

## REVIEW ARTICLE

### ANXIETY DISORDERS INDUCED HYPERTENSION: ISSUE CLINICAL CARE

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**ABSTRACT:** Anxiety is characterized most commonly as a diffuse, unpleasant, vague sense of apprehension, often accompanied by autonomic symptoms such as headache, perspiration, palpitations, tightness in the chest, mild stomach discomfort and restlessness, indicated by an inability to sit or stand still for long. Anxiety disorder is one of important cause of development of hypertension, although it is multifactorial. It increases sympathetic nervous system which causes hypertension due to alterations in baro reflex and chemo reflex pathways at both peripheral and central level. It also increases norepinephrine which acts on  $\beta_1$  receptor (in brain, myocardium and kidney and increases cardiac force, rate of contraction, renin release) and  $\beta_2$  receptor (in pulmonary system and blood vessels and decreases resistance of pulmonary airway and blood vessels)-leading to hypertension.

**KEYWORDS:** Sympathetic nervous system, Baro reflex, Chemo reflex, Norepinephrine.

**INTRODUCTION:** Hypertension is the leading cause of mortality worldwide.<sup>[1,2]</sup> Though it is a multifactorial disease but anxiety plays as a risk factor. Anxiety is an independent risk factor<sup>[3,4]</sup> that increases cardiovascular diseases (CVD) through distinct behavioral and physiological pathways.<sup>[5]</sup>

The fact that hypertension is implicated in the development and progression of CVD. Hypertension seems to be more prevalent in the subject of higher levels of anxiety.<sup>[6]</sup> It has led to the hypothesis that hypertension may be an intermediary link between psychopathology and CVD.<sup>[7]</sup>

**BLOOD PRESSURE CHANGES AND ANXIETY: AUTONOMIC NERVOUS SYSTEM:** The autonomic nervous system plays a central role in maintaining cardiovascular homeostasis via pressure, volume, and chemoreceptor signals. It does this by modifying peripheral vasculature and the function of the kidneys, which affect cardiac output, vascular resistance, and fluid retention. Problems with this system, such as excess activity of the sympathetic nervous system, increase blood pressure and contribute to hypertension.<sup>[8,9]</sup>

In addition, increased activity of the sympathetic accompanied by reduced activity of the parasympathetic has been associated with many metabolic and hemodynamic abnormalities that result in increased cardiovascular morbidity and mortality.<sup>[10]</sup>

The mechanisms of increased sympathetic nervous system activity in hypertension are complex and involve alterations in baro reflex and chemo reflex pathways at both peripheral and central levels. Arterial baroreceptors are reset to a higher pressure in hypertensive patients, and this peripheral resetting reverts to normal when arterial pressure is normalized.<sup>[11]</sup>

Furthermore, there is central resetting of the aortic baro reflex in hypertensive patients, resulting in suppression of sympathetic inhibition after activation of aortic baroreceptor nerves. This baro reflex resetting seems to be mediated, at least partly, by a central action of angiotensin II.<sup>[12]</sup>

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Additional small – molecule mediators that suppress baroreceptor activity and contribute to exaggerated sympathetic drive in hypertension include reactive oxygen species and endothelia.<sup>[13]</sup>

Some studies have shown that hypertensive patients manifest greater vasoconstrictor responses to infused norepinephrine than normotensive controls.

And that hypertensive patients do not show the normal response to increased circulating norepinephrine levels which generally induces down regulation of noradrenergic receptor, and its believed that this abnormal response is genetically inherited.<sup>[14]</sup>

Exposure to stress increases sympathetic outflow, and repeated stress-induced vasoconstriction may result in vascular hypertrophy, leading to progressive increases in peripheral resistance and blood pressure.<sup>[15]</sup> This could partly explain the greater incidence of hypertension in lower socioeconomic groups, since they must endure greater levels of stress associated with daily living.

Persons with a family history of hypertension manifest augmented vasoconstrictor and sympathetic responses to laboratory stressors, such as cold pressor testing and mental stress, that may predispose them to hypertension. Exaggerated stress responses may contribute to the increased incidence of hypertension in this group.<sup>[16]</sup>

**RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM:** Another system maintaining the extracellular fluid volume, peripheral resistance and that if disturbed may lead to hypertension, is the renin-angiotensin-aldosterone system.

Renin is a circulating enzyme that participates in maintaining extracellular volume, and arterial vasoconstriction, Thus it contributing to regulation of the blood pressure, it performs this function through breaking down (hydrolyzes) angiotensinogen secreted from the liver into the peptide angiotensin I, Angiotensin I is further cleaved by an enzyme that is located primarily but not exclusively in the pulmonary circulation bound to endothelium, that enzyme is angiotensin converting enzyme (ACE) producing angiotensin II, the most vasoactive peptide.<sup>[17,18]</sup>

Angiotensin II is a potent constrictor of all blood vessels. It acts on the musculature of arteries and thereby raises the peripheral resistance, and so elevates blood pressure. Angiotensin II also acts on the adrenal glands too and releases Aldosterone, which stimulates the epithelial cells of the kidneys to increase re-absorption of salt and water leading to raised blood volume and raised blood pressure. So elevation of renin level in the blood will lead to hypertension.<sup>[19]</sup>

Recent studies claim that obesity is a risk factor for hypertension because of activation of the renin-angiotensin system (RAS) in adipose tissue,<sup>[20,21]</sup> and also linked renin-angiotensin system with insulin resistance, and claims that anyone can cause the other.<sup>[22]</sup> Local production of angiotensin II in various tissues, including the blood vessels, heart, adrenals, and brain, is controlled by ACE and other enzymes, including the serine protease chymase.

The activity of local renin–angiotensin systems and alternative pathways of angiotensin II formation may make an important contribution to remodeling of resistance vessels and the development of target organ damage (i.e. left ventricular hypertrophy, congestive heart failure, atherosclerosis, stroke, end-stage renal disease, myocardial infarction, and arterial aneurysm) in hypertensive persons.

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**TREATMENT APPROACH:** The above discussion shows that anxiety disorder is one of the leading causes of hypertension and cardiovascular diseases. Before going to treat hypertension, we should treat anxiety first if present. Treatments of anxiety disorder are mainly of two types: Cognitive-behavioral therapy and pharmacotherapy:

1. **Cognitive-behavioural Therapy:** sometimes it acts superior than pharmacotherapy. It removes the misinterpretation of our mind and body. The therapies are-cognitive therapy, applied relaxation, respiratory training, in vivo exposure, family therapy and insight-oriented psychotherapy.
2. **Pharmacotherapy:** Benzodiazepine: The drug of choice are mainly of alprazolam(1<sup>st</sup>) and clonazepam.(2<sup>nd</sup>) Dose of alprazolam is starting dose 0.25-0.5mg thrice daily and maintenance dose 0.5-2mg thrice daily and clonazepam starting dose 0.25-0.5mg twice daily and maintenance dose 0.5-2mg twice daily. Total duration of both drugs for 4-12wks then slowly tapered over 4-10wks.

**SELECTIVE SEROTONIN REUPTAKE INHIBITOR:** Paroxetine is drug of choice. Two types, paroxetine (dose 5 or 10mg daily up to 60mg) and paroxetine CR (dose 12.5 or 25mg daily up to 62.5mg). Others are sertraline, escitalopram. Combination of alprazolam and paroxetine is the best therapy.<sup>[23]</sup>

**CONCLUSION:** Anxiety leads to hypertension because of increased sympathetic nervous system activity and renin-angiotensin-aldosterone system, which ultimately leads to cardiovascular diseases. We must have a look to treat or rule out the anxiety disorders in every patient of hypertension and cardiovascular diseases.

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