

## Review Article

# Hypertension and Its Relation to Headache and Other Craniofacial Neuralgiform Pain

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### Abstract

Both headache and hypertension are widely prevalent in the general population. This has led to a belief that headaches have something to do with hypertension. However, the relationship of headache to hypertension is not a linear one. Mild and probably the moderate chronic hypertension do not seem to produce headache. Acute rise in blood pressure leading to hypertensive crisis can produce headache that is usually temporally related to the onset of hypertension. Acute blood pressure surge may also produce hypertensive encephalopathy and posterior reversible encephalopathy syndrome, which are associated with severe headaches. Headache is also one of the cardinal features of pheochromocytoma and preeclampsia/eclampsia. Craniofacial neuralgiform pains, especially trigeminal neuralgia (TN), have also been shown to worsen with hypertension and relieved with antihypertensive medications in a subset of patients, thereby necessitating a need to understand the relationship of hypertension to TN and possibly with other neuralgiform pains.

**Key words:** Hypertensive crisis, hypertensive encephalopathy, posterior reversible encephalopathy syndrome, trigeminal neuralgia

### Introduction

Patients who suffer from headache are anxious to know the cause of their headache. Majority of the patients relate their headache to either a refractory error or high blood pressure. However, despite correction of hypertension and the refractory error, they continue to have headaches. The relationship of headache with hypertension has interested the headache specialists for nearly one century. T.C. Janeway first suggested the causal relationship of hypertension to headache in 1913.<sup>[1]</sup> However, the relationship of headache with hypertension does not appear to be linear. There are many unanswered questions. Can mild-to-moderate hypertension produce headache? Does headache produce high blood pressure? Can acute rise in blood pressure produce headache? Is headache related to chronic hypertension? Is headache an invariable symptom in conditions associated with acute hypertension such as pheochromocytoma, eclampsia, and preeclampsia? Is headache a symptom of hypertensive encephalopathy or malignant hypertension? What is the possible mechanism of a hypertensive

headache? Are there any specific headache characteristics that can be attributed to hypertensive headache?

These are some of the questions that the researchers have tried to answer in the last century. In this review, we will take up individual case scenarios and try to address some of these questions.

### Case 1

A 40-year-old gentleman complained of low-grade continuous headache for 1 year. He had headache few hours after waking up in the morning. His headache was bilateral, non-pulsating, not related to physical activity, and not associated with photophobia, phonophobia, or vomiting. He was relieved of his headache for few hours after taking a tablet of acetaminophen, but he usually avoided medicines. Incidentally, during a routine physical checkup 6 months back, he found that his blood pressure was 140/90 mmHg. Since then, he has been keeping a record of his blood pressure, which varied from 140 to 160 mmHg systolic and 80 to 95 mmHg diastolic. He had a history of episodic migraine

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that lately became less mild but more frequent for past 18 months. He was not adequately relieved on amitriptyline and propranolol. He came with his blood pressure record and asked whether the use of antihypertensive medicines will relieve his headache? The patient was prescribed amlodipine (5 mg/day) that controlled his blood pressure but did not relieve his headache. Gradual uptitrating the dose of amitriptyline relieved his headache.

### Headache Attributable to Mild-to-Moderate Chronic Hypertension

This case scenario is not uncommon in the headache specialty clinics. Most headache experts believe that mild chronic hypertension (140–159/90–99 mmHg) and moderate chronic hypertension (160–179/100–109 mmHg) does not produce headache. The evidence came from the studies on ambulatory blood pressure monitoring in patients with headache.<sup>[2,3]</sup> They found that the patient's mean blood pressure values during headache periods and headache-free periods were not significantly different. The blood pressure values 1 h before onset were not different from blood pressure values at the time of onset of headache, thereby suggesting that even if the blood pressure was high in a subgroup of patients during headache periods, it was not the headache that produced hypertension. More importantly, they also found that the maximal blood pressure recordings in majority of these patients were outside their headache periods. The above patient suffered from tension-type headache that gradually evolved in frequency from his usual migraine attacks (transformed migraine).

Based on these observations, international classification of headache disorder 3<sup>rd</sup> edition suggests that the mild and moderate hypertension may not cause headache.<sup>[4]</sup> However, since 30% of patients with headache in the above study had moderate hypertension, the relationship of headache secondary to moderate chronic hypertension is still controversial.

#### Case 2

A 46-year-old gentleman complained of mild dyspnea on exertion, swelling over feet for 1 week, and acute severe, bilateral, and pulsating headache for 2 days. Headache was associated with occasional vomiting but without photophobia and phonophobia. The patient experienced exacerbation of headache on physical activity. He was a chronic smoker, tobacco chewer, and chronic alcoholic. He was not a known hypertensive or diabetic. He had headaches very occasionally in the past. On examination, he had blood pressure of 190/130 mmHg, high jugular venous pressure, and tachypnea on supine position, mild pedal edema, and mild hepatomegaly. His chest auscultation revealed S3 gallop, Electrocardiogram (EKG) showed the left ventricular hypertrophy with strain pattern, normal troponin I levels, and a two-dimensional echo was suggestive of signs of hypertensive heart failure. His fundus examination and a cranial computed tomography (CT) were also normal. He was admitted and started on the infusion of sodium nitroprusside that gradually reduced his blood pressure to 140/80 mmHg over 1 day that also promptly relieved his headache and features of heart failure.

### Headache Attributable to Acute Arterial Hypertension Without Hypertensive Encephalopathy

ICHD 3<sup>rd</sup> edition classifies headache attributable to hypertension with blood pressure  $\geq 180$  mmHg systolic and  $\geq 120$  mmHg diastolic with appearance of headache in temporal relation to rise in blood pressure with/without relief from headache with reduction in blood pressure and without evidence of pheochromocytoma, eclampsia/preeclampsia, or any other conditions that could better explain the headache as headache attributable to arterial hypertension (10.3). When these hypertensive surges are not associated with end-organ damage like hypertensive encephalopathy, ICHD 3<sup>rd</sup> edition refers these as headache attributable to hypertensive crisis without hypertensive encephalopathy (10.3.2).<sup>[4]</sup> The short-lasting headaches are reported with acute blood pressure surges in the absence of evidence of pheochromocytoma.<sup>[5]</sup> These hypertensive attacks are also referred to as hypertensive urgencies where it may present with headache, epistaxis, and psychomotor agitation without evidence of end-organ damage secondary to hypertension.<sup>[6,7]</sup>

#### What is the Mechanism of Hypertension-related Headache?

The mechanism of headache by acute rise in blood pressure is not precisely known. It is believed that with the acute rise in blood pressure, the cerebral autoregulation comes into play to maintain cerebral perfusion and neurological functions. When the blood pressure is high but amenable to cerebral autoregulation, the neurological functions remain intact, but there is vasoconstriction of small cerebral arterioles (site of cerebral autoregulation). Therefore, the increased vascular resistance that is produced by cerebral small arteries and arterioles results in the increased transmural pressure in the large cerebral arteries that mainly occupy the base of the brain largely in the posterior fossa. The cervical nerve roots supply these arterial walls and the stretching of the walls of these arteries due to increased transmural pressure produces a referred pain to occipital and neck region. That possibly also explains the reason of occipital/nuchal headaches secondary to hypertension. However, these headaches can be global or frontal as seen in children with acute hypertension.

#### Are there any Specific Characteristics of Hypertension-related Headache?

The ICHD 3<sup>rd</sup> edition recommends that the headache occurring secondary to hypertensive crisis without hypertensive encephalopathy (10.3.2) has to be bilateral, pulsating quality, and it exacerbates with physical activity. The case 2 described above showed all these characteristics. People have also described bioccipital headaches, but headache can be generalized or frontal especially in children. Nuchal headaches and headaches on waking up in the morning or headaches causing early morning awakening are also described as features of hypertensive headaches.<sup>[5,8,9]</sup>

#### Case 3

A 72-year-old gentleman presented with headache, altered behavior with irrelevant talks, episodes of loss of recent memory, social

disinhibition, imbalance, and altered sleep-wake cycles for 12 days. His headache was bilateral occipital, nuchal, and throbbing and used to exacerbate on walking and bending forward and was associated with vomiting at the peak intensity of headache. He was a known hypertensive (on amlodipine 5 mg daily) with poor compliance on drugs. On examination, he was confused. His blood pressure was 200/130 mmHg, with tachycardia, episodic diaphoresis, and episodes of extreme anxiety. Rest of the neurological and systemic examination was normal. His fundus showed signs of early papilledema. His cranial magnetic resonance imaging (MRI) showed bilateral (right>left) occipital white matter hyperintensity on T2-weighted and fluid-attenuated inversion recovery images [Figure 1] with punctate hemorrhages on susceptibility-weighted images. He was promptly treated with IV sodium nitroprusside infusion that reduced his blood pressure to 150/90 mmHg within 24 h. He completely recovered from headache and the higher mental dysfunction. A repeat MRI scan showed near complete resolution of posterior white matter hyperintensities [Figure 1].

#### Headache Attributable to Hypertensive Encephalopathy

ICHHD 3<sup>rd</sup> edition refers headaches that are temporally related to high blood pressure  $\geq$  180/120 mmHg and encephalopathy (confusion, lethargy, seizures, or visual abnormalities) as “headache attributable to hypertensive encephalopathy (10.3.3). Additional features required are relief from headache with recovery from hypertensive encephalopathy and, in addition, two of three headache characteristics - diffuse pain, throbbing character, and aggravation of headache on physical activity. When these patients have characteristic MRI picture as shown in Figure 1, the condition is called “posterior reversible encephalopathy syndrome (PRES).” Unlike hypertensive crisis without hypertensive encephalopathy, the blood pressure here rises beyond the range of cerebral autoregulation. Hence, failure of cerebral autoregulation results in cerebral hyperperfusion and vasogenic cerebral edema. Poor sympathetic innervation of posterior circulation results in predominant posterior predilection of vasogenic edema. Headache may be present in up to 50% of patients with PRES. Patients with chronic hypertension can also have papilledema, thereby referring the condition as “malignant hypertension.” Those without history of chronic hypertension may develop hypertensive encephalopathy with  $<$ 180/120 mmHg of blood pressure. The examples of such conditions are pheochromocytoma and eclampsia.

#### Headache Attributable to Pheochromocytoma (10.3.1)

Pheochromocytoma produces episodic short-lasting headaches due to episodic surge in blood pressure. It usually produces other signs of enhanced adrenergic drive such as palpitation, anxiety, sweating, and pallor. If the acute rise in blood pressure produces symptoms of hypertensive encephalopathy, then the diagnosis of headache is coded as 10.3.3 (headache attributable to hypertensive encephalopathy). The most important characteristic is episodic short duration of headache that usually lasts  $<$ 1 h.<sup>[10]</sup> The headache is usually very severe, occipital, or may be frontal especially in children, throbbing with increase in headache on exertion. The accompanying symptoms may be facial flushing,

tremors, impending doom with severe anxiety, abdominal and chest discomfort, dyspnea, and vomiting.<sup>[11]</sup> Diagnosis requires demonstration of high urinary excretion of catecholamines or catecholamine metabolites in a 24-h urinary sample. Abdominal CT scan demonstrates adrenal masses. Medical management requires adequate sympathetic blockade by alpha-blockers followed by beta-blockers. Definitive treatment is the excision of adrenal masses. The features of adrenergic drive and headache usually resolve with the definitive treatment of pheochromocytoma.

#### Headache Attributable to Eclampsia/Preeclampsia (10.3.4)

Headache is not unusual in pregnancy, and it is very common to have a mild heaviness of head with other tension-type like headache characteristics. However, if the headache is severe, occurring for the 1<sup>st</sup> time in pregnancy, or with the recent change in character and severity and with new found high blood pressure, then these headaches should be considered as a cardinal features of preeclampsia.<sup>[12]</sup> It is important to identify such headaches because majority of patients will have headache prior to the onset of seizures. For ICHD 3<sup>rd</sup> edition diagnosis of “headache attributable to preeclampsia/eclampsia (10.3.4),” headache should appear during pregnancy or postpartum period (up to 4 weeks) in a woman with diagnosis of preeclampsia or eclampsia, and there should either be temporal correlation of occurrence of headache with preeclampsia/eclampsia or relief of headache in the postpartum state.

#### Case 4

A 45-year-old female complained of brief episodes of electric shock-like pain on the left side of face (V2 and V3 distribution) for 1 month. These episodes ranged from few seconds to 2 min. Chewing, talking, and touching the face on affected area precipitated these pain attacks. She had 10–15 such pain attacks daily. Incidentally, she was found to have hypertension during the evaluation of these pain attacks. Her neurological examination was normal. Her cranial MRI revealed anterior inferior cerebellar artery loop abutting the trigeminal nerve root [Figure 2]. She was started on amlodipine 5 mg and atenolol 50 mg. Her blood pressure was normal on the subsequent visits. Interestingly, her pain episodes also disappeared. She continued to remain normotensive and pain free for past 1 year.

#### Craniofacial Neuralgiform Pain And Hypertension

Among craniofacial neuralgiform pains, trigeminal neuralgia (TN) has been shown to have some association with hypertension. The phenomenon of TNs worsening/precipitating by hypertension can possibly be explained by the fact that hypertension can lead to increase tortuosity of blood vessels.<sup>[13]</sup> Most patients with TN show compression of trigeminal nerve root entry zone by a tortuous blood vessel. This compression leads to focal demyelination and ephaptic transmission within the nerve fibers, thereby producing the typical symptomatology.<sup>[14]</sup> Uncontrolled hypertension may increase the blood vessel tortuosity, thereby worsening the compression and aggravation of symptoms. The

reverse is probably responsible for amelioration of pain attacks with antihypertensive medications.

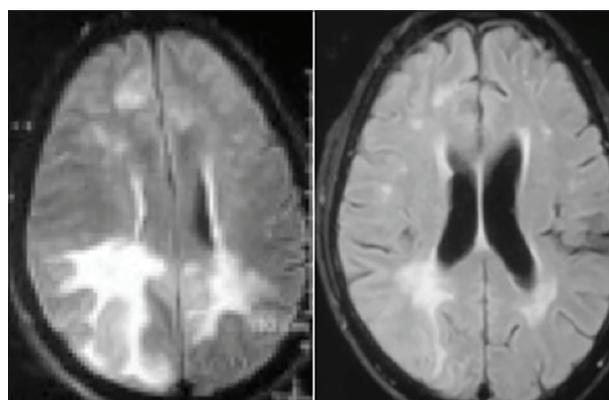
The relationship of TN and hypertension has been assessed in few studies but with ambiguous results.<sup>[15,16]</sup> Recently, a population-based study clearly demonstrated significantly higher risk of developing TN in hypertensive patients.<sup>[17]</sup> Many authors have shown pain attacks of TN improving with antihypertensive medicines [Table 1].<sup>[18-21]</sup> However, a systematic and a relatively large-scale study is required to bring up a clear relationship of TN with hypertension.<sup>[22]</sup>

### Antihypertensive Medicines Causing Headache

A systematic review on antihypertensive drugs effect on headache shows that the antihypertensive medicines reduce headache, but the effect is dependent on the class of medicines.<sup>[23]</sup> However, some antihypertensive medicines may produce headache as a side effect. These medicines include angiotensin-converting enzyme inhibitors, angiotensin receptor blockers II, calcium channel blockers, alpha-blockers, and direct vasodilators. The likely mechanism is their common property to produce intracranial vasodilatation. The headache is generally mild and may improve with cold pack, hot bath, breathing exercises, or regular physical exercises. If the headache is severe and frequent, then there is a need to change the antihypertensive medication.

### Headache And Ischemic Stroke

Headache may be a presenting feature of cerebellar infarcts. However, headache has been documented in other strokes. In a recent meta-analysis, 27% of patients with ischemic stroke had headaches.<sup>[24]</sup> The headache was associated with female sex, younger age, cerebellar stroke, history of migraine, and blood pressure <120/80 mm of Hg. The pathophysiology of headache in



**Figure 1:** (a) Cranial magnetic resonance imaging (MRI) fluid-attenuated inversion recovery image showing predominant parieto-occipital white matter hyperintensity that showed near complete resolution on a follow-up MRI (b)



**Figure 2:** Axial images of fast imaging employing steady-state acquisition sequence show the left anterior inferior cerebellar artery loop (straight arrow) abutting trigeminal nerve root (curved arrow)

**Table 1:** Published case reports of trigeminal neuralgia that improved with antihypertensive therapy

S.n.	Reference	Description	Imaging
1.	Uniyal et al. <sup>18</sup>	A 55-year old woman developed left trigeminal neuralgia pain (V3 territory) and incidently found hypertensive. Amlodipine normalized blood pressure and ameliorated pain attacks. Noncompliance to amlodipine produced relapse of TN episodes.	Anterior-inferior cerebellar artery loop around left trigeminal nerve root. Left vertebral artery compressing anterolateral medulla causing neurogenic hypertension.
2.	Lanzino et al. <sup>19</sup>	A 59-year old man experienced painful exacerbations of left sided trigeminal neuralgia in parallel with hypertensive crises which relieved by clonidine administration.	Vascular loop of dolichoectatic basilar artery compressing the left trigeminal nerve root entry zone.
3.	Conforti et al. <sup>20</sup>	A 56-year old woman presented with typical trigeminal neuralgia pain in V2 and V3 territory. The pain episodes started during uncontrolled hypertension and improved with calcium channel blockers.	Persistent trigeminal artery abutting the right trigeminal nerve root.
4.	Sahin et al. <sup>21</sup>	A 60-year-old man presented with trigeminal neuralgia pain in V2 and V3 area. The pain episodes worsened during unstable hypertension.	Vascular loop abutting to the left trigeminal nerve root.

ischemic stroke could be distention or distortion of blood vessels, thereby stimulating the intracranial nociceptive afferents, arterial dissection (intracranial and extracranial), and involvement of trigeminal vascular and cervical vascular systems.<sup>[25]</sup>

## Conclusion

Hypertension may produce headache in certain circumstances. Acute rise in blood pressure in hypertension naïve or chronic hypertensive patients may produce headache in temporal relation to rise in blood pressure. Hypertension when very severe may break the boundary of cerebral autoregulation and produces hypertensive encephalopathy and other organ dysfunctions in addition to acute headaches. Certain hypertensive emergencies such as pheochromocytoma and eclampsia/preeclampsia have headache as an initial and a cardinal feature that sometimes is a reason for the diagnosis of these conditions. Cranial and facial neuralgiform pains, especially TN, are now shown to have some association with hypertension at least in a subset of patients, but their relationship needs to be established in the future studies.

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