ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN — POLONIA
VOL. LI, 20 SECTIO D 1996

Katedra i Klinika Neurologii Akademii Medycznej w Lublinie
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Uraemic Autonomic Neuropathy

Mocznicowa neuropatia autonomiczna

Uraemia leads to the damage of autonomic nervous system and the emergence of uraemic autonomic neuropathy. Consequences of uraemia may be dangerous for life, therefore its early diagnosis and prevention is essential.

Pathogenesis of uraemic autonomic neuropathy is to a great extent unclear. However, its development is believed to depend on many factors which overlap one another. From among the pathogenic factors, the age of patients is taken into consideration. Frequency and intensity of symptoms of uraemic autonomic neuropathy are considerably higher in older patients than in younger ones (15). This correlation is clearly manifested in patients prophylactically treated than in those who were dialysed (12). The impact on the duration of chronic renal insufficiency is controversial. The majority of authors do not confirm the relation of the uraemic autonomic neuropathy intensity to the duration of the dialysis' treatment (15, 17). Rozentryt (12) believes that more significant is the duration time of chronic renal insufficiency before dialyses are on.

Anaemia, one of the most common complications of chronic renal insufficiency, has for a long time been considered a pathogenic factor in uraemic autonomic neuropathy (2). The introduction of erythropoetine into the treatment of anaemia in chronic renal insufficiency allowed to evaluate the functioning of the autonomic system after anaemia had been corrected. It appears that in patients effectively treated with

erythropoetine, together with the improvement of haematological parameters there occurs normalisation of functions in the autonomic nervous system. After an effective treatment with erythropoetine, Stojceva-Taneva (14) had observed patients for two years and did not find any irregularities in the functioning of their autonomic nervous system. Biochemical changes taking place in patients with chronic renal insufficiency, without doubt have an influence on the development of uraemic autonomic neuropathy. Earlier postulated influence of high urea and/or creatinine concentration, was not confirmed in new research (8). An unfavourable effect of parathormone on peripheral nerves is unquestionable (5), but the pathogenic influence on the autonomic system has not been proved yet. It is assumed that a harmful factor for nerves and receptors of the autonomic nervous system is not directly a hormone, but rather a calcium-phosphoric disorder secondary to its surplus (4). Less proved in the literature is the influence of other factors, whose unfavourable effects are taken into consideration in the development of uraemic autonomic neuropathy. Accumulation of aluminium in patients with chronic renal insufficiency causes damage to the functioning of their neurotransmitters. Lai and others (7) found that aluminium slows down acquisition of dopamine, noradrenaline and serotonine as well as damages the functioning of the neurotransmitting system of glutamic and γ-aminobutyric acids. Perry and others (11) described a decrease of acetylcholine synthesis in patients with accumulation of aluminium. These neurotransmitters determine the proper performance of uraemic autonomic neuropathy and their deficiency may cause changes, mainly functional ones, in the operation of the system.

Similar role may be considered in relation to the concentration of magnesium, calcium and hydrogen ions, which play a very important role in excitability and nervous conductivity. In patients with chronic renal insufficiency the ions' concentration is not stable and undergoes big fluctuations (13). One may also consider a harmful influence of medicines, which in patients with chronic renal insufficiency have changed pharmakinetics and often reach toxic concentrations (10), as well as hypoxaemia encountered during the dialysis, which in consequence leads to a nervous ischaemia. The changes may be intensified by a disturbed autoregulation of cerebral vessels found in dialysed patients (9). In the

pathogenesis of uraemic autonomic neuropathy the influence of patients' nourishment should be emphasised. Chronically dialysed patients are often emaciated, have calorific deficiency, mainly albuminous. Hirsch (6) showed that in emaciated patients autonomic neuropathy develops more often and is stronger expressed. Taking into consideration the above mentioned data it is nowadays assumed that in the pathogenesis of uraemic autonomic neuropathy one is to deal with the summation of the influence of different factors, both preceding the development of chronic renal insufficiency and those appearing as its consequence. Their action is most probably intensified by changes in autoregulation of the cerebral circulation as well as a defect of the blood-brain barrier, that are disclosed and intensified in the course of uraemia.

The most common symptoms of uraemic autonomic neuropathy are diaphoresis' disturbances, hypotension after a change to a perpendicular position, frequent hypotension during the dialysis, impotence, feeling of sustained satiety after eating, difficulties with evacuation, diarrhoea especially at night, hypersensitiveness to warmth and coolness (15, 16, 17). Frequency of these symptoms in chronic renal insufficiency patients is approximately 43—54% (12, 15, 17).

Table I. The ranges of norms of the Ewing's tests set

	NORM	BORDER	PATHOLOG
VALS	$\geqslant$ 1,21	1,11 — 1,20	$\leqslant$ 1,10
WSP odd.	$\geqslant$ 15	11 — 14	$\leqslant$ 10
MIN/MAX.	$\geqslant$ 1,04	1,01 — 1,03	$\leqslant$ 1,00
PION (mm Hg)	$\leqslant$ 10	11 — 29	$\geqslant$ 30
HGP (mm Hg)	$\geqslant$ 16	11 — 15	$<$ 10

In order to diagnose uraemic autonomic neuropathy, it is essential to carry out diagnostic tests to evaluate the functioning of the autonomic nervous system. The set of five Ewing's tests (3) with a modification done by the American Diabetes Association (1) is commonly accepted. The following tests should be carried out:

1. The Valsavy's trial — the tested patient blows into a mouthpiece with a leak. The mouthpiece is connected to a manometer, maintaining

a pressure of 40 mm Hg for 15 sec. The ECG is registered during the trial and for 45 sec. after its termination. A result of the test is Valsavy's coefficient (VALS) — a quotient of the longest R — R after the trial and the shortest R — R from the period of exertion, extended of 5 s.

2. Deep respiration test — in a half-recumbent posture the tested patient breathes deeply 6 times per minute. The result is the difference between the mean frequency of the heart rhythm while aspiration and the mean frequency while respiration during one minute, expressed as a number of heartbeats per minute (WSP. odd).

3. Perpendicular position test — testing the heart rhythm. After a few minutes' rest in a recumbent posture the patient gets up by himself within 3—4 sec. Acceleration of the heart rhythm is evaluated. The result is a time quotient of the longest and the shortest R — R segments after reaching the perpendicular position within 45 sec. (Min/Max.).

4. Perpendicular position test — measuring the maximal blood pressure. Before the change to the perpendicular position the maximal blood pressure is measured three times, and the mean value of the measurements constitutes the basic figure. After an unaided change to the perpendicular position the maximal blood pressure is measured every 30 seconds for 3—4 minutes. The result is the biggest difference between the basic maximal blood pressure and the observed one after the change to the perpendicular position within 3 minutes (PION).

5. Squeezing test — measuring the minimal blood pressure. Before the test is carried out, the maximum strength of the dominant hand is defined and the minimal blood pressure is measured three times in order to establish the basic value. Then, the patient squeezes the dynamometer using 30% of his maximum strength in the course of 3—5 min or until considerable tiredness. The minimal blood pressure is measured on the opposite arm every 30 sec. The result of the test is the difference between the highest minimal blood pressure during the test and the mean value of the measurements when the patient is at rest.

REFERENCES

1. American Diabetes Association and American Academy of Neurology: Consensum statement: report and recommendations of the San Antonio conference on diabetic neuropathy. Diabetes Care 1988, 11, 592—597.
2. Bach C., Iaina A., Eliahau H. E.: Autonomic nervous system disturbance in patients on chronic haemodialysis. Isr. J. Med. Sci. 1979, 15, 761—764.
3. Ewing D. J., Clarke B. F.: Diagnosis and management of diabetic autonomic neuropathy. Br. Med. J., 1982, 285, 916—818.
4. Goldstein D. A., Chui L. A., Massry S. G.: Effects of parathyroid hormone and uraemia on peripheral nerve calcium and motor nerve conduction velocity. J. Clin. Invest., 1978, 62, 88—93.
5. Goldstein D. A., Massry S. G.: Effects of parathyroid hormone administration and its withdrawal on brain calcium and electroencephalogram. Miner. Electrolyte Metab., 1978, 1, 84—91.
6. Hirsch et al.: Heart rate variability as a measure of autonomic function during weight change in humans. Am. J. Physiol., 1991, 261, 1418—1423.
7. Lai J. C. K., Lim L., Davison A. N.: Effect Cd, Mn, Al on rat brain synaptosomal uptake of noradrenaline and serotonine. J. Inorg. Biochem., 1982, 17, 215—225.
8. Malik S., Winney R. J., Ewing D. J.: Chronic renal failure and cardiovascular autonomic function. Nephron, 1986, 43, 191—195.
9. Nielsen A. L., Jensen H. E.: Oxygen status: A standard evaluation in uremic patients? Dialysis Transplant., 1994, 23, 288—302.
10. Orłowski Z.: Choroby nerek a dawkowanie leków. Ośrodek Informacji Naukowej „Polfa", Warszawa 1993, 3—13.
11. Perry T. L. et al.: Neurochemical abnormalities in brains of renal failure patients treated by repeated haemodialysis. J. Neurochem., 1985, 45, 1043—1048.
12. Rozentryt P.: Czynność autonomicznego układu nerwowego u chorych z przewlekłą niewydolnością nerek w świetle tradycyjnych testów i widmowej analizy zmienności rytmu serca. Praca doktorska AM w Łodzi, 1992.
13. Savazzi G. M.: Lights and shadows on the pathogenesis of uraemic polyneuropathy. Clin. Nephrol, 1982, 18, 219—229.
14. Stojceva-Taneva O., Masin G.: Erythopoetin and autonomic nervous system dysfunction. XXIX Congress of EDTA, 203, Paris 1992.
15. Wang et al.: Sympathetic skin response and R—R interval variation in chronic uraemic patients. Muscle Nerve 1994, 17, 411—418.
16. Vita G. et al.: Uraemic autonomic neuropathy. J. Auton. Nerv. Syst. 1990, 30, 179—184.
17. Vita G. et al.: The time course of autonomic neural function in chronic uraemic patiens during haemodialysis treatment. Nephrol. Dial. Transplant, 1992, 7, 1022—1025.

STRESZCZENIE

Przedstawiono neuropatię autonomiczną występującą u chorych z przewlekłą niewydolnością nerek. Szczególną uwagę zwrócono na próby wyjaśnienia patogenezy oraz metody rozpoznawania mocznicowej neuropatii autonomicznej.