



## Combined Hyperactive Dysfunction Syndrome of the Cranial Nerves: A Retrospective Systematic Study of Clinical Characteristics in 44 Patients

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**BACKGROUND:** Combined hyperactive dysfunction syndrome (HDS) is defined as the combination symptoms arising from overactivity in cranial nerves, specifically, trigeminal neuralgia (TN), hemifacial spasm (HFS), and glossopharyngeal neuralgia (GPN), without an obvious explanatory structural lesion. This study retrospectively analyzes the clinical characteristics of combined HDS treated with microvascular decompression (MVD) in a single institution.

**METHODS:** A total of 1450 patients with HDS were treated with MVD in our department during a 10-year period, among which 44 cases of combined HDS were identified. Clinical records and follow-ups were reviewed.

**RESULTS:** Combined HDS comprised 3.03% (44/1450) of all HDS in our series, with female predominance compared with single HDS ( $P = 0.002$ ), including combined TN-HFS (14 cases), combined TN-GPN (26 cases), bilateral TN (2 cases), and combined TN-HFS-GPN (2 cases). The average age at diagnosis of patients with combined HDS (60.9 years) was significantly older than that of patients with single HDS (53.5 years) ( $P = 0.035$ ). Hypertension was closely associated with the prevalence of combined HDS compared with single HDS ( $P = 0.009$ ). The curative rate was 97.7% (43/44) after MVD, and the recurrence rate was 3.33%. The incidence rates of postoperative cardiac, pulmonary, thromboembolic, and

delirium complications were higher in combined HDS than in single HDS ( $P < 0.05$ ).

**CONCLUSIONS:** Combined HDS is a rarely occurring syndrome usually observed in older females, and the most common types are combined TN-GPN and combined TN-HFS. Age and gender seemed to be causes for developing combined HDS, and MVD shows potential as a favorable treatment choice.

### INTRODUCTION

Hyperactive dysfunction syndrome (HDS) is defined as symptoms arising from overactivity in cranial nerves, specifically, trigeminal neuralgia (TN), hemifacial spasm (HFS), and glossopharyngeal neuralgia (GPN), without an obvious explanatory structural lesion. Combined HDS of cranial nerves is defined as the combination of HDSs that might or might not occur on 1 or both sides. These symptoms can sometimes occur synchronously or metachronously.<sup>1,2</sup>

Previous studies indicated that combined HDSs are extremely rare. To our knowledge, isolated case reports or several small case series have thus far been studied,<sup>3-7</sup> demographic characteristics, risk factors, and treatment effect after microvascular decompression (MVD) needs further study. In addition, the current study is the first to describe the incidence of several complications that occur after MVD with combined HDS. A total of 1450 cases of HDS

#### Key words

- Combined hyperactive dysfunction syndrome
- Microvascular decompression
- Postoperative complications
- Risk factors

#### Abbreviations and Acronyms

- AICA:** Anterior inferior cerebellar artery  
**GPN:** Glossopharyngeal neuralgia  
**HDS:** Hyperactive dysfunction syndrome  
**HFS:** Hemifacial spasm  
**MVD:** Microvascular decompression  
**PICA:** Posterior inferior cerebellar artery  
**PV:** Petrosal vein  
**REZ:** Root entry/exit zone  
**SCA:** Superior cerebellar artery  
**TN:** Trigeminal neuralgia

**VA:** Vertebral artery

**VTE:** Venous thromboembolism

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underwent MVD in our department from January 2006 to September 2016, among which were 44 cases of combined HDS.

## METHODS

### Diagnostic Criteria and Data Source

Diagnostic criteria were as follows<sup>2</sup>:

- 1) Patients with combined onset of involuntary and asynchronous TN, HFS, and GPN, which may or may not occur simultaneously on 1 or both sides, were included.
- 2) Brain tumor, arteriovenous malformation, other space-occupying lesions in the cerebellopontine area, and other forms of facial or oromandibular dystonic movements, focal seizures, tardive dyskinesia, history of Bell palsy, dystonia, blepharospasm, and metabolic diseases were excluded.

To satisfy the diagnostic criteria and determine the potential offending vessels, all 1450 cases of HDS treated with MVD underwent preoperative brain three-dimensional time-of-flight magnetic resonance imaging, and all those diagnoses of HDS were made by trained neurosurgeons. The diagnostic basis of TN, HFS, and GPN is primarily based on typical clinical manifestations. Preoperative brain magnetic resonance imaging is a subsidiary examination, which is important for excluding space-occupying lesions and discovering potentially offending vessels. For the 44 cases of combined HDS, operative findings and surgical outcomes were reviewed. For comparison, information regarding age, sex, blood pressure, blood glucose level, blood cholesterol level, as well as postoperative complications of 44 cases of combined HDS and 1406 cases of single HDS, were obtained from the medical records. In addition, the diagnoses of hypertension, hypercholesterolemia, and hyperglycemia were performed by veteran physicians in accordance with relevant specific diagnostic criteria in Chinese patients.

### Effectiveness Evaluation, Follow-Up, and Ethics

The effectiveness evaluation criteria of surgical outcomes within 1 month after MVD were classified according to the following 4 grades:

- 1) Clinical cure: complete disappearance of HFS and being pain free without medication for TN and GPN
- 2) Obvious alleviation: intermittent mild twitching for HFS and mild pain not requiring medication for TN and GPN
- 3) Partial alleviation: persistent mild twitching for HFS, mild pain, and pain that is well tolerated with medication for TN and GPN
- 4) No alleviation: no alleviation or even aggravation of the symptoms

In addition, recurrence of symptoms was diagnosed whenever the symptom reappeared and persisted for more than 1 month and was poorly tolerated without any other intervention after a period of disappearance or alleviation postoperatively. Outcomes and prognoses for all 43 patients with combined HDS were obtained by

postoperative observation, interview at the outpatient department, or telephone, except for 1 female who died of acute postoperative cerebellar hemorrhage 10 hours after surgery. Approval for this retrospective study was obtained from the Shandong University Qilu Hospital institutional review board. All 1450 participants provided written informed consent.

### Statistical Analysis

A Student *t* test was used to compare the mean age at the time of diagnosis in patients with combined HDS and patients with single HDS. The  $\chi^2$  test was used to compare the difference in gender distribution between the patients with combined HDS and those with single HDS. A *P* value <0.05 was considered statistically significant. Analyses were carried out using SPSS version 23 (IBM Corp., Armonk, New York, USA).

## RESULTS

Relevant demographic information, type of disease, vessels identified by the surgeon as compressing the root entry/exit zone (REZ), follow-up, and the surgical outcomes of patients with combined HDS are summarized in **Tables 1–3**. The demographic data, chronic comorbidities, and postoperative complications of combined HDS in **Tables 3** and **4** were generally comparable with those of single HDS.

### Incidence

Among these 1450 cases of HDS, 44 were of combined HDS, constituting 3.03% of all HDS. In addition, 2 cases of bilateral TN (4.5%) and 42 cases of combined symptoms occurred on the same side, which included 14 cases of combined TN-HFS (31.8%), 26 cases of combined TN-GPN (59.1%), and 2 cases of combined TN-HFS-GPN (4.5%) (**Table 1**). Of 14 patients with combined TN-HFS, 8 developed TN first, and 5 developed HFS first. One patient reported unbearable synchronized pain resulting from HFS. Of 26 patients with combined TN-GPN, 7 developed TN first, and 19 developed GPN first. HFS occurred first, and then TN and GPN occurred simultaneously for both patients with combined TN-HFS-GPN. Regarding the 2 patients with bilateral TN, the right TN occurred first for all (**Table 2**). In addition, of 1406 cases of single HDS, 310 were of HFS, constituting 22.0% of all single HDS, which is significantly lower than that of TN (73.3%) in the comparative group of patients with a single cranial nerve disorder.

### Demographics

Combined HDS seemed to occur mostly in old patients, with a mean age of 60.9 years (range, 33–83 years) on initial diagnosis, compared with 53.5 years for patients with single HDS (*t* test, *P* = 0.035). Females (39 cases, 88.6%) are more likely to have combined HDS, compared with males (5 cases, 11.4%) ( $\chi^2$  test, *P* = 0.002), and a significant difference in sex ratio was indicated between the combined HDS subgroup and the single HDS subgroup (*P* = 0.035) (**Table 4**).

### Chronic Comorbidities

Among the 44 patients with combined HDS, 40.9% (18 of 44) had a history of hypertension, which is significantly higher than that of single HDS (23.8%; *P* = 0.009). However, when multivariate

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