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Effects of haemodialysis and continuous ambulatory peritoneal dialysis on P300 cognitive potentials in uraemic patients

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ABSTRACT

The aim of this study was to determine the effects of haemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) on P300 cognitive potentials in patients with chronic renal failure (CRF) and to find out if P300 potential is a valuable marker for following subclinical cognitive disorder.

This study was performed in 42 patients with chronic uraemia, of whom 25 were on HD and 17 on CAPD, and in 25 healthy subjects. All the subjects were investigated in terms of P300 cognitive potential obtained from auditory stimuli with the oddball paradigm and the Mini-Mental State (MMS) examination. Patients undergoing HD were evaluated before (pre-dialysis) and after (post-dialysis) standard HD treatment. P300 latency was longer in HD patients than in the control group and CAPD patients. The MMS score was greater and P300 latency was shorter after a standard HD session when compared to pre-dialysis values in HD patients ($p < 0.001$ for both values). There was a negative correlation between P300 latency and MMS scores, and a positive correlation between P300 amplitude and MMS scores.

In conclusion, P300 is useful for evaluating cognitive function in uraemia, even in asymptomatic patients, and CAPD is superior to HD in the management of cognitive impairment.

INTRODUCTION

Peripheral neuropathy and central nervous system (CNS) dysfunction are well known complications of chronic renal failure (CRF) (6, 12, 16). Quantification of the neurological abnormalities can be evaluated by electrophysiological and psychometric testing in patients with CRF (6).

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Measurement of cognitive event-related potentials (ERPs) is an objective electrophysiological tool that has been used to investigate the cognitive faculty (7, 9). Event-related potentials are specific electroencephalogram (EEG) deflections appearing only in response to voluntary, task-related cognitive function, and are generated by patients' responses to visual, auditory or sensory stimuli. Event-related potentials are related to some aspect of the cognitive events associated with the distinction of the target from nontarget stimuli (7). The P300 cognitive potential obtained from auditory stimuli with the oddball paradigm is the best-known type of ERP (10). In normal young adults, the largest positive-going peak occurring at approximately 300 msec was designated as the P300 component (11). A positive correlation has been shown between P300 latency and the degree of cognitive decline in various clinical populations (7, 8, 14). Prolongation of P300 latency was shown to be the earliest sign of cognitive dysfunction in metabolic encephalopathies including uremic (13, 17) and hepatic encephalopathies (13).

The Mini-Mental State (MMS) examination is one of the most commonly used psychometric tests for detecting cognitive impairment and following cognitive changes over time (5).

The aims of this study were [1] to investigate P300 cognitive potential and MMS tests in HD patients, CAPD patients and healthy controls; and [2] to evaluate the acute effects of HD treatment on these tests.

METHODS

Subjects

Forty-two patients with chronic renal failure (25 on haemodialysis [HD], 13 male and 12 female, mean age 37.3±2.7 years [range 19–64], and 17 on continuous ambulatory peritoneal dialysis [CAPD], 7 male and 10 female, mean age 44.2±3.9 years [range 20–75] and 25 healthy subjects (14 male and 11 female, mean age 41.2 ± 3.5 years [range 22–83]) were included in the study. Patients with diabetes mellitus or another metabolic disease leading to encephalopathy were excluded.

Primary renal diseases were known in 11 HD patients (glomerulonephritis 5, autosomal dominant polycystic kidney disease 3, hypertension 2, and amyloidosis 1) and in 7 CAPD (glomerulonephritis 3, autosomal dominant polycystic kidney disease 1, amyloidosis 1, hypertension 1, and systemic lupus erythematosus 1). Mean time on dialysis was longer among HD patients compared to CAPD patients (62 versus 16 months). The duration of one HD session was 4 hours and 18 of the 25 HD patients were on HD treatment thrice weekly and the remaining was on twice weekly. All CAPD patients were receiving standard 2 litres solution 4 times a day. Daily urine volume was higher than 200 ml in 3 HD patients and 3 CAPD patients. The target KT/V was 1.3 for HD patients and 2.0 for CAPD patients. Other clinical and biochemical parameters are presented in Table 1. Informed consent was obtained from all patients.

Table: 1. Some Clinical and Biochemical Parameters among HD and CAPD Patients

Parameters	HD Patients	CAPD Patients
Hypertension	68%	65%
Number of antihypertensive drugs*	2.4	1.6
Haemoglobin (g/dl)*	9.6	10.7
Epoetin treatment	88%	100%
Parathormon (pg/ml)*	625	290
Calcium (mg/dl)*	7.9	9
Phosphorus (mg/dl)*	5.9	5.2

* Mean values

Testing procedure

P300 cognitive potential was measured and the MMS examination was carried out in all subjects. All tests were performed twice in HD patients, two hours before and after a standard HD session.

Event-related potentials were recorded with an EMG machine (Nihon Kohden Neuropack-8 EMG/Evoked Potential) in a silent room. P300 cognitive potential was obtained from auditory stimuli with the oddball paradigm. Event-related potentials were elicited by binaural acoustic stimuli: 200 clicks were delivered randomly by the computer. The frequent tones comprised 80% of the signal frequencies, which were set at 1 kHz, while the remaining 20% comprised the rare tones at 2 kHz (Intensity: 80 dB, rise-fall time: 10 msec, plato: 20 msec). During the examination, the subjects were asked to count upon perception of the rare tones, the designed target stimuli. The recording was performed with silver disk electrodes (according to the 10–20-system) placed on the scalp, placing the active recording electrodes Cz, and the reference electrodes to both the linked ear lobes and the ground electrode Fpz. The electrode-to-skin resistance was maintained below 5 kΩ for each electrode.

The latency of P300 cognitive potential was measured from the onset to the peak of the largest positive-going peak. The amplitude was measured peak-to-peak of the P300 wave. The MMS examination was performed as described by Folstein et al. (5).

Statistical analysis

Mann-Whitney U-Wilcoxon Rank Sum W, Wilcoxon Matched-Pairs Signed-Ranks, and Spearman correlation tests were used for statistical analysis and a p value less than 0.05 was considered statistically significant.

RESULTS

The results of P300 latency and amplitudes, and MMS are shown in Table 2. The MMS score was significantly lower in dialysis patients than in the control group. P300 amplitudes were similar in all groups.P300 latency was longer in HD patients

Table: 2. The MMS Score, P300 Latency and Amplitude Values of Patients and Healthy Controls

Parameters	Control	CAPD Patients	HD Patients	
			Pre-dialysis	Post-dialysis
MMT (score)	30±0.2	29±0.3[a]	26±1.5[b,d]	28±0.3[b]
P300 Latency (msec)	323±5.2	337±14.1	378±8.9[b,e]	349±9.2[c]
P300 Amplitude (μV)	14±1.3	15±1.5	12±1.5	14±1.2

Results are expensed as mean ± standard error of mean.
[a] $p < 0.01$ versus control group
[b] $p < 0.001$ versus control group
[c] $p < 0.05$ versus control group
[d] $p < 0.001$ versus CAPD patients
[e] $p < 0.05$ versus CAPD patients

than in the control group and CAPD patients. The MMS score was greater and P300 latency was shorter after a standard HD session compared to pre-dialysis values in HD patients ($p < 0.001$ for both values).

There was a negative correlation between P300 latency and MMS scores in the both patient and control groups (respectively r=–0.447, p=0.003; r=–0.166, p= 0.427). This was statistically significant in the patient group.

There was a positive correlation between P300 amplitude and MMS scores in the both patient and control groups (respectively r=0.109, p=0.491; r=0.405, p=0.045). This was statistically significant in the control group.

DISCUSSION

This study documents the presence of electrophysiological and psychometric test abnormalities in uraemic patients, and shows that CAPD patients may have some advantages over HD patients.

Previous studies evaluating P300 latency and MMS scores in uraemia mainly focused on HD patients. The number of studies evaluating P300 in uraemic patients is limited and different study designs have been used. Gallai et al. (6) demonstrated improvements in P300 latency following dialysis in 20 patients undergoing HD treatment. Abnormal P300 and pattern visual evoked potential latencies were found in 22 patients (13 were maintained on chronic haemodialysis and 9 were receiving only a low-protein diet) in a study by Cohen et al. (3). Tennyson et al. evaluated long-latency event-related potentials and the Symbol Digit Modalities Test in 10 haemodialysis patients. Significant increases in N200 and P300 amplitude were demonstrated following dialysis treatment in these 10 patients. In their study, ERP component latency and the Symbol Digit Modalities Test were not affected by dialysis. Control groups were not used (15). Evers et al. investigated visually evoked ERPs in 33 neurologically asymptomatic patients before and after they underwent hemodialysis. They compared the data with those of age-matched healthy subjects. Before hemodialysis, the patients' P300 latency was significantly prolonged as

compared with that of the control group. After hemodialysis, P300 latency of the patients decreased, this was statistically significant (4).

The study design used by Buoncristiani et al. was similar to ours, and, to the best of our knowledge, P300 latency in CAPD patients has only been studied in their study. They demonstrated better neurocognitive function in CAPD patients and improvement in neurocognitive function after a dialysis session in HD patients (2).

Our study shows transient improvements in MMS scores and P300 latency after a standard HD session, but these improvements are limited when compared those in CAPD patients. The beneficial effects of CAPD over HD on neurocognitive functions may be due to the following: [1] better removal of middle molecules; [2] its continuity, avoiding the 'peak hypothesis'; and [3] better control of anaemia.

In conclusion, P300 is useful for evaluating cognitive function in uraemia, even in asymptomatic patients, and CAPD is superior to HD in the management of cognitive impairment.

REFERENCES

1. Brown, W.S., Marsh, J.T., Wolcott, D., Takushi, R., Carr, C.R., Higa, J. & Nissenson, A.R.: Cognitive function, mood and P3 latency: effects of the amelioration of anemia in dialysis patients. Neuropsychologia 29 (1): 35–45, 1991.
2. Buoncristiani, U., Alberti, A., Gubbiotti, G., Mazzotta, G., Gallai, V., Quintaliani, G. & Gaburri, M.: Better preservation of cognitive faculty in continuous ambulatory peritoneal dialysis. Perit Dial Int 13 Suppl 2: 202–205, 1992.
3. Cohen, S. N., Syndulko, K., Rever, B., Kraut, J., Coburn, J. & Tourtellotte, W. W.: Visual evoked potentials and long latency event-related potentials in chronic renal failure. Neurology 33: 1219–1222, 1983.
4. Evers, S., Tepel, M., Obladen, M., Suhr, B., Husstedt, I.W., Grotemeyer, K.H. & Zidek, W.: Influence of end-stage renal failure and hemodialysis on event-related potentials. J Clin Neurophysiol 15 (1): 58–63, 1998.
5. Folstein, M. F., Folstein, S. E. & McHugh, P. R.: Mini-Mental State: A practical method for grading the state of patients for the clinician. J Psychiatr Res 12: 89–98, 1975.
6. Gallai, V., Alberti, A., Buoncristiani, U., Firenze, C. & Mazzotta, G.: Changes in auditory P3 event-related potentials in uremic patients undergoing HD. Electromyogr Clin Neurophysol 34: 397–402, 1994.
7. Goodin, D. S.: Event-Related (Endogenous) Potentials. In: Electrodiagnosis in Clinical Neurol. (ed. M. J. Aminoff), pp. 627–648. Churchill Livingstone, New York, 1992.
8. Goodin, D. S., Starr, A., Chippendale, T. & Squires, K. C.: Sequential changes in the P3 component of the auditory evoked potential in confusional states and dementing illnesses. Neurology 33: 1215–1218, 1983.
9. Kramer, L., Madl, C., Stockenhuber, F., Yeganehfar, W., Eisenhuber, E., Derfler, K., Lenz, K., Schneider, B. & Grimm, G.: Beneficial effect of renal transplantation on cognitive brain function. Kidney Int: Mar 49 (3): 833–8, 1996.
10. Oken, B. S.: Endogenous event-related potentials. In: Evoked Potentials in Clinical Medicine (ed. K. H. Chiappa), pp. 529-563. Lippincott-Raven Publishers, Philadelphia, New York, 1997.
11. Polich, J. & Squire, L. R.: P300 from amnesic patients with bilateral hippocampal lesions. Electroencephalogr and Clin Neurophysiol 86: 408–417, 1993.
12. Raskin, N. H. & Fishman, R. A.: Neurologic disorders in renal failure. N Engl J Med 294: 143–148, 1976.
13. Ruzicka, E., Tesar, V., Jelinkova, E., Mmerta, M., Nevsimalova, S. & Kucerova, O.: Event-related potentials in evaluation of metabolic encephalopathies. Schweiz Arch Neurol Psychiatr: 144 (4): 378–84, 1993.

14. Stivelman, J.C.: Benefits of anaemia treatment on cognitive function. Nephrol Dial Transplant 15 Suppl 3: 29–35, 2000.
15. Tennyson, T. E., Brown, W. S., Vaziri, N. D., & Jennison, J. H.: Event-related potential changes during hemodialysis. Int J Artif Organs 8: 269–276, 1985.
16. Tyler, H. R.: Neurologic disorders in renal failure. Am J Med 1: 888–890, 1978.
17. Weissenborn, K., Scholz, M., Hinrichs, H., Wiltfang, J., Schmidt, F.W. & Kunkel, H.: Neurophysiological assessment of early hepatic encephalopathy. Electroencephalogr Clin Neurophysiol: Apr 75 (4): 289–95, 1990.

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