CYPROHEPTADINE, PIZOTIFEN AND AMITRYPTILINE AS PROPHYLACTIC THERAPY IN CYCLIC VOMITING SYNDROME

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BACKGROUND AND AIM. Cyclic vomiting syndrome (CVS) is a functional gastrointestinal disorder of unknown origin that causes severe recurrent attacks of intractable nausea and vomiting, and for which no established and effective therapy exists. In the last 2 decades, uncontrolled trials of various anti-migraine agents have demonstrated rates of efficacy of 40% to 90%. The aim of our study was to verify the clinical response to prophylactic therapy with the drugs cyproheptadine (CYP), pizotifen (PIZ) and amitriptyline (AMI) in children with CVS.

MATERIALS AND METHODS. The charts of patients referred to our Unit over the last 10 years for recurrent vomiting and diagnosed as having CVS were retrospectively reviewed. All patients with ≥6 (range 6-20) attacks per year who were subjected to long-term (≥6 months) prophylactic therapy with the anti-HT2/anti-H1 drugs CYP (0.25-0.5 mg/kg/die divided in 2 doses) or PIZ (0.5-1.5 mg/die divided in 1 or 2 doses), or with the tricyclic antidepressant drug AMI (0.5-1.5 mg/kg/die divided in 2 doses) were included. Response to treatment was defined as a ≥50% reduction in the number of acute attacks of vomiting. In those patients who had been treated with different drugs, each drug treatment was considered separately. Side effects leading to treatment withdrawal were also considered. The statistical evaluation was carried out using χ2 test and the difference was considered significant when p<0.05.

RESULTS. Overall 92 treatments were carried out in 66 patients. A positive response to therapy was reported in 49/92 (53.3%) patients, as follows: CYP 26/49 (53%), PIZ 16/30 (53.3%), AMI 7/13 (53.8%). Full remission during the treatment period was achieved in 32/92 (34.8%) patients, namely CYP 19/49 (38.8%), PIZ 8/30 (26.6%), and AMI 5/13 (38.5%). The evaluation of response to first and second treatment showed that 20/66 patients did not respond to the first drug and needed a change in prophylaxis. In 10 of these 20 (50%) a positive response was achieved with the second treatment. No significant association was found between response and age at onset of symptoms, frequency and length of the attacks. On the other hand, a positive response to the first line of treatment was observed more frequently in females than in males: 25/39 females vs. 9/27 males (p<0.05). Significant side effects were reported in 5 (5.4%) cases: 2 sleepiness with CYP and 3 excessive and distressing weight gain with PIZ, all leading to change of treatment.

CONCLUSIONS. Prophylactic therapy with CYP, PIZ and AMI results in significant symptom improvement or resolution in nearly 50% of patients with CVS, with similar efficacy among all drugs and an acceptable rate of moderate side effects. Females appear to have a positive response more often than males, but the reasons are unclear. In case of failure of a first line of therapy, a second drug is often beneficial. Although an uncontrolled evaluation does not allow to quantify the placebo effect of these drugs, a prophylactic therapy is recommended in children with CVS.