Topiramate and its Use in the Therapy of Epilepsy in the Elderly

a report by
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Introduction

Epilepsy in the elderly is defined as first onset of epileptic seizures in patients from the age of 60[1,2] or, according to other authors, from the age of 65,[3,4] respectively. It has been established that approximately one-third of patients with newly diagnosed epilepsy are older than 60 years and also half of all adult patients with known epilepsy are beyond an age of 60.[5] The symptomatic focal epilepsy is the most frequently diagnosed type. Main causes are strokes[6,7] followed by brain tumours[4] and degenerative diseases of the brain.[2] Regarding anticonvulsant therapy, physicians have to be aware of differences in the therapy of older patients. The brain of the elderly patient has a high sensitivity to centrally acting medication which may lead to fatigue and somnolence as well as cognitive side effects even at a low dose. Furthermore, physicians should be aware of a reduction in renal clearance and impaired hepatic metabolism of anti-epileptic drugs in the elderly. In addition, many patients of advanced age are suffering from chronic diseases requiring extensive non-anticonvulsant co-medication that can cause significant drug interactions. Therefore, an anti-epileptic drug used in the elderly patient ideally should have a low potential for cognitive impairment, an adequate clearance despite reduced metabolism and a low possibility for drug–drug interaction. Furthermore, the anticonvulsant used should be effective as monotherapy.

Taking these considerations into account, it is surprising that carbamazepine is still the most widely prescribed anti-epileptic drug in the German-speaking area, despite the advantages of recently approved anticonvulsant drugs. There are several studies investigating the efficacy or efficacy respectively of new anticonvulsants such as gabapentin, lamotrigine, levetiracetam, oxcarb-azepine, tiagabine, topiramate and zonisamide in the epilepsy of the elderly.[8–18] Unfortunately only two of these are randomized, controlled, double-blind studies.[8,9] The aim of this report is to discuss the significance of topiramate in the therapy of epilepsy in the elderly.

Efficacy

In general, topiramate has advantages over previously established anticonvulsant drugs. A prospective, randomised double-blind study conducted by Privitera et al.[19] investigated the efficacy of topiramate 100mg or 200mg/per day compared with carbamazepine 600mg/day and valproic acid 1250mg/day in patients aged six and above. Prior to randomisation, in accordance to current clinical practice, patients with focal epilepsy were assigned to the carbamazepine arm and patients with generalised epilepsy to the valproic acid arm. In this study 10% (62 out of 621 patients) of the participants were older than 65 years. The results show a similar efficacy of topiramate compared to carbamazepine or valproic acid, however higher retention in the study.

Other studies investigating the effectiveness of topiramate in the elderly were conducted as open-label studies and revealed variable seizure-free rates for patients treated. Mehta et al.[13] reported a seizure-free rate of 41.2% in 34 patients older than 60 years with newly diagnosed or previously treated focal epilepsy following a topiramate monotherapy (50–100mg daily) during six months of treatment. In the study conducted by Mauri,[14] seizure-free rates of 90% in patients suffering from focal or generalised epilepsy while on topiramate monotherapy for six months were reported. Patients included were older than 65 years; the mean daily topiramate dose was 91mg. Two other studies by Groselj et al.[15] and Stefan et al.[16] included patients with previously treated or untreated focal or generalised epilepsy. In the study of Groselj et al. 64 % of patients remained seizure-free during the seven-month study while on topiramate monotherapy (mean dosage 121mg, range 50–450mg daily). Stefan et al. treated elderly patients (mean age 69 years) for 12 months in combination or monotherapy of topiramate. Fifty-six of 107 patients (52%) were seizure-free at the end of the study and 44% remained seizure-free throughout. The effective topiramate dosage was 98 + 50mg for topiramate monotherapy and 153 + 87mg for add-on therapy. In our study[17] we evaluated the effectiveness of topiramate in patients older than 65 years with newly diagnosed focal or generalised epilepsy.

patients older than 65 years with newly diagnosed focal or generalised epilepsy. Topiramate was prescribed for six months with a mean daily dose of 95mg (range 25–400mg). At the end of the study 42.7% of the patients remained seizure-free for at least six months.

Tolerability

Based on the low reported number of patients withdrawing from clinical trials and studies with naturalistic designs, due to adverse events (AEs), topiramate has a good tolerability up to the mid dosage range. Withdrawal rates due to AEs while on topiramate were 14%[15] for monotherapy and 15.9%[16] as add-on therapy during open label studies. These rates compare well to published rates in the elderly for lamotrigine (12.1–20%)[8,9], levetiracetam (19%)[10] and gabapentin (21.6%)[8], and are lower than rates reported for oxcarbacepine (27%)[11] and carbamazepine (31–50%).[8,9] The most common AEs reported for topiramate were paresthesia, dizziness, nausea, loss of appetite, depression, difficulty with memory, weight decrease, localised numbness, insomnia and palpitations. All AEs improved following dose reduction or withdrawal of medication.

Recommendation for Practice

According to available data and the author's own clinical experience, topiramate is a broad-spectrum, well-tolerated AED effective in the treatment of focal or generalised epilepsy in the elderly. Even at a low daily dosage of 25–100mg it is effective in most patients. At this point, no randomised, double-blind controlled trials in the elderly using topiramate have been conducted, therefore there is no class I or II evidence available to support this recommendation further. ■

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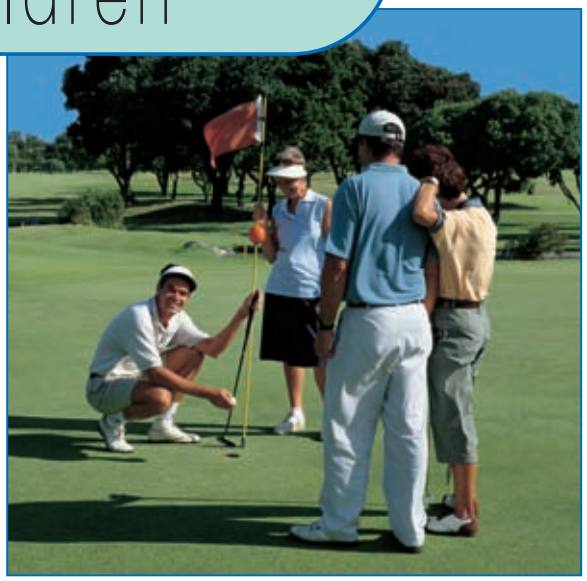
Broad-spectrum efficacy in adults and children



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