Topiramate: Is it More Than Prophylaxis of Migraine? From Neurological to Gynecological Indications

Migren Profilaksisinden Daha Fazlası mı? Nörolojik Endikasyonlardan Jinekolojik Endikasyonlara

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Abstract

Topiramate is an anticonvulsant indicated for the treatment of epilepsy and migraine. More recently, it has been used for weight loss with significant success in some populations who have other indications, such as seizure disorders, in addition to obesity, but has not been reported in female patient with PCOS. I present a case of migraine patient whose PCOS symptoms (amenorrhoea, obesity) improved with topiramate. *Turk Jem 2009; 13: 29-30*

Key words: Topiramate, PCOS, weight loss

Özet

Topiramat bir antikonvulzan olarak epilepsi ve migren tedavisinde endikedir. Yakın zamanda nöbet sorunu olan obez hasta gruplarında kilo kaybı amacıyla başarıyla kullanılmıştır. Fakat polikistik overli kadın hastada kullanımı henüz bildirilmemiştir. Migrenli, topiramat kullanıyla polikistik over semptomları (amenore, obezite) düzelen bir vaka sunulmaktadır. *Türk Jem 2009; 13: 29-30*

Anahtar kelimeler: Topiramat, Polikistik over, kilo kaybı

Case Study

I present a 35-year-old woman with migraine who had 4 attacks per month. She was treated with topiramate as a prophylactic treatment, 25 mg nightly and the dose was titrated up to 50 mg two times daily (BID) over 4 weeks. At follow -up, after 3 months of receiving topiramate, she noted improvement in her migraine. She also noted weight reduction (her previous trials to reduce her weight failed) and had menstruation after 7 months of amenorrhoea; she reported that she was diagnosed as having PCOS when she was 29 years old and she did not take any other medication during topiramate therapy.

Discussion

The precise mechanism of action of topiramate as an anticonvulsant is not known. However, studies have shown that topiramate blocks the action potentials elicited repetitively by a sustained depolarization of the neurons in a time-dependent manner, suggesting a state-dependent sodium channel blocking action. Topiramate also augments the activity of the neurotransmitter gamma-aminobutyrate (GABA) at some subtypes of the GABAA receptor. Topiramate also demonstrates antagonism of the AMPA/kainate subtype of the glutamate excitatory amino acid receptor. It also inhibits carbonic anhydrase (1).

The exact mechanism of action regarding weight loss has not been delineated. However, several mechanisms have been proposed, including: 1) energy expenditure elevations in the face of reduced caloric intake secondary to anorexia; 2) reduction in the activity of salivary enzymes, which are partially responsible for taste; 3) reduction in leptin and corticosteroid concentrations; and (4) reduction in serum glucose and insulin concentrations (2).

Polycystic ovarian syndrome (PCOS) is an extremely common disorder affecting 4% to 12% of women of reproductive age (3). Despite being heterogeneous in nature, the hallmarks of the disease are hyperandrogenism or chronic anovulation in the absence of specific pituitary and/or adrenal disease. Chronic anovulation often presents as oligomenorrhea, amenorrhea,

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dysfunctional uterine bleeding, and/or infertility. Other women may only develop menstrual problems later in life, perhaps after significant weight gain (4).

Recent insights into the pathophysiology of PCOS have shown insulin resistance (IR) to play a substantial role and as such have brought the long-term issues of type 2 diabetes mellitus (5). When clinically evaluating a patient for the possibility of PCOS, it is also important to search for signs of IR. Upper-body obesity is a key component of the IR syndrome (6). Many PCOS patients had a 31% rate of impaired glucose tolerance and 7.5% met the criteria for type 2 diabetes mellitus (7).

Because of the central role IR plays in PCOS, it is understandable that improving insulin sensitivity can restore normal menstrual function. This might be looked at as treating the "root cause" of the problem rather than simply using oral contraceptives to regulate the cycles (8).

Much has been done to evaluate the effects of insulin sensitizers in this regard. Metformin is perhaps the most widely studied agent (9).

Weight loss itself can reduce hyperinsulinemia and subsequently hyperandrogenism result in improvement in menses. Kiddy et al. (10) showed improvement in menstrual function in 9 of 11 patients (82%) with oligomenorrhea who lost >5% initial body weight (range 5.9 to 22%) on a 1000 kcal/day, low-fat diet over 6 to 7 months.

As topiramate therapy can reduce weight and increase insulin sensitivity, it is unsurprising that my case showed improvement in her menstrual function. Is it reasonable to address researches to examine the consequence of topiramate use on PCOS patients?

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