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Systemic autonomic involvement in episodic cluster headache: a comparison between active and remission periods

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Abstract In this study we compared systemic autonomic involvement in episodic cluster headache during active and silent periods. Seventeen patients were studied with sympathetic skin response, lying to standing test, Valsalva manoeuvre, deep breathing test and orthostatic hypotension evaluation. Each of them underwent these tests during active and silent periods. Values were then compared with normal controls. Our data show a parasympathetic, but not sympathetic, involvement. Moreover, this impairment seems to be "chronic", as it persists beyond the active period.

Key words Cluster headache • Autonomic tests • Vegetative nervous system

Introduction

Cranial autonomic involvement in episodic cluster headache (ECH) is known. Some vegetative symptoms are part of the diagnostic criteria for ECH and other trigemino-autonomic cephalalgias in the IHS classification [1]. Less is known about systemic autonomic impairment. Some authors [2–7] have described a derangement of cardiovascular responses during attacks of ECH. Moreover, a few authors have studied the differences between active and remission phase. We present a case-control study on systemic autonomic nervous activity, in particular its cardiovascular function, in ECH, during cluster periods and during remission phases.

Methods

Seventeen ECH patients (14 males, 3 females, mean age 36.2 years, range 22–55) underwent a series of vegetative tests (Table 1), according to Ewing's protocol [8], to evaluate parasympathetic cardiovascular responses: lying to standing test (LST), Valsalva manoeuvre (VM) and deep breathing test (DBT); we also performed two tests, sympathetic skin response (SSR) and measurement of postural changes of blood pressure (PH), to assess vasoactive sympathetic pathway. Each patient was studied during either the active or silent period. We considered as active period when the last attack had occurred no more than 2 days before the study and silent period if the patient had been attack-free for the last 3 months and the following 2 months. Seventeen sex- and age-matched healthy subjects were also evaluated as controls. During the active phase patients were drug-free; only symptomatic agents were allowed. The day of the study patients did not take coffee, tea or other foods containing sympathicomimetic amines. No patient suffered from diseases other than ECH; nobody was a smoker.

Results

Values are shown in Tables 2 and 3. SSR and PH showed no difference either between the active and the silent period or between ECH and normal controls. On the contrary, we found significant ($p<0.01$) differences in VM, LST and

Table 1 Synopsis of autonomic tests in the study

Test	Technique	Significance	Marker	Reference values
SSR	Potential obtained simultaneously on 4 limbs by means of clapping, gasping and supraorbital electric stimulation	Assessment of sympathetic activity	Detection of the potential	Presence (normal) or absence (pathologic) of the potential
LST	EKG recording during fast movement from clinostatism to orthostatism	Assessment of parasympathetic cardiovascular responses	"30/15" ratio: RR interval at 30th beat/RR interval at 15th beat after standing up	Normal: ratio≥1.03; pathologic: ratio≤1
VM	15 s expiration against manometer; test repeated three times with a 2-min interval between each of them; simultaneous EKG recording	Assessment of parasympathetic cardiovascular responses	Valsalva ratio: ratio between the maximal RR interval after the strain and the minimal RR interval during it	Normal: ratio>1.20; pathologic: ratio<1.11
DBT	1 min deep breathing (6 cycles/min), with simultaneous EKG recording	Assessment of parasympathetic cardiovascular responses	E:I: ratio of the longest RR interval during expiration to the shortest RR interval during inspiration, on 6 consecutive cycles	Normal: ratio>1.20; pathologic: ratio<1.11
PH	Performed together with LST: measurement of blood pressure during clinostatism, then at 30, 60, 120 and 180 s after standing up	Exploration of vasoactive sympathetic pathway	Measurement of BP during orthostatism	Normal: systolic BP <-20 mmHg; pathologic: systolic BP >-30 mmHg

Table 2 Values during active period

Patient	Age	Sex	LST	PH	VM	DBT	SSR
1	34	M	1.04	-13	1.08	1.24	Yes
2	22	F	1.03	-15	1.08	1.06	Yes
3	36	M	1.00	-12	1.22	1.23	Yes
4	34	M	0.98	-8	1.09	1.02	Yes
5	22	M	1.05	-4	1.11	1.19	Yes
6	29	F	0.96	-7	1.04	1.04	Yes
7	53	M	0.97	-19	1.03	1.06	Yes
8	28	F	1.01	-17	1.07	1.05	Yes
9	42	M	0.94	-18	1.19	1.19	Yes
10	30	M	0.96	-10	1.07	1.03	Yes
11	43	M	1.01	-8	1.23	1.22	Yes
12	35	M	1.05	-5	1.10	1.27	Yes
13	55	M	1.01	-13	1.04	1.01	Yes
14	43	M	0.92	-14	1.03	1.20	Yes
15	51	M	1.02	-16	1.05	1.03	Yes
16	28	M	1.02	-16	1.10	1.28	Yes
17	24	M	0.89	-12	1.09	1.01	Yes

DBT if we compared values of the active period with the control group. In fact, we could observe a significant change in 76.4% (LST), 82.3% (VM) and 52.9% (DBT) of patients during the active period. The same statistical difference was observed when we examined values of the silent period. The rate of patients with abnormal values during the silent phase was only slightly reduced: 70.6% (LST), 58.8% (VM) and 47% (DBT).

Table 3 Values during remission period

Patient	Age	Sex	LST	PH	VM	DBT	SSR
1	34	M	1.04	-11	1.21	1.23	Yes
2	22	F	1.05	-12	1.07	1.04	Yes
3	36	M	1.01	-12	1.22	1.25	Yes
4	34	M	0.99	-10	1.09	1.07	Yes
5	22	M	1.06	-13	1.15	1.24	Yes
6	29	F	0.95	-9	1.03	1.09	Yes
7	53	M	0.97	-18	1.02	1.27	Yes
8	28	F	1.01	-17	1.05	1.07	Yes
9	42	M	0.94	-19	1.19	1.23	Yes
10	30	M	0.96	-13	1.08	1.05	Yes
11	43	M	1.01	-8	1.25	1.26	Yes
12	35	M	1.06	-4	1.10	1.25	Yes
13	55	M	1.00	-11	1.02	1.08	Yes
14	43	M	0.91	-13	1.16	1.19	Yes
15	51	M	1.01	-15	1.05	1.07	Yes
16	28	M	1.02	-16	1.10	15	Yes
17	24	M	0.89	-16	1.09	9	Yes

Conclusions

Despite many investigations focusing on systemic vegetative changes in ECH, results are often controversial. While cranial vegetative symptoms of cluster headache seem to be related to an orthosympathetic hypofunction, often persisting during the silent period [9, 10], our knowledge of the systemic vegetative system is still poor and results are often controversial. There are several reasons for this: (1) studies are carried out using different tests and in different periods (i.e., during attack, outside attack but within an active phase, outside the active period); (2) there is no standardised method as regards the study of the autonomic nervous system and it has been explored neurophysiologically, pharmacologically or by means of other techniques [7]; and (3) obtained values are often poorly comparable, as they are frequently influenced by internal and external factors (temperature, drugs, smoke, psychic conditions of the patient). Most of these studies have described changes in the systemic autonomic system, varying from an orthosympathetic hyperactivity [5] to a parasympathetic hyperactivity [2, 4, 6]. In our study we used a standardised protocol [8] that explores mainly the parasympathetic cardiovascular system. Moreover, we performed two tests (SSR, PH) to assess orthosympathetic function. Our findings confirm a systemic autonomic impairment affecting the majority of patients during the cluster period. This impairment seems to involve the parasympathetic more than the orthosympathetic side, as we found changes in LST, MV and DBT, but not in SSR and PH. The same changes persisted beyond the cluster phase, suggesting that this vegetative derangement could be “chronic”. Our data confirm a diffuse autonomic imbalance in ECH patients, in the active and silent periods, far from being completely understood and more complex than hitherto known.

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