Tetanic crisis and antiepileptic drugs. A case report.

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Abstract

OBJECTIVE AND METHODS: We presented a rare case of tetanic crisis in a 23-year old mentally retarded woman with epilepsy after treatment by oxcarbazepine, the new anticonvulsant agent. We reviewed laboratory, radiographic and medical examinations and recommend a proper treatment in such cases.
RESULTS AND CONCLUSION: The laboratory tests revealed only severe hypocalcemia. We described the potential role of oxcarbazepine in the induction of activity of cytochrom P 450 system of hepar and increases of less active metabolin of vitamin D. Supplementation of vitamin D and calcium in patients taking antiepileptic drugs is in the same case crucial.

Abbereviations
OXC – oxcarbazepine

Introduction

Epilepsy is a common disease. In the USA about 2 mln people have epilepsy [1]. The implementation of new anticonvulsant drugs has enabled this illness to be controlled, including the reduction in frequency of tonic-clonic seizures and partial seizures and reduction of occurrence of adverse events at the same time, and, as a consequence, better tolerance of applied pharmacotherapy [2]. One of the new antiepileptic drugs is oxcarbazepine (OXC) which derives from commonly used carbamazepine. The mechanism of the action of OXC hasn't been well known. It is assumed, that depending on its potential, this drug blocks sodium channels and calcium channels in cortical and striatal neurons. In comparison to carbamazepine it is less biotransformed by the cytochrome P 450 system of hepar and after glucoronidation it is excreted mainly by kidneys. Side effects such as dizziness, headache, diplopia, ataxia, nausea and vomiting are less noticed than during using carbamazepine. OXC can cause occurrence of electrolyte balance disturbance – first of all, hyponatremia. Kayemb Kay's et al. [6] have shown that using carbamazepine and vigabatin during pregnancy, induces a significant decrease of calcium concentration in serum in newborns. The occurrence of hypocalcemia led to opisthotonos, nausea and vomiting. The administration of calcium and vitamin D had the effect of complete subsidence of these symptoms. Describing our case we would like to draw attention to the possibility of the existence of severe and symptomatic hypocalcemia during the use of OXC. Moreover, we think that it is important to highlight that the administration of vitamin D and calcium is a very effective treatment of such patients.

CASE REPORT

Case report

A 23-year-old woman with oligophrenia and epilepsy since her childhood was admitted to the District Hospital complaining of nausea, vomiting (vomiting was a few times a week, usually after eating) and mild pain in the lower abdomen. The interview was difficult not only because of her mental handicap but also because of her parent's handicap. The information was mainly given by her own neurologist. According to this information, it appeared that the patient was taking orally 600mg per day oxcarbazepine (Trileptal, Novartis Pharma) for 4 months. Before that she was treated irregularly using mainly carbamazepine, which she had stopped taking about one year before present therapy. On admission, physical examination revealed normal heart rate, blood pressure was 14,63/9,31 kPa and very little tenderness and pain on the lower part of the abdomen wall. Laboratory tests revealed the following values: serum calcium – 1.4, 1.52, 1.65 mmol/l (2.15–2.55), parathyroid hormone – 29.20 pg/ml (12–72), alkaline phosphatase – 1.85, 2.42 ukat/l (< 4.5), serum phosphate – 1.32 mmol/l (0.87–1.45). The daily excretion of calcium and phosphate were 6.02 mmol/l (2.5–8.0) and 5.72 mmol/l (11–32) respectively. Other biochemical tests including urea, liver and renal function tests, serum concentration of sodium, potassium, chlorine, magnesium, magnesium in the blood, triiodothyronine (FT3), TSH, thyroxine (FT4), blood gas analysis were within normal limits. These designations were done when the patient was on a low-calorie diet with a limited amount of sodium. She was also examined with: X-rays of chest and bones of feet and hands, ECG, ultrasonography of abdomen, thyroid, heart and gastroscopy. These examinations revealed mild gastritis and an ovarian cyst with a diameter 5 cm to 6 cm. During the patient's stay at the hospital symmetrical, tonic seizures were observed about 2–3 times a day, which was typical for a tetanic crisis. These attacks lasted 20 to 30 minutes, but the patient was conscious all the time. The attacks subsided after intravenous administration of 10 ml calcium glubionate (Calcium Pliva, Pliva Kraków, PL). Several times tetanic turned into typical tonic – clonic epilepsy stopped by intravenous 10 mg diazepam (Relanium, Medana Pharma Trepol Group). Because of such a process of disease, she was treated with 0,25 ug/day vitamin D (Kalcytrol, Instytut Farmaceutyczny, PL) and 600mg/day calcium gluconate (Calcium300, Pharmavit, PL). The cyst of the ovary was removed by operation. The patient's condition after the operation was without any complication and tetanilla weren't noticed. According to one-month out-patients observation the patient is in good condition, with no experience of a seizures. She takes vitamin D, calcium and oxcarbazepine, her serum and urine calcium is within normal limits.

Discussion

The influence of anticonvulsant drugs, among others phenobarbital, phenytoin, vigabatrin and also carbamazepine with a concentration of calcium in the serum is quite well-known. Hypocalcemia which is very rare in those cases, comes from the increase of metabolin of vitamin D as a result of the induction of activity of hepatic microsomal enzymes. In the hepar vitamin D is converted to a compound of medium activity of 25 hydroxyvitamin D (25-OH-D3). The increased production of less active metabolin vitamin D, as well as the increase of the excretion of gall with 1,25-dihydroxyvitamin D, metabolin which is said to be the most active kind of it, can cause serious disorders of calcium balance in people treated with anticonvulsant agents [6,7]. In the process of epilepsy, regardless of the form of treatment, there is an increase of concentration of potassium (K+) and chlorine (Cl-) and decrease in concentration of calcium (Ca+) strictly before the seizure. Then, the increase in the high concentration of serum citrate, connected with stress, sometimes may intensify the current hypocalcemia [8]. In the case which we described, except from the decreased level of calcium, the concentration of the rest of the ions were within normal range. We also didn't notice hyponatriemia – typical for OXZ. The blood gas analysis were correct. Moreover, we excluded hypoparathyroidism, as a possible cause. The serum concentration of parathyroid hormone, phosphate and urinary calcium and phosphate excretion were correct. There were not any osteodystrophy in the bones of hands and feet which could suggest pseudohypoparathyroidism. That's why we assumed that hypocalcemia was mainly caused by OXZ. As a matter of fact, OXZ is little metabolized by the cytochrome P 450 system of hepar, but when there are proper circumstances which influence the decrease of the level of calcium, its activity which stimulates the change of vitamin D to less active metabolin, may cause the appearance of tetany. According to Ali's et al [1] work we assume that those favorable circumstances in the mentally retarded are: physical inactivity, reduced exposure to sunlight and a low calcium diet. It seems that because of rather mild gastritis and quite a mild ovarian cyst, disorders of absorption of vitamin D and calcium were not so important. Besides, as the laboratory test revealed, the role of vomiting concomitant with the diseases was not big. Reporting that case, we wanted to pay attention to the possibility of the occurrence of severe symptomatic hypocalcemia after treatment with OXZ, when the concomitan ilnesses predispose to electrolyte disorders. Moreover, it seems to us that the supplementation of calcium and vitamin D is effective during treatment of such patients.

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