Labile Hypertension….
What we Know

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General Background

Most guidelines for treating hypertension focus on the average blood pressure (BP) assessed from either home or office readings.

Little attention is paid, however, to BP lability. Virtually all physicians are familiar with the term labile hypertension, yet there are no quantitative criteria to define or diagnose it.

Its effects on cardiovascular (CV) outcome are unclear, and there are no guidelines for its treatment.

The effect of treating the labile component of hypertension on CV outcome is also unknown.

Despite this, labile BP elevation is a common place of clinical dilemma.

It is normal for BP to fluctuate from moment to moment and from day to day. BP fluctuation is related to many factors such as physical activity, emotion, position, respiratory cycle, diet, salt intake, alcohol ingestion, sleep deprivation, and others.

Even in otherwise normotensive individuals, BP fluctuation can be substantial during moments of physical or emotional stress or even without overt provocation.

In physicians' offices, readings can be very stable in some patients, while varying markedly in others.

BP Variability , Reactivity, And Lability

In describing the tendency of BP to fluctuate, the terms variability, reactivity, and lability have been widely used.

BP variability is usually defined as the average variation of BP throughout the day, quantitated as the standard deviation of ambulatory BP readings. It is increased in hypertensive individuals and increases with aging.

Bp Reactivity

BP reactivity is defined as the response to environmental stressors, usually quantitated as responses to standardized laboratory stressors.

- In both the laboratory and clinical real life , individuals with increased reactivity are sometimes referred to as ‘‘hot reactors.’’
- BP reactivity is difficult to quantitate because an individual’s reactivity differs from stressor to stressor and even upon retesting with the same stressor.

Bp Lability

BP lability is a characteristic of human BP, and there is no clear definition that differentiates normal from abnormal lability.

The term labile hypertension, although widely used, also lacks an accepted definition and is more a clinical impression than a specific diagnosis.

LABILE COMPONENT OF BP AS A CLINICAL DILEMMA

- The alerting phenomenon (white coat hypertension)
- Labile hypertension (including preprocedural hypertension)
- Paroxysmal hypertension
- Normal lability in patients with vulnerable underlying conditions
  - 1-Cerebral aneurysm
  - 2-Chronic aortic dissection
  - 3- Amyloid angiopathy
  - 4-Marfan syndrome
  - 5-Angina

The Alerting Phenomenon

The alerting phenomenon is the tendency of BP to rise at the time of measurement, usually, but not always, due to consciously perceived anxiety over the measurement.

Although typically described as occurring during measurement by a physician, it can also occur during measurement at home.

When limited to physician's offices, it is regarded as white coat hypertension.

Surprisingly, studies show that patients with white coat hypertension do not have abnormal lability outside of physicians' offices

Labile Hypertension

Patients with labile hypertension experience transient but substantial increases in BP.

The increases often, but not always, occur in the setting of emotional distress, particularly anxiety, and are likely mediated by sympathetic activation.

Labile hypertension can be asymptomatic or can be accompanied by symptoms such as headache, palpitations or flushing.

The BP usually falls spontaneously without intervention.

Paroxysmal Hypertension (Pseudopheochromocytoma)

In contrast to patients with labile hypertension, inpatients with "paroxysmal hypertension" (pseudopheochromocytoma), BP elevation generally occurs in the absence of overt emotional distress, with most patients describing the paroxysms as having occurred "out of the blue".

Paroxysms characteristically begin very abruptly and can last minutes, hours, or even days . Abrupt BP elevation is accompanied by prominent and very distressing physical symptoms, such as headache, palpitations, flushing, weakness, or dyspnea .

Biochemical screening for a pheochromocytoma is mandatory, although such a tumor is found in<2% of patients with paroxysmal hypertension.

Catecholamine studies are usually normal but can be mildly abnormal either during or even between paroxysms, reflecting activation of the sympathetic nervous system

Normal Lability in Patients with Vulnerable Underlying Conditions

Although fluctuation of BP is a normal phenomenon, even normal lability would seem potentially harmful in patients with certain medical conditions. For example,

1-chronic aortic dissection,
2-Marfan syndrome,
3-angina
4-cerebral aneurysm,
5-Recurrent nonhypertensive cerebral hemorrhage from amyloid angiopathy,

Transient BP elevation might be deleterious and reduction of even normal lability could be beneficial.

TREAT MENT

- To date, the treatment of hypertension has focused on measurement of resting BP. Virtually no attention has been given to the indications for, and benefit of, treatment of the labile component of BP elevation or to the drug treatment strategies that might best reduce BP lability.

Treatment of BP Variability and BP Reactivity

Little attention has been paid to the effect of drug treatment on BP variability or reactivity or to the effect of such treatment on CV outcome.

Antihypertensive drug therapy does not appear to reduce BP variability. Monotherapy with either a diuretic, angiotensin-converting enzyme (ACE) inhibitor, α blocker, or β-blocker does not reduce BP reactivity to stressors, although lowering of resting BP will predictably lower peak pressure as well.

APPROACH TO DRUG THERAPY FOR BP LABILITY

Eliminating BP lability is not possible but reducing it is often achievable.

A regimen that antagonizes sympathetically mediated BP elevation would seem more logical than treatment with agents directed at other mechanisms, such as ACE inhibitors, ARBS or diuretics, the mainstays of treatment of sustained hypertension

The effect of combined α/β-blockade on sympathetically mediated BP reactivity to laboratory stressors suggest a role for combined α/β-blockade in treating patients with labile hypertension.

Carvedilol and labetalol each provides both α and β-blocking effects but might not be ideal because of unpredictable response resulting from first-pass hepatic metabolism.

Alternatively, two separate agents, a β-blocker, preferably one whose β-blocking effect is not greatly affected by hepatic metabolism (e.g., atenolol, nadolol, bisoprolol, or nebivolol), combined with an α-blocker, such as prazosin, can be prescribed.

The Alerting Phenomenon and White Coat Hypertension

The treatment of white coat hypertension has gained considerable controversy. It would seem unnecessary, and perhaps harmful, to prescribe antihypertensive drugs if home readings are truly normal, as treatment could confer the risk of iatrogenic hypotension.

However, given the increased likelihood of developing sustained hypertension, patients need to be observed for progressive elevation of home readings over time. Treatment should be aimed at reducing home BP, if it is elevated, using the usual pharmacologic agents.

Labile Hypertension (Including Preprocedural BP Elevation)

There are no recognized criteria for treating labile hypertension, other than the mean 24-hour BP observed on ambulatory monitoring.

Frequent home monitoring, which can foster anxiety and elevated readings, should be discouraged. In patients whose hypertension is characterized by frequent severe elevations, e.g., systolic readings >180mm Hg, or who have runaway anxiety about their BP, treatment to achieve more normal readings can be helpful both in lowering BP and in reducing the vicious cycle of anxiety.

Here, institution of a regimen combining an α- and β-blocker, at their usual dosages, would seem preferable.

Contrary to widespread belief, studies consistently show that β-blocker monotherapy does not reduce BP reactivity to stressors. It mitigates the increase in heart rate and cardiac output but does not reduce BP reactivity, which is maintained instead by an increase in peripheral resistance.

Similarly, α-blocker monotherapy blocks the increase in peripheral resistance, but BP reactivity is unaltered due to an increase instead in cardiac output.

In contrast, studies suggest that the combination of an α- and β-blocker, which blocks increases in both cardiac output and peripheral resistance, does reduce BP reactivity

In patients who repeatedly experience marked and problematic BP elevation when presenting for medical or surgical procedures, intravenous administration of an anxiolytic agent and/or the α/β-blocker labetalol can acutely lower BP.

A prophylactic regimen consisting of an α- and aβ-blocker (any standard β-blocker given in combination with an α-blocker, such as prazosin , given for 2 or 3 days, can often mitigate the preprocedural elevation in BP. If necessary, an anxiolytic agent, such as lorazepam (0.5–2 mg), or alprazolam (0.25–1 mg), can also be administered shortly before the procedure.

Paroxysmal Hypertension

Pharmacologic, psychopharmacologic, and psychologically based interventions alone or in combination can eliminate paroxysms in most patients and enable resumption of a normal life.

Acute Management of Hypertensive Paroxysms

A rapid-acting intravenous agent, such as labetalol can be administered. An intravenous bolus of 10 mg to 20 mg can be given, followed by repeat boluses of 20 mg to80 mg at 10- to 15-minute intervals until a response is seen. In the absence of a response or in the presence of extreme BP elevation nitroprusside can be administered.

In patients with less severe BP elevation, oral therapy with clonidine or the combination of an α and aβ-blocker can be given as an alternative to intravenous treatment.

A α-/β-Blockade can be given as labetalol 100 mg to 300 mg every 6 to 8 hours, with response expected within 1.5 to 2.5 hours or alternatively as a β-blocker with fairly rapid onset of action, such as metoprolol (25–50 mg orally every 6 hours), combined with prazosin (1 mg orally every 8–12 hours).

Milder paroxysms can be managed in some patients with a rapid-acting anxiolytic agent, such as alprazolam, given alone or in combination with an antihypertensive agent.

Chronic Preventive Management

- Chronic therapy with an α-blocker combined with a β- blocker given orally has been reported to reduce severity of BP elevation during paroxysms.

- The use of antidepressant and anxiolytic agents to prevent attacks was suggested by the similarity of the syndrome to panic disorder.

Antidepressant agents, including selective serotonin reuptake inhibitors and tricyclic antidepressants, have been reported to prevent recurrent paroxysms in most patients at dosages recommended for treating panic disorder.

CONCLUSIONS

Although the management of labile forms of hypertension is a frequently encountered clinical dilemma, specific criteria for diagnosing labile hypertension and clinical trials to guide management do not exist.

The clinical spectrum of this problem and a treatment approach based on published reports and physiologic principles has been presented.

Studies to assess the effects of labile hypertension and outcome of treatment are needed.

Thanks