Case Report

Synergic Effect of Fludrocortisone and Disopyramide in an Elderly Patient with Orthostatic Syncope

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Summary

Orthostatic hypotension (OH) is a debilitating condition very common in the elderly that may lead to syncope. There is no single drug able to limit the fall in blood pressure in patients affected by OH when standing. In addition, the presence of hyperkinetic arrhythmias may worsen the fall in orthostatic blood pressure especially in elderly patients affected by OH. Unfortunately most of antiarrhythmic therapies lead to a decrease in blood pressure contrasting the effect of OH treatment. By contrast, disopyramide seems to have an anticholinergic effect that could play an important role in limiting the fall in blood pressure in participants with hyperkinetic arrhythmias and OH. We report a case of successful combination therapy of fludrocortisone, disopyramide and nonpharmacologic treatment in an elderly participant affected by neurogenic orthostatic OH and hyperkinetic arrhythmias with a poor quality of life and frequent syncope episodes.

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1. Introduction

Orthostatic hypotension (OH) is defined as a reduction in systolic blood pressure of \( \geq 20 \text{ mm Hg} \) or diastolic blood pressure of \( \geq 10 \text{ mm Hg} \) within 3 minutes upon standing which often leads to syncope\(^1\). OH, a common condition in the elderly, results in a cerebral hypoperfusion when passing from supine to upright position\(^2\). Although OH may be easily diagnosed, therapeutical approach is difficult, leading to a markedly reduced quality of life especially in elderly participants\(^4\). Furthermore, OH may be worsened by supraventricular cardiac arrhythmia\(^5\).

We report a case of successful combination treatment in an elderly participant affected by neurogenic OH and supraventricular cardiac arrhythmia resulting in frequent episodes of syncope.

2. Case report

A man aged 65 years reported a 5-year history of episodes of syncope occurring by changing position (i.e., rising from the bed or chair). Together with a previous myocardial infarction and subsequent revascularization with preserved diastolic and systolic cardiac function (ejection fraction = 65%), the patient was affected by depression, hypercholesterolemia, bilateral hearing impairment, and decreased visual acuity. Cerebral neurodegeneration was not reported. Current therapy was salicylate, paroxetine, and simvastatin. A dual-chamber pacemaker was previously implanted for a marked sinus bradycardia. However, the patient reported dizziness, blurred vision and nausea, often preceding episodes of syncope. At the admission, in supine position the patient had a resting heart rate (HR) of 70 bpm and a blood pressure (BP) of 140/80 mm Hg. However, after 2 minutes in a standing position, BP reduced to 70/40 mm Hg and HR was 65 bpm with a disoriented state that rapidly reverted in clinostatic position. Since his HR did not increase during standing, neurogenic OH was suspected and successively confirmed by Valsalva manoeuvre. Multidimensional geriatric assessment evidenced a mild cognitive impairment, a mild...
Multiple Approaches in the Elderly with Orthostatic Syncope

Table 1

<table>
<thead>
<tr>
<th>Procedures or Drugs</th>
<th>Clino-BP (mmHg)</th>
<th>Ortho-BP (mmHg)</th>
<th>Syncope/week (n.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>120/70</td>
<td>70/40</td>
<td>4</td>
</tr>
<tr>
<td>Dietary and behavioral approaches</td>
<td>130/70</td>
<td>80/50</td>
<td>4</td>
</tr>
<tr>
<td>+ Application of the compression stockings</td>
<td>125/75</td>
<td>80/35</td>
<td>3</td>
</tr>
<tr>
<td>+ Midodrine 10 mg/d</td>
<td>140/80</td>
<td>80/55</td>
<td>3</td>
</tr>
<tr>
<td>+ Fludrocortisone 0.3 mg/d</td>
<td>170/90</td>
<td>90/60</td>
<td>1</td>
</tr>
<tr>
<td>+ Disopyramide 200 mg/d</td>
<td>160/90</td>
<td>105/70</td>
<td>0</td>
</tr>
</tbody>
</table>

BP = blood pressure.

* Discontinued (see text for details).

Table 1

Therapeutical sequence in treating orthostatic hypotension and syncope.

BP – blood pressure.

*A Discontinued (see text for details).

orthostatic symptoms and depression, a severe impairment of quality of life, and, more importantly, a complete disability of basic activities of daily living (4/6 lost). Blood tests showed normal age-related findings. Echo-cardiography showed a mild cardiac hypertrophy and mild aortic insufficiency. Carotid Doppler ultrasound showed no significant alterations. The 24-hour Holter electrocardiogram (ECG) showed frequent episodes of atrial tachycardia with a ventricular rate of 150 bpm. Thus, the diagnosis was orthostatic syncope in a participant with neurogenic OH and supraventricular arrhythmia. Fluid intake (up to 2 liters 24 hours) and salts increased, time spent in upright position reduced, abrupt passage from supine to standing position avoided and application of the compression stockings accomplished poor results. Midodrine (10 mg/day) was administered but quickly discontinued because of scalp paresthesias and no effect on OH. Fludrocortisone 0.1 mg up to 0.3 mg daily was prescribed. The patient no longer experienced episodes of syncope but dizziness and blurred vision were reported. Orthostatic BP test revealed a fall of BP from 165/90 mm Hg to 90/60 mm Hg without changes of HR (HR from 70 bpm to 68 bpm; Table 1). Because of supraventricular arrhythmia (Fig. 1), the patient started therapy with disopyramide 200 mg/day with the resolution of arrhythmias associated with a reduction of symptoms related to orthostatic stress after 10 days. Over 3 months, the patient reported supine hypertension of 185/95 mm Hg and fludrocortisone was discontinued. After 1 month, symptoms worsening and an increase in the number of syncopal episodes (three per month) were observed. Fludrocortisone 0.3 mg daily was resumed and symptoms rapidly improved. During in-hospital stay ECG did not show arrhythmias and disopyramide therapy was discontinued. However, after 72 hours the patient presented orthostatic symptoms and disopyramide was promptly resumed. After 3 years of follow-up, only five episodes of presyncope were observed (Table 1) and the patient fully recovered basic activities of daily living (1/6 lost).

3. Discussion

Management of OH should aim to raise orthostatic BP without concomitant rising in supine BP, and, more importantly, to reduce orthostatic symptoms and to improve the ability to perform daily activities, especially in the elderly6,8. Volume expansion, compression garments, and education about orthostatic stressors and warning symptoms are used to reduce the degree and the symptoms of OH6,7. In our case all these procedures had poor effects on preventing syncope caused by OH.

Several drugs, such as midodrine, fludrocortisone and disopyramide, have been used to treat recurrent vasovagal syncope with poor efficacy, especially in the elderly6. Fludrocortisone is a synthetic mineral corticoid with an action on both volume plasma expansion and increase of vascular alpha-adrenoceptor sensitivity6. Recently, POST II, a multicenter, international, randomized, placebo-controlled study, has been designed to assess the effects of fludrocortisone in the prevention of neurally mediated syncope with time to first recurrence of syncope as primary end point9. However, hypertension may limit the use of fludrocortisone. In our case, even in the presence of clinostatic hypertensive values, an improvement in orthostatic BP was observed and no episode of syncope occurred. It has also been suggested that agents with anticholinergic, antiarrhythmic and negative inotropic effects, such as disopyramide, can be effective in patients with syncope caused by OH6,7. It has been reported that oral disopyramide therapy in patients with recurrent episodes of syncope was effective in preventing inducible and spontaneous neurally mediated syncope10. Successively, a double-blind randomized trial demonstrated that both intravenous and oral administration of disopyramide were ineffective for the prevention of neurally mediated syncope provoked by head-up tilt testing11. In our patient, disopyramide was basically prescribed to treat arrhythmias. At the second admission the effect of disopyramide on orthostatic BP was not related to the action on arrhythmias: when the drug was discontinued orthostatic BP worsened in the absence of arrhythmias.

In our case, fludrocortisone and disopyramide seemed to act synergistically as demonstrated by the reduction of OH, of the

Fig. 1. (A) Supraventricular tachycardia before; and (B) after disopyramide administration.
number of syncope episodes, and by the recovery of basic activities of daily living. The stiffness and less compliance of cardiovascular system may make similar reduction of intravascular volumes more prone to hypotension development in which the prescription of fludrocortisone and disopyramide may play a role.

References