referenceable paper within the next six weeks. The manuscript will also appear in print form within two-four months following the web reference.

Thank you for your fine contribution. On behalf of the Editors of the American Journal of Nephrology, we look forward to your continued contributions to the Journal.

Sincerely,

Dr. George Bakris
Editor-in-Chief, American Journal of Nephrology



Thanks for your
attention!