Medication adjustment in a diabetic patient with orthostatic hypotension and nocturnal arterial hypertension

Ajuste farmacológico en una paciente diabética con hipotensión ortostática e hipertensión arterial nocturna

Dear Editor:

Dysautonomy in patients with diabetes mellitus affects their quality of life and darkens their prognosis[1,2]. Orthostatic hypotension (OH) is frequent [1] and may be associated with supine arterial hypertension or high blood pressure (HBP), known as the Hip-Hop phenomenon[3]). In addition, the anti-hypertensive drugs administered during the day may cause or worsen an inversion of the circadian rhythm of blood pressure (BP) with the appearance of nocturnal HBP, increasing the cardiovascular risk [2,4,5] and worsens the damage on target organs.[5]

We present here the case of a 36-year-old woman with long-standing diabetes complicated with cranial multineuritis, polyneuropathy, retinopathy and nephropathy with kidney transplant for which she received immunosuppresie treatment with prednisone and everolimus. She also suffered Cushing's syndrome due to a pituitary microadenoma that required surgery, an infection by chronic HCV and HBP, for which she had received treatment with doxazosin 8 mg/24 hr and amlodipine 10 mg/24 hr.

She was admitted to the neurology department because of a two-month-long progressive condition of intolerance to orthostatism and syncopes, which was aggravated in the preceding two weeks, in which the patient had been bedridden.

Examination revealed a reduction in vibratory sensitivity and absence of osteo-tendinous reflexes in the lower limbs. OH (table 1) was confirmed. The variability in heartrate and BP were normal on application of the Valsalva manoeuvres and deep breathing. The isometric contraction test was pathological with an increase of 7 mm Hg in Diastolic BP. She presented low figures for catecholamines in blood, both while lying down (decubitus) and standing (bipedestation) (table 1).

The neurophysiological study detected a polyneuropathy with alteration in the sympathetic-cutaneous reflex test in the lower limbs. The cardiac MIBG SPECT (MIBG-I-123) revealed major hypouptake (early heart/mediastinum ratio of 1.53 and a late ratio of 1.37), without structural or electric flow alterations (Tc 99m MIBI SPECT was normal) (normal echocardiogram and electrocardiogram).

The cerebral MR scan, porphyria study, cryoglobulinaemia and the analysis of the dysimmune infectious process did not reveal any relevant anomalies; the persistence of the HCV infection was the only finding.

Anti-hypertensive medicaiton was withdrawn and her BP was monitored for 24 hours using a Holter system (table 2). There was no improvement in OH and nocturnal HBP was recorded; this revealed a *riser* pattern (nocturnal increase in BP). A week after admission, she was given midodrine up to a morning dose of 10 mg and 10 mg at lunchtime. In order to control the nocturnal HBP, she was administered clonidine 0.15 mg and captopril 25 mg, both with a single bedtime dose. A further 24-hour BP recording (table 2) was then performed and revealed a *non-dipper* pattern (decrease of between 0 and 10% in nocturnal BP). The patient in a week and recoved the ability to walk.

Our patient suffered from a post-ganglionar sympathetic alteration corroborated by the complementary tests. Monitoring using a 24-hour holter system allowed the real values and the circadian pattern of her BP to be known in order to adjust treatment. That adjustment was complicated by the presence of severe OH with nocturnal HBP, which worsened after the withdrawal of the anti-hypertensive drugs.

Table 1 BP values (mm Hg), heartbeat (bpm) and catecholamines in blood (pg/mL) in decubitus and after standing upright for three minutes

	Systolic BP	Diastolic BP	Heartbeat	Noradrenaline	Adrenaline	Dopamine
Decubitus	136	91	81	44	14	14
Standing	75	49	56	218	17	15

Table 2 BP values on the pre-treatment and post-treatment 24-hour Holter recordings for treatment adjustment (mm Hg) and the circadian pattern

	Pre-	Post-
Mean daytime systolic BP	139	131
Mean daytime diastolic BP	91	86
Mean night-time systolic BP	162	128
Mean night-time diastolic BP	103	85
Decrease in Systolic BP	-17%	2%
Decrease in Diastolic BP	-13%	1%
Circadian pattern	*Riser*	*Non dipper*

This adjustment and the non-pharmacological measures were ineffectual for the control of OH, which improved after the introduction of midodrine. Nocturnal HBP in turn improved with clonidine and captopril with a single bedtime dose.

Midodrine is a selective 1-adrenergic alpha agonist causing venous and arterial constriction, with the subsequent increase in blood pressure. [6] Although there is some controversy about the aggravation of supine nocturnal HBP due to midodrine, its short half-life and the possibility of associating it with equally short half-life anti-hypertensives (for example clonidine and captopril) with a single bedtime dose are f ndings in favour of its administration in this kind of patient, particularly in diabetics with dysautonomic symptoms.[7] Although it was approved by the FDAin 1996 for this indication, the same agency has recently announced its possible withdrawal due to the lack of post-authorization studies after the clinical trial leading to its approval.[8] Other authors have already written of their concern over this and point to the existence of patients who might be left unprotected with this measure. [8] This will oblige us in the near future conduct controlled studies into this and other "orphan drugs" for neurogenic OH.

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Peripheral neuropathy as a f rst sign of microscopic polyangiitis ☆

Neuropatía periférica como forma de presentación de poliangeítis microscópica

Dear Editor:

The emergence of peripheral neuropathy is an important characteristic in both primary and secondary systemic vasculitides and is often observed during the f rst stages of the illness, thus giving it a major diagnostic valueAlterations in the peripheral nerve between the group of small-vessel vasculitides are highly variable; they make up a group with shared histological characteristics and frequently positive anti-neutrophil cytoplasmic antibodies (ANCA) in serum. The initial clinical characteristics of these vasculitides are very similar, and the differential diagnosis between them is on many occasions diff cult.

Microscopic polyangiitis (MPA) mainly affects the lungs and kidneys, and so has been studied particularly by rheumatologists and nephrologists; the criteria of the Chapel Hill Conference, however , do not limit MP A only to these organs, and alterations in the peripheral nervous system is no exception.

We report here the case of a 43-year-old woman without any signif cant history of pathology who attended our hospital as a result of a progressive condition lasting for two months and involving paraesthesias and mostly distal weakness in all four limbs, as well as asthenia, anorexia and slight fever The most signi f cant f ndings during systematic anamnesis were nicturia and occasional oliguria. The general examination was normal and the neurological examination revealed asymmetric weakness predominantly in the distal muscles of all four limbs, as well as hyporre f exia, distal tactile hypoaesthesia and distal abolition of sensitivity to vibration.

At the onset of her condition, the analytical studies showed her kidney function to be within the normal range (urea 34 mg/dL and creatinine 0.82 mg/dL), which slowly and gradually deteriorated until she presented, two months later, 64 mg/dL of urea and creatinine 1.4 mg/dL, with creatinine clearance of 48 mL/minute, as well as haematuria and proteinuria of 2.9 g/L that had not previously been present.

The neurophysiological study (tables 1 and 2) showed an axonal motor and sensory alteration in multiple nerves studied, compatible with multiple mononeuritis. The biopsy of the sural nerve showed evidence of severe axonal degeneration.

The initial determination of anti-nuclear antibodies, anti-DNA antibodies, anti-cardiolipins and ANCA, as well as angiotensin conversion enzyme and cryoglobulins was negative.

Treatment with oral corticosteroids (prednisone 1 mg/kg of bodyweight/day *per os*) gave rise to a slight increase in her neurological condition, without changes in her kidney

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