CYCLIC VOMITING SYNDROME (CVS): DEMOGRAPHIC AND CLINICAL REVIEW OF AN ITALIAN COHORT

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BACKGROUND AND AIM. CVS is a brain-gut disorder characterized by recurrent severe vomiting episodes that may affect the patients' quality of life. Very few and scattered studies have been published on the epidemiology and clinical features of the disease. We hereby report the demographic and clinical data of a large cohort of pediatric patients with CVS.
MATERIALS AND METHODS: The charts of 163 patients referred to our Unit for suspected CVS according to the Rome III criteria were reviewed. Following a thorough biochemical, metabolic, allergological, endoscopic, and radiological evaluation in order to exclude every known etiology of cyclic vomiting, 102/107 patients were unequivocally diagnosed as having true, idiopathic CVS. On these patients the following demographic and clinical features were reviewed: gender, age of onset, frequency and length of episodes, time from onset to final diagnosis, family history of migraine and cyclic vomiting, and clinical features. Statistical significance was evaluated with T test, Fisher's exact test and $\chi 2$ test.
RESULTS. Gender and age of onset: 50/107 patients were males (M) and 52/107 females (F), with a mean age of onset at 5.2 years (yr). A significantly earlier onset was observed in M compared to F (mean age 4.21yr vs. 5,83 yr respectively, $p<0.05$) and a predominance of M was observed in children whose symptom onset was before 2 yr of age (14 M vs. 4 F). Time from onset to final diagnosis: 24% of patients received a diagnosis <1 yr, 39% between 1 and 4 yr, 25% between 4 and 8 yr, and 12% >8 yr since the onset of symptoms. Frequency of episodes: 31% of patients reported ≤5 episodes/yr, 36% 6-10 episodes/yr, 17% 11-15 episodes/yr; 16% >16 episodes/yr. Length of episodes: in 26% of patients attacks had a mean length of <12 hours (hr); in 24% between 13 and 24 hr; in 20% between 25 and 48 hr; in 30% >49 hr; an association was found between length and frequency of episodes, in that children with >10 episodes/yr also had more frequent episodes lasting >24 hr ($p<0.05$). Time at onset: 39% of episodes occurred in the morning, 26% at night (until 6 a.m.), 4% morning or night, 9% at other times of the day, and 22% had episodes at variable times. Clinical features: apart from vomiting, the commonest clinical symptoms were nausea and drooling (84%), pallor and a "miserable" appearance (83%), lethargy (70%), abdominal pain (64%), phono- and photophobia, intolerance to smell (48%), headache (42%), tachycardia and mild hypertension (20%), watery stools (19%), and mild pyrexia (19%). Family history: 64% of patients had at least one relative with migraine (66.6% of whom only matrilinear, 20,6% only non-matrilinear, 12,8% both; $p<0.01$ for matrilinear vs. non-matrilinear). Migraine was reported by 45% of mothers and 12% of fathers. Furthermore, 11.2% of patients had a relative with CVS, which was significantly more represented in matrilinear relatives (83.8%, $p<0.05$).
CONCLUSIONS. In our large cohort of patients CVS is equally frequent in M and F, but the disease occurs earlier in M than F, due to a significant preponderance of M in infancy throughout pre-school age. A severe phenotype of CVS with longer and more frequent attacks can be identified in 20% of patients, in whom a prophylactic treatment is definitely indicated. Vomiting episodes mostly begin at night or in the morning, and are often associated with lethargy, abdominal pain and autonomic manifestations. In over 1/3 of patients there is a severe delay (>4 yr) before a formal diagnosis is established. The prevalence of migraine in mothers of CVS patients is significantly higher than that of the general female population, and migraine and cyclic vomiting are significantly more common in the matrilineage, strongly suggesting a maternal (mitochondrial DNA-related) inheritance of these two historically linked disorders.