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CLINICAL STUDY

Dialysis headache in patients undergoing peritoneal dialysis and hemodialysis

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Abstract

Objectives: Headache is among most frequently encountered neurological symptom during hemodialysis (HD), but still under investigated in peritoneal dialysis (PD) patients. The aim of this study was to assess the incidence and clinical characteristics of dialysis headache (DH) in HD and PD patients. *Material and methods*: A total of 409 patients (91 on PD and 318 on HD) were interviewed using a structured questionnaire, designed according to the diagnostic criteria of the International Headache Classification of Headache Disorders from 2004. Patients with DH underwent a thorough neurological examination. *Results*: DH was reported by 21 (6.6%) HD patients and 0 PD patients. PD patients had significantly lower serum sodium, potassium, calcium, phosphate, urea and creatinine, calcium–phosphate product, and diastolic blood pressure than HD patients. HD patients had significantly lower hemoglobin compared to PD patients. Primary renal disease was mostly parenchymal in HD patients, and vascular in PD patients. DH appeared more frequently in men, mostly during the third hour of HD. It lasted less than four hours, was bilateral, non-pulsating and without associated symptoms. *Conclusion*: Biochemical alterations may be implicated in the pathophysiology of DH. Specific features of DH might contribute to better understanding of this secondary headache disorder.

Keywords

End-stage renal disease, hemodialysis, headache, peritoneal dialysis

History

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Introduction

Dialysis prevents development and/or progress of uremia-related complications, such as neuropathy and encephalopathy, but the treatment itself may bring about acute or long-term neurological complications. Although headache is among the most frequently encountered neurological symptoms during hemodialysis (HD), studies reporting its features are limited. Even scarcer are data on headache associated with peritoneal dialysis (PD).[1]

According to the International Headache Society (IHS) criteria, dialysis headache (DH) is characterized by occurring during at least half of HD sessions, resolving within 72 h after dialysis or altogether after successful transplantation and by at least three attacks with these properties.[2] All criteria are related to HD.

The pathophysiology of DH is still unresolved. One suggestion was that the large water and electrolyte shifts during dialysis could induce headache. This is particularly important for HD, which is associated with more remarkable variations of hemodynamic parameters than PD. The headaches described in HD patients may represent an integral part of the so-called post-dialysis disequilibrium syndrome.[3] Another possible associated cause may be the presence of hypertension during HD. A positive correlation between the severity of hypertension and the likelihood of headache to occur during HD was reported, even though the absence of hypertension does not necessarily preclude the occurrence of DH.[4] There is still very little data available on headaches related to PD treatment.

In this study, we aimed to assess the frequency and clinical features of DH in HD and PD patients.

Material and methods

This prospective study included 409 patients from four dialysis centers in Serbia—91 on PD (43 females and 48 males, mean age 59.75 ± 11.53 years) and 318 on HD (119 females and 199 males, mean age 59.90 ± 12.73 years). All PD patients were on continuous ambulatory peritoneal dialysis with four daily exchanges of 2 L of glucose-based dialysate. All HD patients were on standard bicarbonate HD, performed thrice weekly for 4 h, using polysulfone dialyzers. Time on dialysis ranged from 3 to 60 months in PD patients and from 3 to 240 months in HD patients. Majority of patients on both dialysis modalities were treated with recombinant

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human erythropoietin. All patients gave their informed consent for participation in the research. The study was conducted in compliance with the Declaration of Helsinki.

All patients were interviewed by a single experienced neurologist, using a questionnaire based on the International Headache Classification diagnostic criteria. The questionnaire provided details on the time of headache onset, monthly incidence of symptoms, pain severity assessed by verbal-analogue scale (0 representing ''no pain'', 10 representing ''the strongest pain'' as estimated by the patient), quality of the pain (pulsating/throbbing and non-pulsating), location (anterior and posterior aspects of the head), lateralization (unilateral, bilateral, and diffuse), duration of the pain (in minutes) and associated symptoms (photophobia, phonophobia, osmophobia, nausea, vomiting, vertigo, and weakness of body parts). All patients with repeated headaches underwent thorough neurological examination and in some cases further diagnostic procedures were indicated.

Blood samples were drawn following 12-h overnight fasting, that is, after the night exchange in PD patients and before heparin administration at the beginning of HD session. Serum urea nitrogen was measured by complete enzymatic method (urease–glutamate-dehydrogenase), reference range was 3.5–7.5 mmol/L. Serum calcium concentration was determined by photometric color test (Arseniko), reference range was 2.20–2.65 mmol/L. Serum phosphates were determined by photometric UV-test, reference range being 0.80–1.45 mmol/L. Serum calcium and phosphates were calculated as mean values from two measurements in two consecutive months, performed prior to laboratory investigations and interview. Serum creatinine was determined by the Jaffe's kinetic method without deproteinization on multichannel analyzer. Serum sodium and potassium concentrations were determined by flame photometry. Hemoglobin concentration was determined by cyanmethemoglobin method on Coulter's analyzer. Peritoneal dialysis adequacy was assessed based on Kt/Vsp index, calculated from formula: Kt = total Kt = peritoneal Kt+renal Kt; peritoneal Kt = −h dialysate urea nitrogen content/serum urea nitrogen; renal Kt = −h urine urea nitrogen content/serum urea nitrogen.

V (by Watson formula): $V = 2.447 - 0.09516\,A + 0.1074\,H + 0.3362\,W$ (in males),

$V = -2.097 + 0.1069\ H + 0.2466\,W$ (in females), where A = age (years), H = height (cm), and W = weight (kg). Hemodialysis adequacy was assessed based on Kt/Vsp index, calculated from Daugirdas second-generation formula:

$$\mathrm{Kt/Vsp} = -\ln(C_2/C_1 - 0.008 \times T) + (4 - 3.5 \times C_2/C_1) \times \mathrm{UF}/W$$

where C_1 is predialysis serum urea, C_2 is postdialysis serum urea (mmol/L), T is duration of dialysis session in hours (h), UF is interdialysis weight gain (L), and W is the patients' postdialysis weight (kg).

Reference values for adequate dialysis according to KDOQI guidelines are weekly Kt/V >2 for PD patients and Kt/Vsp ≥1.2 for HD patients.[1] Arterial blood pressure (BP) was calculated as mean value from 12 measurements taken before and after mid-week HD session or first daily exchange in PD patients. Results were statistically analyzed with Chi-square test, *t*-test for parametric and Mann–Whitney test for non-parametric data. $p < 0.05$ was considered significant.

Results

Basic demographic and clinical data and underlying renal disease are shown in Table 1. No statistically significant differences were found regarding age and sex between PD and HD patients. However, underlying renal disease in HD patients was mostly parenchymal, while in PD patients it mostly had vascular etiology (Table 1). Majority of patients had adequate dialysis (Table 1).

PD patients had significantly lower serum sodium, potassium, calcium, phosphate, calcium–phosphate product, urea and creatinine, and significantly higher serum hemoglobin than HD patients (Table 2). Systolic BP did not differ significantly among PD and HD patients, while diastolic BP was significantly lower in PD patients (Table 1).

Only three patients (2 men and 1 woman) had headaches before starting CAPD. Two subjects had episodic tension-type headache and one had occipital neuralgia. None of the patients observed changes in headache characteristics following the beginning of PD treatment (Table 3). Preexisting headaches were present in 53 (16.7%) HD patients (31 women and 22 men), mostly diagnosed as tension-type (43.4%) and migraine (26.4%). Most HD patients observed no changes in the characteristics of primary headache in connection to the

Table 1. Demographic and clinical characteristics.

Characteristic	HD	PD	*p*
Age (years)	59.9 ± 12.73	59.75 ± 11.53	0.776
Sex			
Male	199	48	0.091
Female	119	43	
Kt/V			
Satisfactory[a]	139	29	0.838
Non-satisfactory[b]	131	29	
BP systolic (mmHg)	141.26 ± 23.189	137.42 ± 21.705	0.137
BP diastolic (mmHg)	88.5 ± 24.37	79.78 ± 12.315	0.029
Underlying renal disease			
Vascular	86	49	0.000
Parenchymal	141	20	
Unknown	91	22	

Notes: BP = blood pressure.
[a]Kt/V >1.2 for HD, Kt/V >2 for PD.
[b]Kt/V <1.2 for HD, Kt/V <2 for PD.

Table 2. Biochemical characteristics of the study groups.

Variable	CAPD	HD	*p*
Hgb (g/L)	112.1 ± 10.29	93.63 ± 15.53	0.000
Ca (mmol/L)	2.245 ± 0.224	2.335 ± 0.24	0.004
P (mmol/L)	1.598 ± 0.451	1.857 ± 0.565	0.000
Ca × P ($mmol^2/L^2$)	3.602 ± 1.057	4.324 ± 1.332	0.000
K (mmol/L)	4.392 ± 0.828	5.335 ± 0.868	0.000
Na (mmol/L)	138.78 ± 3.61	141.26 ± 3.81	0.000
Urea (mmol/L)	17.875 ± 6.235	29.028 ± 8.115	0.000
Creatinine (umol/L)	766.81 ± 206.91	886.73 ± 243.98	0.000

Notes: Hgb—hemoglobin, Ca—calcium, P—phosphate, Ca × P—calcium–phosphate product, K—potassium, Na—sodium.

beginning of chronic HD treatment (Table 3). None of the patients with primary headaches experienced attacks of their typical headache during HD. Statistically significant difference was found between HD and PD patients regarding types of primary headache (Table 3).

Dialysis headache was more frequent in males, it typically began during the third hour of HD, and lasted less than four hours. It was mostly bilateral, non-pulsating and without associated symptoms, resembling tension-type headache and without migrainous features (Table 4).

Discussion

HD and PD are well established modalities for treating end stage renal disease patients in Serbia, with some 7,000,000 inhabitance and nearly 5000 patients on HD and 300 patients on PD.

Dialysis headache was present in 6.6% of HD patients in this study. None of the PD patients had DH. Previous studies reported 70% incidence of DH on HD,[4] while more recent researches registered DH in 50% of HD patients.[3,5] Substantial decrease in DH incidence may be explained by advances in HD quality. DH was more frequent on acetate HD due to negative base excess following acetate dialysis and decrease in carbon dioxide partial pressure.[4,6] Furthermore, earlier studies on this subject[3,5] did not apply diagnostic criteria from the revised ICHD from 2004, which were used in our research classifying DH as a secondary headache disorder attributed to the disorder of homeostasis.[2] It is therefore possible that these studies included headaches which were present before the beginning of chronic dialysis treatment, such as migraine or hypertensive headache, as DH.[7] HD and PD vintage had no significant influence on occurrence of DH in our study. The same finding regarding HD patients was reported by other authors.[8]

Dialysis headache characteristics in our study (male preponderance, appearance during the third hour of HD session, less than four hours duration, bilateral localization and non-pulsating quality) were somewhat different from those reported by Goksan et al., where DH on HD was more often present in female patients, had moderate intensity, throbbing quality and bilateral localization.[3]

Statistically significant difference was found between PD and HD patients in distribution of underlying renal disease. Patients treated with HD mostly had parenchymal diseases, while patients undergoing PD mostly had vascular diseases. This can be partially explained by the fact that vascular disease patients are referred to PD due to problems creating and maintaining adequate vascular access.

HD patients in this study had significantly higher calcium, phosphate and calcium–phosphate product than PD patients. High calcium–phosphate product is an important risk factor for development of extraskeletal calcifications, namely diffuse, longitudinal calcifications of tunica media (Monckeber's medial sclerosis).[9] Such calcifications may decrease elasticity of cerebral blood vessels, thus decreasing their autoregulatory ability and contributing to appearance of DH.[1]

Patients undergoing HD in our study had significantly higher predialysis serum sodium, potassium, urea and creatinine than PD patients. Several studies of disequilibrium syndrome as a possible cause of DH reported significantly lower serum sodium and urea in HD patients with DH.[3,4,7,8] The disequilibrium syndrome may appear during HD, but it is most common at the end or following a HD session. It is attributed to acute cerebral edema in inadequately dialyzed patients, which appears due to fast elimination of substances from extracellular fluid.

Patients on regular HD in this study had significantly higher diastolic BP levels than PD patients. Systolic BP was also higher in HD patients, but without statistical significance. In their study of DH in HD patients, Goksan et al. reported significantly higher systolic and diastolic BP in patients with HD related headache even before starting HD session.[3] On the other hand, they did not observe difference in BP after HD, concluding that sudden decrease of arterial BP during HD may induce headache.[3] Hypertension appears in early stages of renal failure and in majority of patients persists even after commencement of dialysis treatment.[10] Being a more continuous process, PD initially offered excellent blood pressure and volume control, especially for hemodynamically unstable patients.[1] It was therefore common practice to allow liberal salt and water intake in PD patients. However, a number of recent studies have shown that subclinical volume expansion causing hypertension is common in PD patients.[11,12] The effects become more obvious once residual renal function is lost. Excessive dietary salt intake contributes to uncontrolled hypertension and volume overload.[1]

Although the cases of caffeine-withdrawal headache have been described in HD patients, none of the patients in our group of patients fulfilled criteria for this disorder.[13]

Intermittent nature of HD demands fluid removal and electrolyte correction to be performed over a short time interval and such rapid removal of fluid is often poorly tolerated.[1] More rapid decrease of extracellular than intracellular urea concentration and consequential osmotic fluid shift lead to more rapid changes of body fluids volume, including cerebrospinal liquid, thus significantly contributing to increased intracerebral pressure, cerebral edema and

Table 3. Types of predialysis headaches.

Predialysis headaches types	HD	PD	*p*
Primary, *n* (%)	41 (12.9)	2 (2.2)	0.002
Symptomatic, *n* (%)	12 (3.8)	1 (1.1)	0.313

Table 4. Dialysis headache features in hemodialysis (HD) patients.

Headache features	*n* (%)
Male sex	16 (76)
Only during HD	15 (71)
Begining in the third hour of HD	11 (52)
Duration less than 4 h	16 (76)
Anterior localization	11 (52)
Bilateral presentation	17 (81)
Pain intensity (VAS $\geq$8)	11 (52)
Quality of pain—non-pulsating	14 (67)
No associated symptoms	14 (67)
Predialysis headache	0 (0)

Note: VAS—verbal-analogous scale.

headache in HD patients. This may also explain why PD patients in our study do not suffer from DH, since removal of particles and fluid during PD is more gradual than during HD.

PD patients in this study had significantly higher hemoglobin than HD patients. Headache may be a symptom of anemia but correlation between complete blood count and headache has seldom been systematically studied. Furthermore, International Headaches Classification does not include anemia as possible cause of symptomatic headaches, but rather includes it in the appendix, together with other metabolic and systemic disturbances.[2] A few epidemiological studies reported contradictory results on the correlation between anemia and headaches. Therefore controlled prospective studies are still needed to determine incidence and properties of headaches associated with these states.[2]

In conclusion, biochemical alterations may be implicated in the pathophysiology of DH. Specific features of DH might contribute to better understanding of this secondary headache disorder.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Daugirdas J, Blake P, Ing T. *Handbook of Dialysis*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.
2. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders. *Cephalalgia*. 2004;24(suppl 1):1–160.
3. Goksan B, Karaali-Savrun F, Ertan S, Savrun M. Hemodialysis-related headache. *Cephalgia*. 2004;24:284–287.
4. Bana DS, Yap AU, Graham JR. Headache during hemodialysis. *Headache*. 1972;112:1–14.
5. Alessandri M, Massanti L, Geppeti P, Belluci G, Cipriani M, Fanciullacci M. Plasma changes of calcitonin gene-related peptide and substance P in patients with dialysis headache. *Caphalalgia*. 2006;26:1287–1293.
6. Neyer U, Woss E, Haller R, Kross R. Headache and EEG changes caused by acetate and bicarbonate dialysis. *Acta Med Austriaca*. 1983;10:15–23.
7. Milinkovic M, Zidverc-Trajkovic J, Sternic N, et al. Hemodialysis headache. *Clin Nephrol*. 2009;71(2):158–163.
8. Goksel KB, Torun D, Karaca S, et al. Is low blood magnesium level associated with hemodialysis headache? *Headache*. 2006;46: 40–45.
9. Fukagawa M, Kazama JJ. The making of a bone in blood vessels: From the soft shell to the hard bone. *Kidney Int*. 2007;5: 533–534.
10. Agarwal R. Hypertension in hemodialysis patients: Hypertension in hemodialysis: A comprehensive review. *Semin Diál*. 2004; 17(4):249.
11. Enia G, Mallamaci F, Benedetto FA, et al. Long-term CAPD patients are volume expanded and display more severe left ventricular hypertrophy than hemodialysis patients. *Nephrol Dial Transplant*. 2001;16:1459–1464.
12. Faller B, Lameire N. Evolution of clinical parameters and peritoneal function in a cohort of CAPD patients followed over 7 years. *Nephrol Dial Transplant*. 1994;9:280–286.
13. Nikic P, Zidverc-Trajkovic J, Andric B, Milinkovic M, Stojimirovic B. Caffeine-withdrawal headache induced by hemodialysis. *J Headache Pain*. 2009;10(4):291–293.