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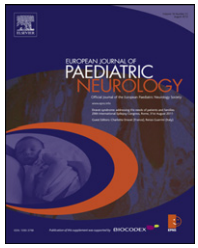

Original article

Comparison of flunarizine and topiramate for the prophylaxis of pediatric migraines

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ABSTRACT

The purpose of this study was to compare the efficacy and tolerability of topiramate and flunarizine for the prophylaxis of pediatric migraines. A retrospective medical-record review of patients who underwent prophylaxis after receiving a diagnosis of migraine with aura and without aura was performed. Only patients who completed at least 3 months of treatment were included in the analysis. Response to treatment was assessed as the total number of headache days/month. Patients with more than 50% reduction in headache days/month were classified as responders. Responder rate, retention rate, and adverse-event rates were also calculated from all patients who started on the prophylaxis. Further analyses were performed using different patient groups with a cut-off age of 12 years. The responder rate was 80% (89/111 patients) for flunarizine and 81% (122/150 patients) for topiramate, based on a comparison among 261 patients. The retention rate was 67% for flunarizine and 63% for topiramate and the adverse-event rate was 6% for flunarizine and 10% for topiramate. The responder rate, the retention rate, and the adverse-event rate were not significantly different between flunarizine and topiramate. These findings were concordant between the preadolescent (6–12 years old) and adolescent (13–18 years old) groups. The efficacy and tolerability of topiramate were not inferior to those of flunarizine for the prophylaxis of pediatric migraines. These findings were observed in preadolescent and adolescent patients.

1. Introduction

Migraines are a common neurological disorder that can significantly impair the quality of life of pediatric patients. The prevalence of migraines in the pediatric population ranges from 3 to 15%, depending on the study population and design.[1–4] It is also common in Korean pediatric populations, with an estimated prevalence of 8.7%.[5] Patients with migraines commonly experience worsening of headaches with routine daily activities and the migraine headaches themselves significantly interfere with the daily activities of patients. Impairment of quality of life, such as absence from

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school, is more common in patients with frequent or severe migraine attacks. Indication for prophylactic treatment was proposed in previous studies, which usually included patients with frequent migraine attacks (more than one or two attacks/week) or severe disabling attacks.[6,7]

Preventive treatment with flunarizine (FNZ) is safe and effective in pediatric patients with migraine[8] and was recommended as a probable effective treatment in the American Academy of Neurology (AAN) practice parameter in 2004.[9] Randomized, double-blind, placebo-controlled trials of topiramate (TPM) also resulted in successful prevention of pediatric migraines.[10,11] However, no study has compared TPM with FNZ as a prophylactic treatment of pediatric migraines in real clinical practice settings. The purpose of this study was to perform a comparison of TPM and FNZ in a large number of patients with pediatric migraines from a single center. A comparison of efficacy and tolerability was also performed in different age subgroups of patients with migraine (preadolescents and adolescents).

2. Materials and methods

This study was approved by the Institutional Review Board of the Seoul National University Hospital. An electronic medical record database search was performed using a clinical data warehouse program. Patients diagnosed with migraines and treated with either TPM or FNZ at the Seoul National University Children's Hospital (SNUCH) and Seoul National University Bundang Hospital (SNUBH) from January 2005 to December 2011 were identified. The diagnosis of migraine was established based on the International Headache Society 2004 Classification[12] after detailed history taking of headache characteristics, disease course, and physical and neurological examinations by pediatric neurologists (HH and YSH). Indications for prophylactic treatment included frequent headaches (more than 10 headache days/month) and frequent prolonged migraine attacks that severely limited daily activities, such as school attendance. Selection and dose adjustment of the specific prophylactic agent were made based on the discretion of the treating physician. After the initiation of prophylactic treatment, patients were evaluated monthly at the pediatric neurology clinic. They were told to keep a headache diary, and the response to treatment was assessed based on the diary regarding headache days/month. Patients were also told to record any adverse events, which were also assessed at the follow-up visit. The starting dose of TPM was 1 mg/kg/day, taken once and at night. An increase in the dosage was decided after at least 1 month of treatment. The starting dose of FNZ was 5 mg/day, once and at night, and the decision to increase the dose was also made after 1 month of treatment.

After the database search, the medical records were reviewed and only the patients with migraines with aura or migraines without aura were included in the analysis. Clinical information regarding sex, age at onset, age at diagnosis and treatment, pre- and post-treatment headache days/month, decrement of headache days after the treatment for each patient, duration of treatment, reasons for withdrawal, and any adverse events were retrieved. Detailed information regarding continuation or discontinuation of treatment was retrieved to analyze the outcome of initiation of the prophylactic treatment in all patients. The outcomes of the initiation of treatment were classified as: (1) continuation of the medication for longer than 3 months, (2) self-withdrawal because of drug inefficacy, (3) withdrawal because of adverse events, and (4) withdrawal without any specific reasons.

To maximize the comparability among the different treatment groups, only the patients who completed at least 3 months of treatment with good compliance and had a period of at least 1 month of post-treatment outcome evaluation were included in the comparison. Response to prophylaxis was categorized as headache free, ≥50% decrease in headache days/month, <50% decrease in monthly headache days, and no improvement. Patients who were headache free and with a ≥50% decrease in headache days/month were considered as responders and the remaining patients were classified as nonresponders for statistical analysis. The rate of adverse events and their profile were also compared. To identify differences in efficacy and tolerability in the different age groups, an additional analysis was performed after dividing the patients according to age at the time of treatment (6–12 years for the preadolescent group and 13–18 years for the adolescent group).

Statistical analysis was performed using SPSS 18.0 for Windows. To compare patient characteristics, Student's t test was used for continuous variables. Pearson's χ^2 test and Fisher's exact test were used for the analysis of discrete variables based on sample size. Statistical significance was set at $P < 0.05$.

3. Results

A total of 475 pediatric patients (206 males and 269 females) who were treated prophylactically with either FNZ or TPM at SNUCH and SNUBH were identified after a search and review of electronic medical records. FNZ was prescribed to 212 patients (99 males and 113 females) and TPM was prescribed to 263 patients (107 males and 156 females). The distribution of each prophylactic agent in each age group is shown in Fig. 1. Forty-six patients from the FNZ group and 24 patients from the TPM group were lost in the follow-up. In the FNZ group, 67% (111/166) of patients were on medication longer than 3

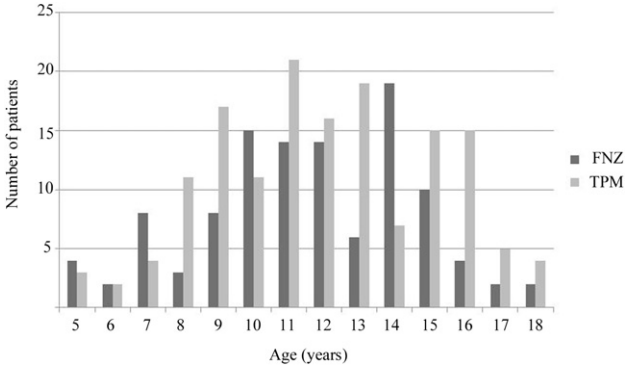

Fig 1 – Age distribution of patients in the FNZ and TPM group.