

Prevalence of hypertension in glossopharyngeal neuralgia patients comparing with the result from the China Hypertension Survey

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Abstract

Background & Objective: Neurogenic hypertension is an important subtype of hypertension but the concept still lacks supporting evidence. By comparing the prevalence of hypertension in glossopharyngeal neuralgia (GPN) patients and the general population, we believe it can provide the evidence for the theory that compression of IX nerve root entry zone can cause hypertension. **Methods:** We retrospectively analyzed patients with GPN and compared the prevalence of hypertension in these patients with the general population. **Results:** A total of 90 patients with GPN were included, in which 40 suffered from hypertension. The adjusted prevalence was 40.3%. The odds ratio (OR) for hypertension between the GPN patients and the general population in China was 1.451. The 35-44 and 45-54 years old GPN patients had a higher prevalence than the general population, with an OR of 2.611 and 1.648, respectively.

Conclusion: Patients with GPN have a higher prevalence of hypertension. The prevalence of hypertension is more pronounced in patients younger than 55, supporting the pathogenesis of vascular compression resulting in neurogenic hypertension.

Keywords: Glossopharyngeal neuralgia, hypertension, microvascular decompression, prevalence

INTRODUCTION

Hypertension is one of the major diseases affecting human health, but its pathogenesis remains unclear. Neurogenic hypertension is a type of hypertension caused by central or peripheral nerve dysfunction. Jannetta *et al.*¹ first proposed that vessel compression on the rostral ventrolateral medulla (RVLM) was a significant cause of neurogenic hypertension. Following this, many studies based on anatomy, imaging, and experiments were conducted to investigate this theory.²⁻⁴ Sendell *et al.*⁵ found that the incidence of hypertension was elevated in patients with hemifacial spasm (HFS) but not trigeminal neuralgia (TN). This was thought to be explained by the compression site of HFS is closer to the RVLM.

Glossopharyngeal neuralgia (GPN) is a rare cranial nerve disease with an annual incidence of 0.2-0.7/100,000.^{6,7} It is mainly caused by demyelination or degeneration of the

glossopharyngeal nerve, and the compression of the pharyngeal nerve at root entry zone (REZ) was thought to be the main pathogenic factor. The pathology is postulated to be from vascular compression induced neurogenic hypertension.

This study explores the prevalence of hypertension in patients with GPN and compared with the general population. If the prevalence of hypertension is higher in GPN patients, we can infer that the compression of blood vessels on the IX nerve REZ can cause hypertension.

METHODS

Study design

This is a retrospective study to investigate the relationship between essential hypertension and GPN. The study compared the prevalence of hypertension in GPN patients and the general population. To be comparable with the control group, the prevalence rate was standardized

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with the 2010 China population census data. Hypertension data for the general population is derived from the China Hypertension Survey (CHS), 2012–2015.⁸

Patients with GPN

This study included all of the patients with GPN who underwent craniotomy operation by the corresponding author during 2011.11–2018.10.

GPN was diagnosed based on clinical history. Patients with GPN were characterized by unilateral sharp, stabbing, and severe pain, which were often triggered by swallowing, chewing, coughing, or talking that lasted from seconds to minutes. The pain occurred in cluster. The intervals between the pain cluster could range from days to years, with patients being asymptomatic during remission.⁹ The pain was usually located at the posterior part of the tongue, oropharynx, angle of the mandible, or the middle ear.¹⁰ The trigger point was always present and was located in the glossopharyngeal nerve distribution.

All the patients underwent routine preoperative examinations after admission. The numeric rating scale was used to evaluate the degree of pain and its improvement after the operation. Head MRI (including Three-dimensional time-of-flight (3D-TOF), 3D constructive interference in steady state (3D-CISS), and 3D reconstruction sequences) were performed to exclude tumors and to find the abnormal vessels before surgery. Pharmacological treatments such as carbamazepine, gabapentin, and pregabalin were usually effective initially, but patient later gradually became resistant to these drugs. So, the microvascular decompression (MVD) surgery was performed.

Blood pressure (BP) was measured twice by a standard method. Before the measurement, the patient should be at rest for at least 5 minutes. The patient adopted a sitting position with the upper arm at the same level of the heart. The same sphygmomanometer was used for measurement. The BP was measured at an interval of 1–2 minutes. If the difference between the two measurements was more than 5mmHg, a third measurement was required and the average BP was taken.

The results from the China Hypertension Survey

The survey was based on a sample of 451,755 residents from 31 provinces in mainland China from October 2012 to December 2015. They were included in the stratified sampling and were divided into 14 strata of 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, ≥ 75 years of age and each

age group was divided into male and female.⁸ In addition, survey results were adjusted according to the 2010 China population census data. The survey was representative of the overall state of hypertension in China due to its large sample size, extensive coverage, and rigorous design.

Similar to the CHS, hypertension in this study was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or patients taking anti-hypertensive drugs in the recent two weeks.

Statistical analysis

The odds ratio (OR), 95% confidence intervals (CIs), and p values were calculated to determine if the prevalence of hypertension in GPN patients was higher than the general population. A subgroup analysis of the incidence of hypertension in all ages was performed to calculate the ORs, 95% confidence intervals (CIs), and p values. A chi-square test was used to find out whether the affected side had an effect on the onset of hypertension. Statistical analysis was performed using the software of SPSS 18.0.

RESULTS

Demographic features

A total of 90 GPN patients who underwent MVD were enrolled. The patients who could not find offending vessel were excluded in this study. The study subjects included 33 males and 57 females with an average age of 57.5 ± 9.7 years (range from 35 to 80 years). There were 41 patients with GPN on the left side and 47 patients on the right side. Of the 90 patients with GPN, 40 suffered from hypertension. The offending vessels found during the operation and the demographic characteristics of the patients are shown in Table 1.

All patients had a typical GPN as described above. There were no abnormalities in routine preoperative tests, and no surgical contraindications. MR imagings were performed in all patients before surgery. None of the patients had other abnormalities during the operation and the operations were all successful.

Prevalence of hypertension in GPN patients

The average BP of patients admitted to the hospital was 132.5 ± 16.2 mmHg systolic BP, 79.6 ± 11.5 mmHg diastolic BP, and average heart rate (HR) was 78.3 ± 4.6 beats per minutes. Of the 90 patients with GPN, 40 had hypertension, and

Table 1: Demographic characteristics of patients with GPN with and without hypertension

Variable	GPN Patients (n=90)	Percent
Sex		
Female	57	63.3
Male	33	36.7
Age (yrs)		
Mean	57.5±9.7	-
Range	35-80	-
35-44	10	11.1
45-54	25	27.8
55-64	31	34.4
65-74	19	21.1
≥75	5	5.6
Side		
Left	41	45.6
Right	47	52.2
Both	2	2.2
Duration of symptoms (months)	50.3±56.8	-
Hypertension		
Yes	40	44.4
No	50	55.6
Average SBP	132.5±16.2	-
Average DBP	79.6±11.5	-
Average HR	78.3±4.6	-
Duration of hypertension (months)	124.3±4.6	-

GPN: Glossopharyngeal Neuralgia. SBP: Systolic Blood Pressure. DBP: Diastolic Blood Pressure. HR: Heart Rate.

the prevalence was 44.4%. Adjusted prevalence according to all age groups of 2010 China population census data was 40.3%. The prevalence of hypertension in patients and the comparison with the general population are shown in Table 2. The odds ratio (OR) for hypertension between the GPN patients and the estimated general population in China was 1.451 (95% CI 1.451-1.452, $p < 0.001$). We also adjusted the prevalence for gender. The prevalence of hypertension was 45.4% in GPN patients and 38.0% in general population (OR=1.356, 95%CI 1.356-1.357, $p < 0.001$). All of the results indicated a higher prevalence of hypertension in the GPN patients.

On admission, the mean systolic blood pressure and diastolic blood pressure of the hypertension patients were 144.2 ± 15.2 mmHg and 87.2 ± 10.7 mmHg respectively. Upon discharge, they were 135.4 ± 14.0 mmHg and 82.1 ± 11.3 mmHg respectively.

Subgroup analysis based on age grouping showed that the prevalence of hypertension in

both the patients and control groups increased with age. When comparing the prevalence of each age group, it was found that the prevalence of hypertension in GPN patients was particularly higher among the younger populations as compared to control. The 35-44 and 45-54 years GPN patients had a higher prevalence than the general population, with an OR of 2.429 (95% CI 2.427-2.430) and 1.586 (95% CI 1.585-1.586). The prevalence of hypertension in patients over 55 years old was similar to that in the general population.

The influence of the affected side on the prevalence of hypertension was shown in Table 3. Of the 90 patients, 41 (45.6%) suffered from left-side GPN, while 47 (52.2%) patients had GPN on the right-side. Of the left side GPN patients, 19 (46.3%) had hypertension, and 22 (46.8%) for the right side GPN patients. The results showed that the side had no effect on the prevalence of hypertension ($p = 0.876$, 2-sided chi-square).

Table 2: Comparison of the prevalence of hypertension in all age groups after standardization

Characteristics	Standard population			GPN		Expected number of patients	CHS HT standardize prevalence (%)	OR	95% CI	P Value
	HT	Non-HT	HT prevalence (%)	HT prevalence (%)						
35-44	242779923	7	30.0	30.0	72833976.9	15.0	2.429	2.427-2.430	<0.001	
45-54	184347724	15	40.0	40.0	73739089.6	29.6	1.586	1.585-1.586	<0.001	
55-64	139979756	16	48.4	48.4	63216664	44.6	1.165	1.164-1.165	<0.001	
65-74	74085679	9	47.4	47.4	31193970.1	55.7	0.716	0.715-0.716	<0.001	
≥75	44805545	3	60.0	60.0	26883327	60.2	0.992	0.991-0.993	<0.001	
Total	685998627	38	40.3*	40.3*	267867028	32.3#	1.413	1.412-1.413	<0.001	

* Standardize prevalence of GPN patients according to age

Standardize prevalence of population older than 35 years according to age.

DISCUSSION

The neurovascular compression type of neurogenic hypertension is caused by abnormal vascular compression of RVLM and/or IX/X nerve REZ.^{1,2} This is because the blood vessel stimulates C1 cells, resulting in increased sympathetic tone and peripheral vasoconstriction, which causes an increase in BP.¹¹⁻¹³ To-date, the theory has not been confirmed reflecting slow progress in research. However, the confirmation of this type of neurogenic hypertension is an essential complement to the cause of essential hypertension.

This study retrospectively analyzed the prevalence of hypertension in patients with GPN and compared it with the general population. The patients were from more than 20 provinces or municipalities in mainland China, and the study subjects can be considered to be characteristic of patients with GPN. They had typical symptoms, and all secondary factors were excluded, which is currently accepted as a diagnostic of the condition.¹⁴ The treatment of the GPN includes drug therapy and surgical treatment in which MVD is generally preferred because of its remarkable and long-lasting effect.¹⁵⁻¹⁷

The results of this study show that the prevalence of hypertension in patients with GPN was significantly increased. After MVD, the average BP of the hypertensive patients decreased. This could be due to the fact that GPN is mainly caused by the tortuous blood vessels compressing the glossopharyngeal nerve REZ, which is similar to the cause of vascular compression type neurogenic hypertension.¹⁸ The IX nerve REZ is close to the RVLM position so that when the IX nerve is compressed, the RVLM is often affected.¹⁹ The C1 cell activity in this region is enhanced, causing an increase in BP. Sandell *et al.*⁵ conducted a retrospective study to investigate the occurrence of hypertension in patients with either HFS or TN comparing with the prevalence of hypertension in the general population. The result showed that hypertension was significantly higher in the patients with HFSs than the general population; while this was not so for patients with TN. This was explained by the facial nerve being closer to the RVLM than the trigeminal nerve. The glossopharyngeal nerve is also closer to RVLM, so it is consistent with the observation that the prevalence of hypertension in GPN patients is also increased. GPN accompanied with hypertension has not been previously confirmed, but there have been many reports of various cranial nerve diseases, including GPN and hypertension.²⁰

Table 3: The influence of affected side on the prevalence of hypertension

		HT		Total	P
		Yes	No		
Side	Left	22	19	41	-
	Right	26	21	47	-
	Both	2	0	2	-
Total		50	40	90	0.876*

* Chi-square test results of the relationship between side and hypertension. Patients with bilateral GPN were excluded because the sample size was too small and was not related to the study analysis.

Previous studies have reported that patients with GPN may be accompanied with some cardiovascular symptoms, such as syncopal episodes, hypotension, bradycardia, or asystole. The explanation was that these symptoms were due to the concomitant involvement of the vagal nerve.^{21,22} These findings do not contradict our results. In these reports, the cause of GPN and syncope is vascular compression of the IX nerve, but not the IX nerve REZ. Thus, it does not cause an increase in the activity of surrounding C1 cells. Among our study subjects, none had a history of syncope or hypotension, although two patients' electrocardiogram showed bradycardia.

Our results showed that there was no significant difference in the prevalence of hypertension between the two sides. When Jannetta first proposed the theory, it was thought that only the left RVLM compression would lead to high BP. In recent years, more and more researchers believe that both left and right compression can lead to high BP.^{2,23,24} As this type of hypertension is not due to advancing age, thus the rise of BP before aging become a dominant factor.

For limitation of our study, for the association between hypertension and GPN, we could not definitely conclude that the GPN has induced hypertension, rather than the hypertension has reduced in the GPN, as this was a retrospective observational study. As such, there was also no preoperative BP related hormone levels performed, nor can we completely exclude a secondary hypertension.

In conclusion, we have shown that the prevalence of hypertension in our patients with GPN was higher than in the general population. We hypothesized that the association was a vascular compression neurogenic hypertension caused by abnormally distorted vascular compression of IX nerve REZ. The association between GPN and hypertension among our patients was particularly pronounced among those younger than 55 years of age. This is also supportive of the vascular compression resulting in neurogenic hypertension.

DISCLOSURE

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Conflict of Interest: None.

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