Seizures after desipramine in nine years old girl with ADHD syndrome

Drgawki po zastosowaniu dezipraminy u dziewięcioletniej dziewczynki z zespołem ADHD

Piotr Gorczyca¹, Agnieszka Kapinos-Gorczyca¹,
Janusz Kwiecinski², Krystyna Pierzchała², Robert T. Hese¹, Ryszard Brus³,⁴

ABSTRACT

The case of seizures in nine year old girl treated with desipramine (40 mg daily) for half year because of ADHD syndrome was presented.

KEYWORDS

Nine years old girl, ADHD, desipramine, seizures

STRESZCZENIE

Przedstawiono opis drgawek u dziewięcioletniej dziewczynki z zespołem ADHD otrzymującej deziipraminę (40 mg na dobę) przez pół roku.

SŁOWA KLUCZOWE

Dziwiekioletnia dziewczynka, ADHD, desipramina, drgawki

Seizures consequent to treatment with tricyclic antidepressant drugs (TAD) have been observed (1–4), and in fact, desipramine appears to be the most common TAD inducing seizures (5–7). Seizure risk after TAD application is approximately 0.4-2%, a rate much greater than for newer generation antidepressants such as selective-serotonin reuptake inhibitors (SSRIs), bupropion and mirtazapine (<0.4%) (8).

We present the case of seizures in a nine year old girl with attention-deficit-hyperactivity disorder (ADHD) in which seizures occurred subsequent to treatment with dizipramine (DMI; 25 mg/day). Diagnosis of ADHD, DSM-IV-TR classification (American Psychiatry Society, 1994), was made when the child was 7-years old. Some pathological changes in electroencephalogram were recorded, notably central and temporal paroxysmal pik waves following slow waves. After 2-year treatment with imipramine (IMI; 40 mg/day) there was some symptom improvement. However, because of
the relative lack of imipramine in pharmaceutical market in Poland, desipramine (40 mg/day) was substituted. After several months of desipramine therapy a non-drug-related head injury occurred. One week later the girl was hospitalized because of left side body seizures, accompanied by unconsciousness, trismus, paresis of the left side, shallow and acidic respiration, and the absence of pain reaction. Additional examinations showed gazometric abnormalities and leucocytosis (15.0 g/L). During the next 1.5 hr the girl regained consciousness, while left-sided paresis disappeared. However, she was alternatively restless or apathetic. On the next day all pathological symptoms disappeared. Physical examination showed a normal condition, except for the electroencephalographic study which showed sharp but frequent theta waves. Examination by means of tomography and magnetic resonance of the head showed no abnormalities. ADHD is a common but controversial syndrome characterized by developmentally inappropriate hyperactivity, impulsivity, and inattention (9, 10). A high genetic contribution, estimated at 30-35%, has been suggested by family studies and the allelic polymorphism of the gene coding for the dopamine (DA) receptors and the DA transporter protein (11, 12). A number of animal models have been developed to explore neural mechanisms underlying ADHD and treatment possibilities (13–16). Another animal model of ADHD was proposed by Kostrzewa et al. (17), namely perinatal destruction of dopaminergic neurons in rats with 6-hydroxydopamine (neonatally) and adulthood destruction of serotoninergic neurons with 5,7-dihydroxytryptamine. In this model of ADHD Brus et al. (18) presented that desipramine, a monoamine transport inhibitor effectively reduced locomotor time. From this, it was concluded that serotonin neurons are a potentially important therapeutic target for treating human hyperactivity and possibly childhood ADHD (18). For that reason desipramine was used for the ADHD treatment in the presented nine years old girl. It should be added that the subject has a 5-years-older sister with ADHD, who had been successfully treated with imipramine and valproic acid. However, that treatment was discontinued because of an adverse effect (baldness), being replaced by desipramine which has been successful and without adverse effect. Although imipramine is a popular drug for ADHD treatment experimentally and in the clinic, the risk of seizures should be taken into account. In animal testing both IMI and amitryptiline (AMI) have been shown to produce dose-related seizures (19). However, this has not been reported for DMI (20). Moreover in the case of DMI, in contrast to IMI and AMI, no activities preventing post-electrical shock seizures were observed in mice (20). The seizure preventive activity of AMI and IMI may have concerned on absence attacks, even though the seizure-genitive activity was observed for large fits (20). Others also have presented advantageous effects of acute injections of antidepressants in hippocampal experimental seizures (21). On the other hand chronic application of antidepressants enhanced electroconvulsions in rats (22), and diminished experimental seizures after flurothyl application to mice (23). Lidocaine-induced convulsion in experimental animals were also diminished by DMI (24). The negative effects of DMI on EEG recorded in the rats with spontaneous petit mal-like seizures was also presented (25). In contrast to AMI and IMI, DMI also did not influence concentration of valproic acid. AMI and IMI strengthened the seizure-preventive activity of valproinian which was not corralled in relation to the MMDA receptor (20). It also must be remembered that the anti-muscarine activity of TADs may be responsible for the strengthened activity of valproinians. Another mechanism of seizure-genitive activity may be the inhibition of GIRK canals through TADs and in the question of DMI has a larger percentage of the inhibition than IMI (26). In the Luchins et al. (27) in vitro tests IMI had a larger epilepsy-genitive activity on an animal model than DMI. In the Malatynska et al. [28] in vitro tests DMI shows the most profitable profile connected with the weaker inhibition of the chloride canals and the smaller frequency of occurrence of seizures in an animal model. Pindea and Russell in clinical study (29) presented theirs observation concern advantageous effects of DMI in the patients with depression and epilepsy. With the report here we wish to focus on the need of being careful in the prescription of DMI in the treatment of children with ADHD, even if they had been treated earlier with medications inside the TADs group without any
side effects, especially when in the interview there is data on fever seizures having taken place, which can precede epilepsy in 13% of the population ill with it (30).

PISMIENNICTWO: