Orthostatic hypotension

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Received: October 29, 2018, Accepted: December 11, 2018

Abstract

Orthostatic Hypotension has been largely underestimated by the medical community. New interest has come from recent evidence that the patients not only run the risk for fainting but also present an increased cardiovascular risk. In this review the clinical picture is described as well as the actual means of management.

Keywords: risk factors, vasoconstrictor drugs, syncope

In contrast to high blood pressure, the field of low blood pressure has attracted less or no attention of the medical and scientific world. Still, low blood pressure can cause profound disturbance of quality of life and substantial increase in risk. Chronic low blood pressure (hypotension) can present as permanent low blood pressure, as orthostatic low blood pressure or a combination of these two. All of these can be found while inspecting 24 hour blood pressure recordings [1] showing in many patients the well-known peaks of high blood pressure (which attract all attention of the clinicians) but also bits of lower pressure (largely ignored by the clinician). In the present paper, we shall deal with orthostatic hypotension (OH).

Lessons from physiology

When shifting from supine to sitting or standing position, several important hemodynamic changes occur. When standing up, there is a substantial shift of blood – at least 500 ml or more – toward the lower parts of the body; blood is accumulated largely in the splanchnic area and in the venous system of the limbs; as a consequence, less blood is returning to the heart causing a decrease in cardiac output and automatically decrease in systolic blood pressure. This is counteracted by the buffering systems we have such as the baroreceptors and volume receptors. They set on vasoconstriction – largely adrenergic-causing systolic pressure to return toward the control value and maintenance or even slight increase in diastolic blood pressure. Heart rate slightly increases due inhibition of vagal tone. Therefore the regular response to standing in normal conditions is a slight decrease in systolic pressure and a slight increase in diastolic pressure and in heart rate.

However, when the buffering systems do not work, or too late or only partially, the above

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mentioned decrease in systolic pressure while standing up is not (or not completely) counteracted leading to a sudden decrease in systolic pressure and no or almost no increase in heart rate. This condition is called “orthostatic hypotension” and can cause substantial clinical repercussions such as dizziness and fainting; these clinical symptoms occur as soon as the cerebral autoregulation is overruled by the hemodynamic changes when standing up.

**Definition of orthostatic hypotension (OH)**

The regular definition is a decrease of 20 mm Hg and/or diastolic pressure of 10 mm Hg within 3 minutes of standing [2].

Although still used by many, this definition has shortcomings. First, in many patients, blood pressure decreases very shortly within the first minute or earlier and recovers quickly toward the control at three minutes and often earlier. Such decrease lasts very shortly and thus, is difficult to record with the regular blood pressure monitors. To overcome this problem, recently a proposal to define OH was based on the difference between sitting and standing pressure; the changes required for the diagnosis in that case are smaller (15/7 mm Hg)[3].

Second: frail patients have great difficulty to maintain the standing position during three minutes.

Third: it is not sure that three minutes are necessary to estimate prognosis as correlation with events is at least as good with blood pressure changes occurring during the first minute standing blood pressure[4]. On the other hand, in some patients the blood pressure fall comes even later than three minutes and can only be detected by prolonged readings or ambulatory recordings. Maybe, this is an early sign of onset of the orthostatic problem. Thus clearly, further studies are required to clarify and improve the actual definition.

**Prevalence**

Orthostatic hypotension increases with age. Still, recent studies are focusing more and more at OH in middle-age [5].

Often cited figures give a prevalence of up to 20% at the age of 65 or above [6]; 2–5 % are symptomatic; however, in many patients symptoms are underestimated or ignored. Moreover, the estimation of prevalence largely depends on the definition of OH and the quality of the blood pressure recording.

**Risk linked to orthostatic hypotension**

Obviously, the best known risk of OH is dizziness and fainting and the problems linked to it such as fractures. That risk is frightening for patients with OH and does decrease their Quality of Life; some of these patients do not dare to stand up anymore without effective help; this aspect also causes a lot of problems in daily life on top of the complications due to less mobility.

Since a few years another aspect has obscured life of patients with OH: evidence is accumulating that the risk for cardiovascular events is substantially increased. In a first paper [7] an increase of heart failure and atrial fibrillation was found and an hypothesis proposed for a link to dementia. These data were clearly confirmed in a very extensive meta-analysis [8] bringing data together coming from 13 observational studies totalling more than 120,000 patients; median follow up was 6 years; in that paper an increase of 41% of coronary artery

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**Table 1. Causes of Orthostatic hypotension.**

<table>
<thead>
<tr>
<th>Causes</th>
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<tbody>
<tr>
<td>Dysfunction of sympathetic-vagal balance caused by Metabolic diseases such as diabetes</td>
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<tr>
<td>Ageing</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Drugs (some anti-hypertensive drugs, alpha adrenergic blocking agents and some others)</td>
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<tr>
<td>Auto-immune systemic diseases</td>
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<tr>
<td>Neurological syndromes: Pure Autonomic Failure, Multiple system atrophy and some others</td>
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<tr>
<td>No evident cause</td>
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</table>
such an to foresee chairs for such people in order to avoid to stand and all its consequences ...

Treatment of orthostatic hypotension

Several steps have to be mentioned here going from prevention of fainting to pharmacotherapy.

Prevention of fainting

*Taking care when raising*

Patients need to be aware of their problem and the way they can prevent it. Essential is to be careful when shifting from supine to sitting or standing. At each step, the patient should take one or two minutes to permit blood pressure to stabilize. One should repeatedly insist on this rule as this is a type of movement they perform many times during the day and night; the typical scenario is that of the patient sitting quietly in his/her armchair and suddenly is coming in or someone is ringing at the door...

*Using easy tricks to prevent blood pressure fall*

Patients used to the early phases of dizziness or even fainting, can stop it by performing easy movements like heel raising, muscle movements of the limbs or leg crossing. A very effective method is performing an handgrip for ex. by compressing a small rubber ball; handgrip increases blood pressure very quickly, can prevent further decrease and the symptoms linked to it.

Non-pharmacological treatment

Several easy advices can help very effectively. Tiltting the bed in head up position at night may be helpful. The mechanism of this is not very clear; a possibility could be that it puts the patient in an intermediate position between supine and sitting and decreases the amplitude of the step between supine and standing; others propose that this position may decrease nocturnal hypertension and the diuresis following.

Some patients drink a glass of water before going to sleep; also here the mechanism is not clear but increasing central volume might counteract to some extent, the consequences of decreased venous return.
Tilt training may also help in severe selected cases where neuro-cardiogenic mechanisms play an important role [10].

**Compression of the limbs or lower parts of the body.**

Clinical experience has learned that an effective prevention against the pressure fall and the symptoms linked to it can be given by firm compression of the limbs (by stockings) and in severe cases, the lower part of the body up to the abdomen [11,12]. By compression, pooling of venous blood in the lower part of the body largely is counteracted and by doing so, drop in systolic blood pressure prevented. Unfortunately, there is a lack of large well-controlled studies in this area and thus room for improvement about our information on the level of pressure needed and a number of other practical aspects!

**Pharmacological treatment**

Several drugs have been proposed (a number of them are listed in table 2) and tested but there is not always proof for efficacy in patients. Moreover, if active, many drugs act by increasing the whole 24-hour pressure profile and not specifically the fall of pressure while standing. Most of them stimulate the peripheral alpha-1 receptors at the arterial or arteriolar level; a few also on the venous wall. Some drugs have been developed because of their action both on venous and arterial part of the circulation. The potential beneficial effect sounds logical, in light of the hemodynamic changes occurring during the shift toward standing (see above); venoconstriction in particular, could improve venous return, keep cardiac output constant and as a consequence, keep systolic pressure within acceptable limits. However, again hard proof for efficacy in the clinical context is often lacking. Also in some other cases, side effects limit regular drug use. [13].

Finally, clinical experience has learned us that several drugs seem to work very well in the beginning phase of treatment but not at longer term. It is not clear what the mechanism of this phenomenon is, certainly knowing that these compounds of them show proven constrictive properties in experimental conditions. The time of intake might be also be important; one may reflect at using them at specific times of the 24 hours circle; maybe they could be administered only at circumstances where the patient is at risk for fainting (see chapter on “triggers leading to fainting”).

Some patients do well with administration of Fludrocortisone with positive effect on the sodium/potassium balance causing and by this way fluid retention and increase in central volume. Restriction is to be kept in mind in patients with some degree of heart failure; also loss of potassium may cause problems.

Recently an interesting paper has been published on the effect of Droxidopa [14], one of the precursors of noradrenaline; encouraging results were given what again should stimulate further research. However, results on longer time period have to be expected.

With many of these drugs, one needs to be careful not to increase the whole 24-hours blood pressure. This is especially the case in patients with concomitant hypertension (keep attention to night blood pressure!) ; patients with OH are known to be very sensitive to a number of stimuli (such as volume load, emotional stimuli, temperature changes) and drugs (vasodilators, diuretics) what can cause unexpected blood pressure changes.

Finally, one should not forget to stop or adapt doses of those drugs that could lead to OH but

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<table>
<thead>
<tr>
<th>Table 2. Drugs Proposed in medical literature to treat Orthostatic Hypotension</th>
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<tr>
<td>• Fludrocortisone acetate</td>
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<tr>
<td>• Ephedrine</td>
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<td>• Coffeine</td>
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<td>• Etilefrine</td>
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<td>• Dihydro-ergotamine</td>
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<td>• Midodrine</td>
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<td>• Droxidopa</td>
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are prescribed for other diseases present in these patients.

Conclusions and suggestions

Orthostatic hypotension (OH) is an entity that indeed is known by clinicians but largely underestimated. There are still several open questions. Although general hemodynamic changes have been described very well, the reactivity of blood vessels to regular vasoactive stimuli in these patients should further be investigated. Clinically, there is room for better clarification of the definition as there are shortcomings in the existing definition (20/10 mm Hg blood pressure drop during three minutes of standing). Such definition, once established, could help setting up much better information on actual prevalence; it could lead to better information on the risks of these patients; there is not only the risk for fainting and fractures but there is also more and more evidence about an increased cardiovascular risk, even in asymptomatic patients. The mechanisms of this risk again is not clear and the relationship to atherosclerosis and myocardial structural changes should be investigated.

There is a pressing need to find new ways for treatment. Prevention to fainting is a most important message that should be repeated regularly to patients and their families.

Many drugs have been used, with an attractive mechanism of action but for many, varying clinical efficacy.

A quite precious tool is compression that should be quite strong and never forgotten by the patients, especially when the danger of fainting is at maximum (see triggers to fainting).

Both physicians and patients should be informed on the problems caused by OH; there is a negative impact on quality of life besides increased cardiovascular risk. The message is that blood pressure in patients at risk should be measured in supine, sitting and standing positions along with 24 hour and/or home blood pressure recordings. All efforts should be made to set on new research programs in order to enable us to improve medical care.

Conflict of interest

The authors confirm that there are no conflicts of interest.

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