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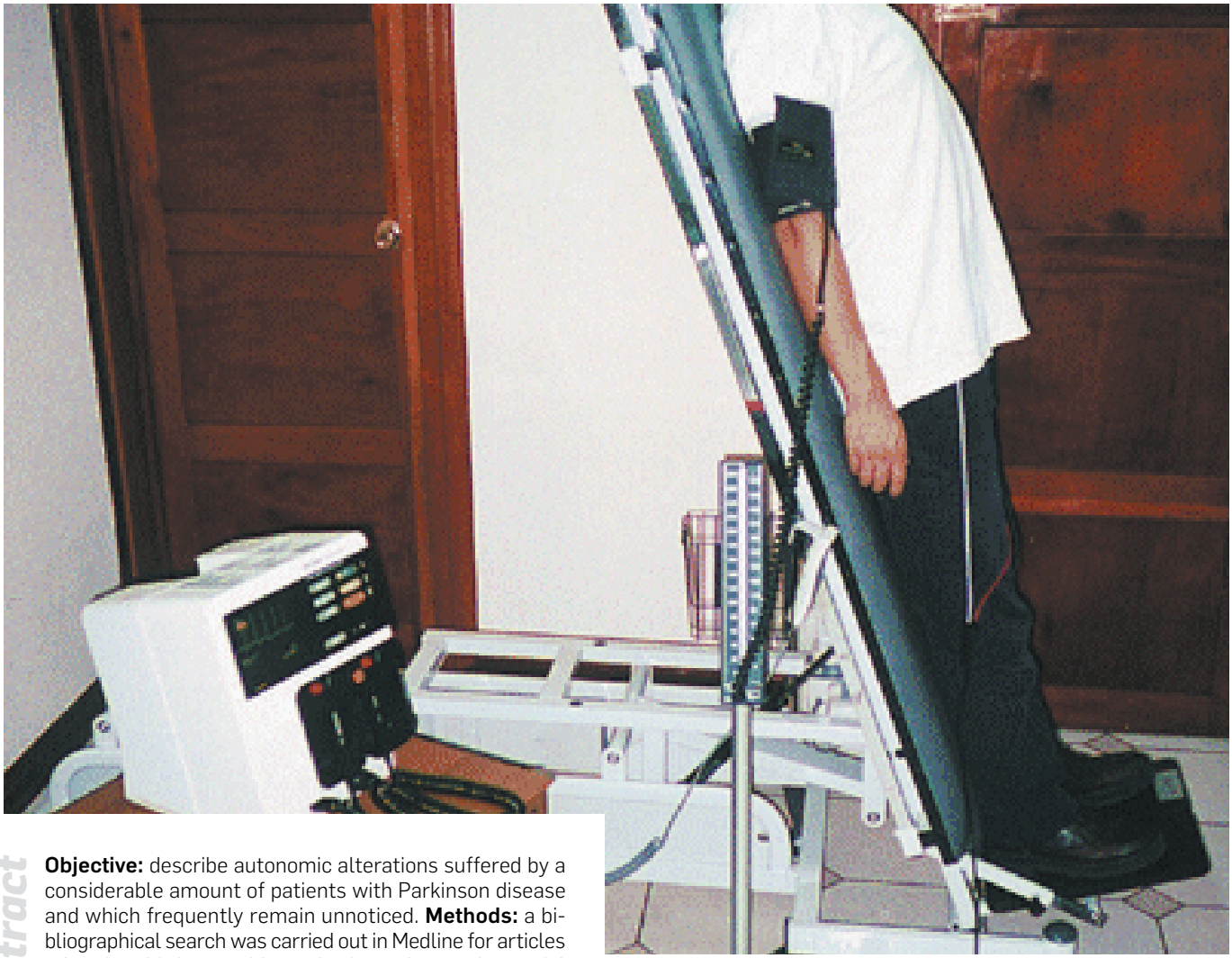

abstract

Objective: describe autonomic alterations suffered by a considerable amount of patients with Parkinson disease and which frequently remain unnoticed. **Methods:** a bibliographical search was carried out in Medline for articles related to this issue, with emphasis on changes in arterial blood pressure and its management. **Results and conclusions:** Parkinson's disease is classically recognised by rest tremor, bradikinesia and rigidity. However many patients present with a group of non-motor symptoms which, due to the appearance of the classical symptoms or their low specificity, are not recognised as a part of the disease. These symptoms can include heart conditions related to sympathetic denervation, or gastrointestinal disorders such as constipation and sialorrhoea, urinary and sexual dysfunction, and conditions affecting blood pressure specifically manifested as orthostatic hypotension. Hypotension is defined as a reduction of 20 mmHg in systolic arterial pressure or 10 mmHg in diastolic pressure during the first 3 minutes after adopting a standing position. Another problem is the presence of supine hypertension which occasionally appears independently of the hypotension or coexists in the same patient. This makes it difficult to establish an adequate treatment as the effective measures for supine hypertension could worsen hypotension, while the response to drugs in the latter is not standard as yet, and varies according to the individual. **Key words:** Parkinson's disease, autonomic dysfunction, orthostatic hypotension, supine hypertension.

Autonomic dysfunction in patients with Parkinson´s disease

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Introduction

Case 1
A 65-year old man presented with a 2-year history of tiredness when standing upright, resting tremor, and clumsiness when walking. Besides resting tremor the physical examination showed a blood pressure of 160/100 mmHg in supine position and heart rate of 65 beats per minute. However, blood pressure fell to 90/50 mmHg on standing, while maintaining the same heart rate.

Case 2
An 83-year old woman diagnosed with Parkinson´s disease 6 years ago presents both motor and non-motor symptoms, and a tendency for orthostatic hypotension. She has suffered two falls when walking attributed to hypotension. Twenty-four hour blood pressure (BP) monitoring showed that, at night, her BP tends to be high, reaching values of 190/95 mmHg.

These patients share the same clinical symptoms published in a monograph in 1871 (An essay of the shaking palsy) by James Parkinson, describing the clinical characteristics of a neurodegenerative disease manifested by resting tremor, bradykinesia and rigidity which has become to be known as Parkinson´s disease (PD). Over time however it has been shown that the disease does not only present the classical symptoms originally described by this Parkinson but also manifests with a wider spectrum of symptoms.

PD can also present with non-motor symptoms (NMS) 1 such as autonomic alterations, and although they have been described for many years, they were not interpreted as part of PD.[2] The cases above mentioned reflect a reality frequently observed in clinical practice: patients with PD who suffer from orthostatic hypotension (case 1) or patients with a tendency to present abnormally raised BP levels at night (case 2).

This disease is associated with an increase in mortality with respect to the general population (2.2 times more, especially those patients who suffer from dementia)[3] and in those who present with postural instability or gait difficulty.[4] The increase in mortality is present in those patients who suffer from diseases at advanced stages, with both motor and non-motor symptoms. The mortality risk is up to 8.3 times higher among the group with frequent symptoms compared to those who present only mild symptoms.[5]

It is estimated that the prevalence of the disease in Europe is 1.8% of the population over 65 years of age, and increases up to 2.6% in patients over 85 years.[6] Diagnosis is infrequent under 40 years and is much higher after 60 years of age. The average age at diagnosis is 70.5 years.[7] It is slightly more frequent in men, and the onset in male patients is usually at earlier ages, 67.5 years (men) compared to 72.6 years (women).

An approach to the pathology

While Parkinson described the clinical picture, he did not do so with regard to the pathological approach to the disease as it has become known afterwards. Today it is known that the clinical picture is related to the loss of dopaminergic neurons within the substantia nigra leading to a reduction in dopaminergic action in the striatum[8] and the presence of cellular inclusions known as Lewy bodies, which are produced by the accumulation of alpha-synuclein protein in the cytoplasm of the neurons of the central nervous system with autonomic functions, the glosso-pharyngeal dorsal motor neurons and vagus nerves.[9] In the case of non-motor symptoms the mechanisms involved are less well known.

The classical symptoms are the tip of the iceberg[10] of other symptoms such as sleep disorders, smell dysfunction, heart sympathetic denervation, constipation, etc which frequently accompany and in occasions precede the traditional clinical picture.[11] Quite often these symptoms are not evaluated as initial symptoms of the disease given their low specificity. On the other hand, it has been suggested that parkinsonism is the clinical expression of different neuropathological lesions.

Physiology of autonomic regulation and its dysfunction in PD

Before describing the characteristics of autonomic dysfunction it is important to know the physiological basis of the autonomous nervous system (ANS) and its components. Samay Jain[12] describes the classification proposed by Langley, namely the sympathetic nervous

system (SNS), the parasympathetic nervous system (PNS) and the somatic nervous system (SoNS).

At the same time, the SNS is divided into subsystems based on the type of neurotransmitter: noradrenaline and adrenaline or acetylcholine. Acetylcholine is a preganglionic transmitter, in both sympathetic and parasympathetic systems, while noradrenaline and adrenaline, with dopamine as a precursor, intervene in the stimulation of the sympathetic system.

At a functional level, the noradrenergic sympathetic system regulates the blood vessel tone and heart stimulation, while the cholinergic sympathetic system regulates sweating. At the same time, the parasympathetic system is responsible for a variety of functions including respiratory sinus arrhythmia, gastro-intestinal and urinary tone, salivary gland secretion, lachrymal secretion and pupil constriction in response to light. On the other hand the adrenomedular sympathetic system employs adrenaline producing chemical effects. Adrenaline along with insulin and glucagon regulate glycemic blood levels.

Dysfunction of the parasympathetic system produces alterations such as xerostomy (dry mouth), mydriasis, constipation, urinary retention and photofobia. When the autonomic system is altered it is difficult, if not impossible, to distinguish whether the symptoms (e.g. constipation, abdominal distension, or oesophageal reflux) are a consequence of somatic, cholinergic parasympathetic denervation or loss in the modulation of autonomic reflexes.

Currently it is known that PD can cause important alterations in the autonomic system and therefore symptoms related to its dysfunction can appear. Sympathetic heart denervation is practically universal in these patients. Secondly, non-heart denervation is very frequent and, for unknown reasons, produces a lower innervation compared to the heart, which ultimately determines the dysfunction observed in the arterial baroreceptor reflex (table 1).

'Non-motor' symptoms are very frequent and even precede 'motor' symptoms

It is also important to know the normal blood pressure response to orthostatic stimulation. When standing up, between 500 and 700 mL of blood abruptly passes to the lower limbs and splenic circulation producing a series of physiological changes as a consequence of the rapid reduction in venous return to the heart, with lower heart fill and a reduction of cardiac output and blood pressure. As a result, activation of a sympathetic response and a reduction in parasympathetic is produced defined as the baroreceptor reflex leading to an increase in peripheral resistance, venous return and cardiac output thus compensating for the fall in BP.

Non-motor symptoms in Parkinson's disease

The clinical picture is much more complicated than the classic triad (tremor, rigidity and bradikinesia), as it is frequently accompanied by non-motor symptoms that are not always adequately evaluated. Among them we find cognitive impairment, sleep disturbances and autonomic dysfunction, the latter representing the main issue to be discussed in this paper. In recent years the description of symptoms related to mental health and the autonomic system are more frequently described in PD.

Table 1. Autonomic nervous system (by Langley and Cannon).

Autonomic nervous system		
System	**Action**	**Neurotransmitter**
Sympathetic	Arterial constriction and heart stimulation. Sweating. Serum glycemic regulation.	Noradrenaline Dopamine Adrenaline Acetylcholine (Cholinergic system)
Parasympathetic	Respiratory sinus arrythmia, gastrointestinal and urinary tract tone, salivary gland secretion, lachrymal secretion, pupil constriction in response to light.	Acetycholine
Somatic	Intestinal functions.	Adrenaline

This alteration includes constipation, urinary retention, erectile dysfunction, excessive sweating, sialorrhea, disorders in blood pressure regulation such as orthostatism and supine hypertension that manifests in varying degrees.[13]

Do these symptoms have any relevance regarding the clinical outcome and prognosis? Is the mechanism causing these symptoms related to the proper physiopathology of the disease or could it be secondary to pharmacological treatment, or both? In the following sections we will try to answer these questions. Besides the aforementioned issues, there is increasing evidence of lower survival in the group of patients with more complex clinical pictures, especially in those who suffer from some cognitive alteration and gait instability.[14]

Autonomic alterations

Heart dysfunction

Heart dysfunction is one of the cardiovascular problems that patients with PD suffer as a consequence of sympathetic heart denervation of chronotropic incompetence. This is manifested by the loss in adaption of the heart rate to physiological requirements throughout the day which can be confirmed when carrying out stress tests.[15] The problem persists even at night during sleep.[16] With the development of neuroimaging it is evident that in PD sympathetic heart denervation occurs with more or less intensity,[17] especially with the loss of postsynaptic noradrenergic nerves. One of the consequences is the alteration of the heart rate. It could also be one of the conditioning factors of early tiredness that PD patients suffer.[18]

The possibility of this alteration representing a predictive element of the disease has been considered. In a study on patients with no known neurological disease, those who did not reach expected maximum heart rates in the stress test developed PD at a higher rate.[19]

Gastrointestinal alterations

In many patients it is common to find constipation, defined as the rate of less than three bowel movements per week or the need for regular use of laxatives. Approximately half of the patients with PD suffer constipation and the severity of this condition increases as the disease progresses. It is not a predictive symptom of the disease as it is common in healthy people, especially women. Some epidemiological studies show there is a greater possibility of developing PD in men presenting with a defecation rate of less than once a day than those with two or more bowel movements per day.[20]

Some episodes of megacolon or intestinal pseudo-occlusive states have been described in these patients.

Among the 'non-motor' symptoms, blood pressure alterations can be observed

Sialorrhea is a frequent symptom accompanied by dysphagia[21] which can be treated with different alternative therapies.[22] To a higher or lower degree, abdominal distension is also common along with nausea, and loss of appetite related to autonomic dysfunction. Up to 63% of the patients can present with digestive symptoms.

Abnormal sweating and heat intolerance

The alteration in sweating appears in half of the patients with PD. Hyperhidrosis, more frequent in the upper half of the body can occur as well as a reduction in sweat secretion more frequent in the lower half of the body. On the other hand, these patients frequently present with heat intolerance.

Urinary and sexual dysfunction

Another of the frequent alterations in PD is the incidence of urinary dysfunction with a prevalence of nearly 50% in some groups of patients. In men at advanced age it is difficult to know to what extent the symptoms are due to PD or related to prostate hyperplasia. Similarly, erectile dysfunction is also frequent in men suffering from PD compared to healthy men of the same age. It could be an early symptom of the disease since men suffering from erectile dysfunction have a 2.7 to 4-fold higher risk of developing PD.[23]

Orthostatic or postprandial hypotension and supine hypertension

Orthostatic hypotension (OH) is defined as a reduction of 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure in the first 3 minutes after a person assumes a standing position.[24] It is a manifestation of a lack of vasoconstriction due to sympathetic system failure. It is frequently produced in patients with PD and it is estimated that it could appear in about 30% of the patients and up to 58% of those presenting symptoms of parkinsonism.[11] Possibly it is the most frequent cardiovascular-related symptom, or at least the most frequently documented given its clinical repercussions.

Table 2. Influencing factors of orthostatic hypotension and non-neurological etiology.[27]

Factors influencing orthostatic hypotension	
Speed in changing posture	
Moment of the day (worse in the morning)	
Prolonged rest periods	
Hot environment	
Increase in intra thoracic pressure (urination, defecation, or cough)	
Eating or alcohol consumption	
Physical exercise	
Position related maneuvers (abdominal compression, squatting position)	
Drugs with vasoactive properties, including dopaminergic agents	
Non neurological causes of orthostatic hypotension	
Low intravascular volumen	Bleeding, burns, haemodialysis
Electrolyte disturbances	Inadequate intake, volumen loss (diarrhoea, vomiting) diabetes insipida, diuretics
Vasodilation	Drugs, alcohol, heat, fever, varicose vein dilation, heart failure
Myocardic	Myocarditis
Insufficient ventricle filling	Auricular myxoma, constrictive pericarditis
Low cardiac output	Aortic stenosis

Orthostatic hypotension is one of the most frequent non-motor symptoms and the most frequent cause of admission to hospital along with infections.[25]

Over the years, there is a loss of baroreceptors affecting up to 50% of the population over 50 years[26] which is independent of PD. Thus the presence of PD can potentiate the symptoms. Apart from these factors there are others, not always related to neurological disorders, that can relate to or increase the symptoms (table 2).

Patients with PD frequently suffer OH and more intensely as the disease advances.

Diagnosing orthostatic hypotension

Although the diagnosis is fundamentally clinical, it can be confirmed and complemented by examinations directed at discovering its mechanism or intensity.[28] The first of them is the head up tilt table test which is carried out on an tilt table (figure 1). The technique employed in this test is simple. Testing conditions include an environmental temperature between 23 and 26ºC where the patient is placed on a table which can be tilted to various degrees from horizontal to vertical position. Once in a horizontal supine position the patient's heart rate (HR) and blood pressure (BP) are monitored. The table is then tilted 60º and the position is maintained for 10 minutes while the HR and BP values are observed from baseline values to every minute during the test up to 20 minutes after recovering the supine position.

A pathological response is considered when the systollic BP falls 20 mmHg or more during the test or in the period after, even though the definition of OH includes a fall of at least 10 mmHg in diastolic BP. Thus the former value is commonly employed. The simultaneous determination of noradrenaline has not shown any significant differences between the group with OH and the group not presenting OH.

Another useful tool is the Valsalva maneuver.[29] This consists of evaluating changes in BP during the manuever. This is good indicator of the integrity of baroreceptors and the adrenergic response to them. The patient is instructed to carry out a prolonged espiration during 15 seconds against a resistance, reaching an intrathoracic pressure of 40 mmHg. Monitoring of BP and HR is carried out before and 15 seconds after the start of the test. The manuever consists of 4 phases: phase I corresponds to the start of the test. Phase II represents the following 10 seconds when the systollic BP falls and the heart rate increases corresponding to the reduction in cardiac output due to the reduction in venous return with the suspension of the heart's vagal tone up to the end of this phase. After about 8 seconds from the start of the test (late phase II), the two parameters recover due to the increase in sympathetic tone. At the end of this maneuver, phase III, there is a sudden loss in pressure in the abdominal cavities with the recovery of blood volume, while in phase IV at rest, both BP and HR reach normal baseline levels.

Figura 1. Test del plano inclinado.

Baroreceptors are considered fundamental in the response to BP and HR, both in the first seconds and during phase III and IV. It is a good test to confirm the integrity of the autonomic system and, although the results can help determine the mechanism involved in OH and the severity related to the loss of baroreceptors, its application is not always comfortable in daily clinical practice.

Another clinical situation frequently associated with OH is postprandial hypotension. It is similar to OH, except for the moment of presentation. It is defined as a fall in BP greater than 20 mmHg 2 hours after eating.[30]

One of the doubts raised when a patient presents an episode of HO is to ascertain the role of pharmacological treatment the patient takes for PD. It is also important to carry out a differential diagnosis with other clinical processes and the role of other drugs the patient may be taking for other ailments, both tasks that could prove arduous. Although treatments may vary we will review the most frequently used.[31]

Drugs most frequently used in PD and their role in blood pressure

One of the first steps in managing OH is to examine whether the pharmacological treatment the patient takes for PD is either a partial cause or precipitates the alterations of the autonomic system. When initiating drug treatment, baseline blood pressure values in upright or standing position should be known. This information may prove useful later on if the patient presents symptoms of orthostatic hypotension. Other treatments taken by the patient including antidepressants, diuretics and antihypertensive agents should also be taken into account.

Levodopa

This drug is considered the most effective in symptom mangement of akinesia in patients with PD. As a precursor of dopamine and noradrenaline it acts by replacing the deficit at basal ganglia and alleviating symptoms. The possible relationship between OH and this drug was first suspected just after its initial use, but the data found in the literature hardly show any conclusive results at cardiovascular level.

The BP lowering effect of the drug varies and is derived from the action of dopamine which at peripheral level produces dilation of peripheral vessels (renal and mesenteric), reducing sodium transport at renal level and eventually increasing natriuresis and diuresis.[32]

Serum levels of the drug are similar in patients suffering from OH and those who do not. Some authors postulate that the loss in sympathetic innervation is crucial in the development of OH. It is important to take into account

If orthostatic hypotension, fluid intake should be regulated and maneuvers causing hypotension should be avoided

that the conversion of levodopa in dopamine outside the CNS increases the serum concentrations of the latter and its active substance, dihydroxyphenylacetic acid which could have a vasodilator effect. In this sense, it is well known in clinical practice that the administration of low dose intravenous dopamine produces vasodilation.

In practice, the effects on the cardiovascular system are reduced by the simultaneous administration of some descarboxylase inhibitor such as carbidopa or benserazide. However, the administration of both drugs is accompanied by a significant reduction in BP, especially the systollic BP with little change in heart rate.[35]

Dopamine agonists

These are a group of synthetic drugs that directly stimulate dopamine receptors. Among them we find cabergoline and bromocriptin with very limited indications given their secondary effects at cardiovascular level. Carbegoline increases the risk of valvular disease, especially in patients with hyperprolactinemia.[33] Other drugs frequently used include pramipexol, ropinirole and rotigotine. Apormophin is a drug administered intravenously and is used as rescue treatment, but rarely for chronic management. It is well known that dopamine agonists can provoke the incidence of OH, and in the case of the tilt test, it can even produce a reduction of systolic BP of up to 12.5 mmHg and diastolic 5.2 mmHg immediately after tilting the table, the effect diminishing after 5 minutes.[34]

Monoaminooxidase inhibitors

Their efficacy in PD is based on blocking enzymes that degrade dopamine in the brain. The use of this group of drugs can delay the need to initiate levodopa or dopaminergic agonists. The MAO B inhibitors are an option in the management of PD although of lower efficacy than levodopa and dopaminergic agonists with regard to the

reduction of symptoms. It seems that their cardiovascular effects are similar to dopaminergic agonists.[35] In a systematic review carried out with selegiline compared to placebo an improvement in symptoms was observed in the group treated with the drug, with no significant differences in mortality.[36]

In summary, drugs administered for PD could be responsible for, or at least potentiate, the OH these patients suffer.

Hypertension in supine position

While it is commonly known that OH is the most frequent alteration affecting blood pressure, in occasions supine hypertension (SH) may coexist. This fact is not well studied and its mechanism of action is not known, although one interpretation is that it may be related to the changes in circadian cycles of these patients. In studies monitoring 24-hour blood pressure, a higher tendency for nocturnal arterial hypertension is observed in patients with OH.[37,38]

Paradoxically this circadian alteration is accompanied by postprandial and orthostatic hypotension which is interpreted as a further and more profound alteration of the autonomic system.[39] While the clinical relevance of this finding involving spells of nocturnal or diurnal hypertension remains unknown, the greater complexity of this condition is a well known challenge when deciding on pharmacological management, even though greater damage to target organs has been observed.[40]

Management of blood pressure alterations

Orthostatic hypotension

Once the diagnosis has been established we should evaluate pharmacological management. Consideration should be made on discontinuing treatment with alpha 1 blockers, diuretics, or tricyclic antidepressants. Once this aspect is evaluated, we should look for alternatives, both pharmacological and non-pharmacological options that could help the patient.

Water and salt

As mentioned above on adopting a standing position it is calculated that approximately 500-700 mL of blood is displaced to the lower limbs and abdomen. In patients with PD and autonomic dysfunction, fluid intake does not seem to significantly influence blood pressure. However, in patients not suffering from PD but with the same dysfunction, an oral intake of 350 to 500 ml of water produces 30 minutes later an increase in systollic BP of 25-31 mmHg and diastolic BP of 15-25 mmHg.[41] For this reason, a supplement of approximately 500 mL of fluid intake in the morning is recommended, especially in patients with symptoms of morning hypotension. There is no sufficient clinical follow-up of this recommendation to conclude on its long term performance.

If supine hypertension, patients should rest with the bed tilted and use compression systems

A similar effect is produced by the intake of salt which also contributes to the increase in plasma volume,[42] despite the fact that a daily intake of 9-12 g of common salt could derive in an increase in cardiovascular problems. Currently this recommendation is under debate[43,44] and thus the measurement of urinary excretion of sodium is advised after which a decision to continue or not with this measure can be made. In any case there are no large studies that support these measures in patients with OH and PD.

Postural measures

Some physical exercises have also been recommended to improve venous return and physical and postural maneuvers such as toe-raising have been advised, although the benefits are rather unclear. Adopting a squatting position could improve symptoms of OH, although no increase of more than 10-15 mmHg in BP has been shown.[45] Some patients can benefit from the use of compression stockings (30-40 mmHg) in the legs or abdomen. Both measures reduce the blood flow to the lower legs or mesenteric region.

Pharmacological management

When changes in lifestyle are not sufficient to prevent orthostatic hypotension, then drugs may be used, although here too the outcome may be uncertain.

Fludrocortisone

At first, monotherapy with fludrocortisone,[46] a synthetic mineralcorticoid that increases circulating blood volume should be considered. This drug improves the sensitivity of blood vessels and can contribute to increasing peripheral vascular resistance. It is initiated with 0.1 mg daily in the morning with progressive increments of up to 0.3 mg per day.

Physicians should look out for the appearance of oedema or supine hypertension, and if so, either a dose reduction or drug withdrawal should be considered. Serum potassium levels should also be checked if the drug is administered at high doses and for the first weeks, as it may be necessary to associate a potassium supplement.

Another limitation for use is that the patient develops SH as a consequence of the increase in peripheral vascular resistance, making the management of these patients rather challenging and complicated.

Sympathetic mimetic drugs

Some present a direct effect and others act indirectly on the vasopressor sympathetic system. The group of sympathetic mimetic agents could be used sporadically or when fludrocortisone is not indicated. The effect is possibly related to the stimulation of adrenergic receptors and the improvement in the receptor affinity which is altered if autonomic system failure.

Ephedrine 25–50 mg/8h has an indirect mechanism of action while midodrine produces direct effects. The latter is an alpha-adrenergic agonist that does not cross the blood-brain barrier and whose main substance is desglymidodrine which acts by increasing vascular tone and BP. The haemodynamic effect of the drug is an increase in BP between 15 and 30 mmHg which is maintained between 2 and 3 hours.

These drugs should not be used in patients with advanced heart disease, uncontrolled hypertension or urinary retention. The presence of SH and the appearance of tachycardia also limit their use.

Others

NSAIDs can be used as an altenative in case of intolerance or lack of efficacy of the previous drugs. Rarely are NSAIDs effective in monotherapy and in occasions they are used in combination therapy along with other measures such as coffee, erythropoietin or pyridostigmine. Erythropoietin can be effective when the patient also presents anaemia.

Caffeine can have a good vasopressor effect by inhibiting adenosine receptors that produce vasodilation. Two or three coffees daily (between 100–250 mg) and especially after meals can alleviate postprandial hypotension.[47] A basis for the use of pyridostigmine is the inhibition of acetylcholinesterase, with an increase in noradrenaline at preganglionar level reducing orthostatic hypotension. However in one double-blind study evaluating its use in monotherapy or associated with midodrine, patients only showed a mild improvement in the episodes of OH.[48]

In some occasions and if all the above fails, vasopressin analogues or dopamine antagonists such as metoclopramide could be used. However the efficacy is rather unclear, frequent side effects are present and these drugs could even worsen the symptoms of PD, thus limiting their use.

When non-pharmacological measures for supine hypertension are not effective then short-acting antihypertensives are indicated

Hypertension when lying down

If the management of OH is sometimes complex, then it is much more complicated when patients suffer SH and especially if both coexist in the same patient, the latter occuring in half of the patients with OH. It is not infrequent that treatment of OH may worsen SH or viceversa, and so patients are advised to maximise the use of non-pharmacological measures. The combination of both blood pressure alterations presents greater risk of organ damage and further caution should be taken when electing pharmacological treatment.

As a first non-pharmacological measure, patients are advised to avoid lying down during the day and to sleep with the upper portion of the bed half raised between 10º and 20º, which is equivalent to the tilt test. In cases where medication is used, it is preferable to employ short-acting drugs such as atenolol, nitroglycerine, captopril[49] or nifedipine. Other authors consider that hydralazine or minoxidil present lower efficacy.50 In any case, the evidence is scarce and low-quality, and thus recommendations should be taken with caution.[51]

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Conclusions

The alteration of blood pressure can manifest as orthostatic hypotension, especially postprandial, supine hypertension, and more frequently, both alterations in the same patient.

It is recommended that all patients diagnosed with PD should undertake a study of their blood pressure profile, including 24-hour blood pressure monitoring if available.

The pharmacological treatment of PD can precipitate vasomotor symptoms and should always be taken into account, and dose adjustments made when necessary.

Fludrocortisone is the first-choice drug for orthostatic hypotension. Alternatives should be considered in case of intolerance or poor clinical response.

Often pharmacological management is complicated because drugs for orthostatic hypotension can cause undesirable supine hypertension and viceversa.

Well designed clinical trials are necessary to study the management of supine hypertension and orthostatic hypotension in patients with Parkinson's disease.

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