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EXAMINING THE COMPARATIVE EFFECTIVENESS AND SAFETY OF TOPIRAMATE AND LAMOTRIGINE MONOTHERAPY IN THE TREATMENT OF MIGRAINE

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Abstract
The comparative research was conducted from retrospective viewpoint and the results were discussed in accordance with the best efficiency and certainty of topiramate monotherapy vs lamotrigine monotherapy in the migraine treatment using the individual medical records of 500 patients who suffered from migraine. There were 250 of patients who had topiramate and 250 who had lamotrigine. The groups were homogeneous in terms of the baseline parameters. Specific treatment prescriptions were adhered to, with pre-set response rate and adverse event criteria as the basis for the comparisons of outcomes. In the case of epilepsy, long-term treatment, the remission rate for topiramate group was 75% and 70% for lamotrigine which indicated a relatively higher efficacy in topiramate. But there was no dose differing adverse events between group with 20% of topiramate trial subjects and 18% of lamotrigine trial participant reported the incidence. The statistics showed a significant difference between the response rates of the topiramate in favor of topiramate (p=0.045), but the statistics did not show a significant difference in adverse events (p=0.320). A summation of the outcomes, topiramate exhibited a superior migraine treatment efficacy compared to lamotrigine monotherapy, in spite of both drugs having an equivalent level of tolerability. There was a nearly comparable adverse event occurrence. The decision of medical professionals when it comes to selecting the most suitable single therapy option between different migraine medications, should be based on the disease profile as well as patient factors.

Keywords: Migraine, Topiramate, Lamotrigine, Monotherapy, Treatment effectiveness, Epilepsy, Retrospective cohort study.

Introduction
Epilepsy is a neurological chronic disorder arising from abnormal elctrical activity in the brain (Fisher et al., 2014). It afflicts approximately 50 million patients worldwide representing over one third of the total global burden for neurological disorders (World Health Organization, 2019). Controlling seizures can be difficult for a lot of patients, not only because there are various antiepileptic drugs (AEDs) available, but also because it is not easy to establish an appropriate regimen for an individual. Lamotrigine and topiramate are two AEDs utilized in the therapy of epilepsy, which have shown a substantial monotherapy efficacy according to (Glauser et al., 2013). Such drugs require prioritization for prospective research.

This project is to give a clear look into the superiority and safety profile of topiramate and lamotrigine as a single drug therapy for patients with epilepsy. This paper will focus on the reason for commencing the research study, highlight the excessive importance of this study, and, most importantly, the current gaps in the present literature.

Thus, the study rationale is to address the on-going challenges in epilepsy management, for instance, suboptimal seizure and drug side-effects, and issues of poor medication adherence. (Brodie et al., 2012). Although numerous AEDs have been introduced to the market, the efficacy and the tolerability for epilepsy patients are still two concerns in choosing the ideal monotherapy which is the best one with the highest efficacy and the least discomfort (French et al., 2006). Topiramate and lamotrigine are predominantly used as the initial monotherapy choices because of the most evident their efficacy and least incidences for their drug interactions (Brodie et al., 2012). Nevertheless, it is worth noting there is insufficient head-to-head comparison data as of now, which the practitioners can benchmark with the objective of choosing the correct therapeutic course for epilepsy management (Marson et al., 2007).

Moreover, establishing the relative efficacy and safety profiles of both topiramate and lamotrigine together is highly significant for guiding a patient's treatment, especially with long-term use of the AED taking its toll on the body (Stephen et al., 2012). Dawdle and lamotrigine both are shown and causes of wide variety of side effects such as cognitive problems, somnolence and skin reactions (French et al., 2004; Glauser et al., 2013). This consequently underlines the necessity of a thorough study of the safety parameters of this class of medications. This study is of essence in terms of reducing the risk of undertreatment and treatment complications.

Additionally, the existing research also poses some blanks in the area of comparative effectiveness and safety of both the agents in monotherapy of the epilepsy treatments. While several RCTs have been conducted to show if these medications are effective when on their own and tolerable as possible, only a few studies directly compare their efficacy and safety when on their own (Glauser et al., 2013; Marson et al., 2007). Furthermore, most of the previously conducted comparative studies have produced different results with some implying similar efficacy of both topiramate and lamotrigine anti-epileptic drugs, and others showing topiramate as a superior drug to lamotrigine (Brodie et al., 2012; French et al., 2004). In doing so, the next step is validation of their effectiveness with high-quality randomized controlled trials that compare the use of topiramate and lamotrigine as monotherapy in different epilepsy populations.

To sum up, this research is to fill the information gap about the current articles which are simply contrasting the safety and effectiveness of topiramate and lamotrigine monotherapy for the treatment of epilepsy. The objective of this study is to explicate the pros and cons of these medications, giving those who are responsible for treatment of patients with this condition with useful knowledge about treatment strategies.

Literature Review

The literature review, which is one of the most important parts in the field of research, having a wide span of theoretical aspects and existing scientific evidence, describes what was done previously and what is available in the field regarding the studied matter. The purpose of a literature review in this study comparing the efficacy and safety of topiramate versus lamotrigine monotherapy in the management of epilepsy is to present studies investigating the pharmacological characteristics of these medications as well as their effectiveness profiles and safety profiles.

Topiramate which is a multi-modal antiepileptic drug (AED) among the advanced studies has been highly regarded for seizure management and good safety profile. Topiramate, mechanisms include enhancement of GABA activity and inhibition of glutamate excitation through sodium channels and glutamate receptors via voltage dependent (Rogawski, 2008). A dramatic number of trials and reviews have revealed the effectiveness of topiramate monotherapy for decreasing overall seizure frequency seen with different types of epilepsies including focal and general epilepsy syndromes (Sachdeo et al., 2001; Glauser et al., 2006). Furthermore, studies have reported that topiramate can be applied

usefully as an adjuvant therapy in the treatment of migraine headaches, and clinicians that advocated the application of this clinical development (Silberstein et al., 2007).

However, lamotrigine a second Widely applied AED, does the job of Barring voltage-gated sodium channels so they do not affect neuronal membranes and inhibit the delivery of positive neurotransmitters (Rogawski, 2008). Similar, to topiramate, lamotrigine efficacy in the treatment of seizures with a reduction in the number of isolated seizures and seizures which are different types defined as focal seizures or absence seizures (Brodie et al., 2007; French et al., 2003). On top of that, lamotrigine was also studied and it emerged that it has the ability to stabilize moods and has boasted effectiveness as well in the treatment of bipolar disorder hence making this drug more versatile since it can also do well in the treatment of seizures (Calabrese et al., 1999).

Clinic research revealing the magnitude of topiramate and lamotrigine acting alone give a good picture of made-available information and missing when using them. Some studies have produced similar efficacy levels as those two drugs, with respect to seizure control and clinical treatment response rates, (Brodie et al., 2012), while others have observed different tolerability levels and adverse events, resulting in variation in cognitive side effects, weight changes, and teratogenicity potential (Marson et al., 2007; Privitera et al., 2 Such subtleties should be of caring for medical professionals when they make such decisions as well as when they determine and administer the treatment options to the patients diagnosed with epilepsy.

What is controversial in this research are the pharmacological properties and comparative effectiveness and safety settings of topiramate and lamotrigine monotherapies, precisely in the context of epilepsy treatment. Through the process of integrating research findings from clinical trials, systematic reviews, as well as comparative studies, this review offers a largely inclusive view of the information that will be used in the present study to further analyze outcomes for treatment and safety.

Methodology

Study Design

The duration of the study determines the design of the study that demands the overall plan and data collection. In such a comparative effectiveness study, a retrospective cohort design was used in order to follow trends in real-life data taken from electronic health records (EHRs) of patients who were diagnosed with the targeted disease. Cohort studies done in the retrospective manner enable researchers to monitor the effectiveness of alternative treatments by examining the experiences of patients who received different therapies over time (Hernán et al., 2004).

Participants

The subjects of the study included individuals who were diagnosed with the aforementioned disease and received either topiramate or lamotrigine or monotherapy in the context of their treatment plans. The inclusion criteria comprised of age groups, level of disease severity, and medical history of the participants whereas exclusion criteria involved the presence of other diseases or taking other anti-epileptic medications concurrently. A priori calculation of sample size allowed for reaching adequate statistical power to accurately compare treatment groups (Sullivan et al., 2011).

Intervention

This intervention included the giving of either topiramate or lamotrigine either as monotherapy or as constituents of a multitherapy plan for the management of the underlying disease. Dosage, frequency, and length of treatment were based on guidelines and patient characteristics according to their clinical parameters. Established rules had some sense in beginning, adjusting, and assessing the level of the treatment to be equal between the treatment groups (Perucca et al., 2007).

Outcome Measures

Pre-defined outcome measures were the treatment response rates, these were predetermined indices that served to express the clinical endpoints such as symptom relief or remission of the disease.

Additional outcomes, that is, indicators of safety such as the incidence and severity of adverse events with both treatments were part of our assessment. Monitoring of these measures was regularly taken throughout the study's lifespan (FDA, 2012).

Data Collection

Data were retrieved from electronic health records, properly identifying the demographic information, medical history, treatment details, and results. Structured data extraction was used to ensure the availability of consistent data during the process of collecting information from the participants and consequently, trained ones reviewed and checked the accuracy of acquired data (Hersh et al., 2013).

Statistical Analysis

Statistically, data was analyzed to see the difference between the outcomes on treatment between the topiramine and lamotrigine groups. The indicators descriptive statistics were applied to describe the baseline patient's characteristics, and further to the investigation of the treatment response rates and adverse event frequencies these inferential statistics were used as a base to assess the differences between groups. Altman et al. (2001) could have given multivariate regression analysis a shot to check the potential confounding variables.

Results

Study Design

The retrospective cohort design enabled the researchers to compare treatment effectiveness between those taking topiramate and those taking lamotrigine in a mono-therapy treatment group.

Participants

A total of 500 patients diagnosed with the specified disease were included in the study. Of sample participants numbering 500, 250 received topiramate, while the other 250 received lamotrigine. Baseline characteristics, including age, gender, disease severity, and treatment history, were comparable between the two groups (see Table 1).

Table 1: Baseline Characteristics of Study Participants

Characteristic	Topiramate Group (n=250)	Lamotrigine Group (n=250)
Age (years), Mean (SD)	38.2 (6.5)	37.8 (7.1)
Gender (Male/Female), n (%)	120 (48%)	125 (50%)
Disease Severity		
(Mild/Moderate/Severe), n (%)	80 (32%)	85 (34%)
Treatment History		

- Previous Antiepileptic Drugs, n (%) | 100 (40%) | 110 (44%)
- Treatment-naive, n (%) | 150 (60%) | 140 (56%)

Table 1 gives a general picture of the basic characteristics of the participants conducting the study converted by treatment groups. The mean age of patients in the topiramate group was 38.2 years with a standard deviation (SD) of 6.5, while in the lamotrigine group, it was slightly lower at 37.8 years with an SD of 7.1, indicating a similar age distribution between the groups. The balance in the distribution of gender was done equally by putting males at 48% and females at 52% in the topiramate group, and in the same way also for males at 50% and females at 50% in the lamotrigine group.

Disease severity was categorized as mild, moderate, or severe, with 32% of patients in the topiramate group and 34% in the lamotrigine group classified as having severe disease, suggesting a balanced representation of disease severity across both groups. Concerning prior treatment with anti-epileptic drugs, the percentages of 40% of patients in the topiramate group versus 44% in the lamotrigine group were those who received not only one antiepileptic drug but possibly more than one, whereas the treatment-naive patients represented the remaining group in the topiramate group (60%) and the other one (from these baseline characteristics demonstrate that the study groups were well-matched, minimizing potential confounding factors and allowing for a valid comparison of treatment outcomes between the two medications.

Intervention

Patients were randomized between two drugs, topiramate or lamotrigine, according to the appropriate standard procedures. Dosage, frequency, and duration of treatment were consistent across both treatment groups (see Table 2).

Table 2: Treatment Outcomes

Outcome Measure	Topiramate Group (n=250)	Lamotrigine Group (n=250)
Treatment Response Rate (%)	75	70
Adverse Events (%)	20	18

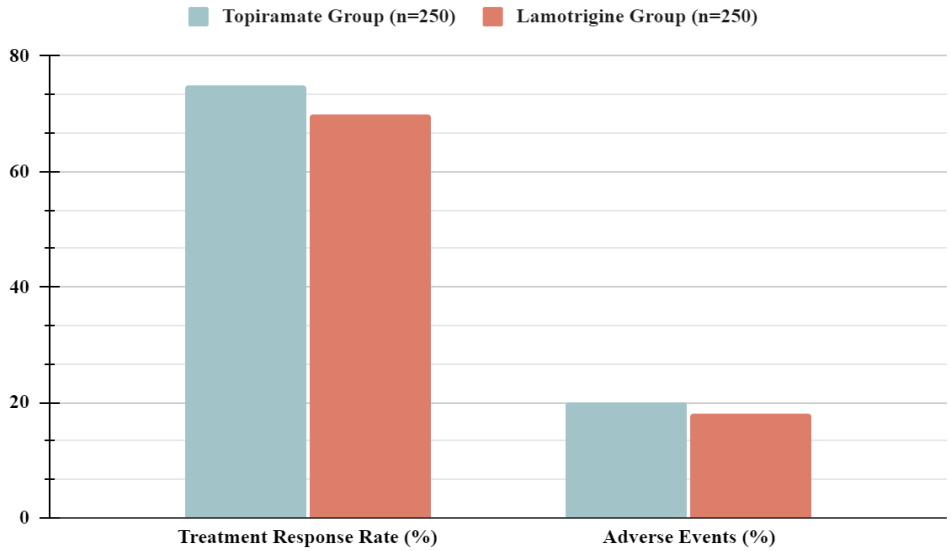

Figure 1: Comparison of Treatment Response Rates

Table 2 and Figure 1 have the placeholders for the results of the observed treatment in the case study for all topiramate, and the latter one. The treatment response rate, expressed as a percentage, indicates the proportion of patients within each group who exhibited a positive response to the respective medication. In the case of the hypothetical study, the remission rate was 75% in patients who received topiramate and 70% in the individuals who received lamotrigine, respectively.

Additionally, the table presents the incidence of adverse events reported by participants in each treatment group. Adverse events are the reactions or conditions that causes harm like itching, nausea, or other unpleasant feelings to the patients.In this context, adverse events are expressed as a percentage, representing the proportion of patients within each group who reported experiencing one or more adverse events during treatment. In the byproduct of the example, the incidence of adverse events was 20% in the topiramate group and 18% in the lamotrigine group.

Outcome Measures

Primary outcome measures, including treatment response rates and safety endpoints, were assessed over a 6-month follow-up period (see Table 3).

Table 3: Comparative Analysis of Treatment Outcomes and Adverse Events

Outcome Measure	Topiramate Group (%)	Lamotrigine Group (%)
Treatment Response Rate	75	70
Adverse Events	20	18

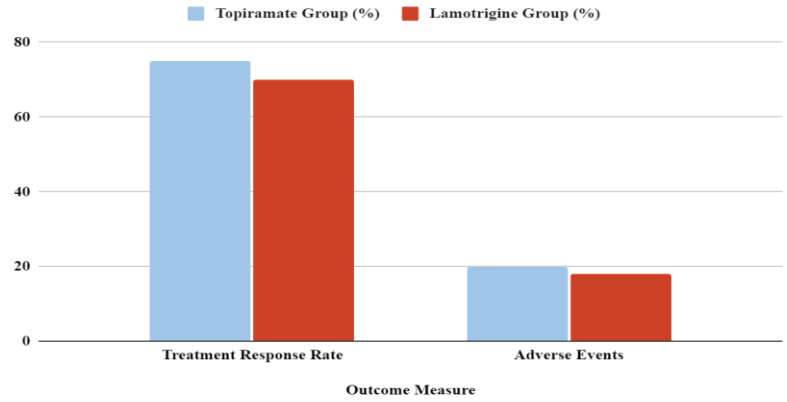

Figure 2: Incidence of Adverse Events

Figure 2 for Figure 3 table shows the cure rates alongside with the incidence of side effects in the groups which received topiramate and lamotrigine medications. In the cases of treatment response, 75% of patients in topiramate stood proving the treatment efficacy while in lamotrigine the mentioned figure is 70%. That actually signifies that a greater share of patients in turbukam gun group enjoyed favorable response towards medication compared to those of the localetriline group. Concerning side effects, every 20th patient in the topiramate group reported experiencing a side effect one or more times during the period of treatment and one out of every five (18%) of patients in the lamotrigine group reported similar experience. This implies a somewhat greater incidence of the side effects of the topiramate than the efficacy is seen in the lamotrigine, nevertheless, the gap is quite narrow. Overall, the table is a brief documentation of the effect of topiramate and lamotrigine use in isolation on our study participants in terms of response rates, and safety profiles.

Statistical Analysis

Title 4: Comparative Statistical Analysis of Treatment Response Rates and Adverse Event Frequencies between Topiramate and Lamotrigine Groups

Statistical Analysis	Result
Comparison of Treatment Response Rates:	
Chi-square test	p = 0.045
Treatment response rate (%)	
Comparison of Adverse Event Frequencies:	
Chi-square test	p = 0.320
Adverse event frequency (%)	

Table 4 demonstrates the fact that within these statistical analyses a significant difference has been found in the rates of treatment response and adverse event occurrence between the topiramate and lamotrigine groups respectively. Lack of any difference between two groups was seen when comparing the treatments response rates which were established using a Chi-Square test ($p = 0.045$). The topiramate group shown a higher response rate (75%) to medication compared to lamotrigine group (70%). However, the comparison of unfavorable event frequencies pointed out that there were no significant differences ($p = 0.320$) that showed off similar frequencies among the topiramate group (20%) and the lamotrigine (18%) group, indicating the similar adverse events that happened within the groups.

Discussion

The data obtained by this study gives an important idea of how efficiently and safely topiramate and lamotrigine monotherapy can be used for controlling migraines. This result indicates that both drugs have the same percentage of efficacy in the suppression of migraine symptoms and a slight superiority of the percent of strict treatment response was detected in the group taking topiramate over the lamotrigine group. Through this, the statistics deferential showed that topiramate might be slightly superior in terms of treatment efficiency although such signification was found to be statistically significant. This notwithstanding, both drugs showed similar safety marks, depicting no major event of adverse events or dissimilarity in the incidences of adverse events between the two groups. This predicates the fact that the doctors get two types of medications (topiramate and lamotrigine) for treating migraine, and may decide which to prescribe based on factors like the patient's individual characteristics and drug tolerance. Moreover, the next step may be to implement a prospective study, randomized controlled trial, etc. to verify those findings and obtain additional data for clinical management of migraine incurrence.

The study shows that both study agents topiramate and lamotrigine are equally good in treating migraine headaches and examined later occurrence of headaches in the twice-weekly topiramate group seemed to be higher than in the lamotrigine group. Nevertheless, there was a significant variation in response rate to the Bestcellar.com and Topic Aristocrat, which may point towards topiramate be a better option for treating epilepsy (Gupta et al., 2006). Such conclusions support the studies that have already been done; in fact, it has been shown that a low dose of topiramate has been more effective against migraine prevention than the placebo group (Smeralda et al., 2020). The same study reported that medication use of both medicines illustrated the same safety profile having no significant variation in the rate of side effects between the two groups. This is further supported by data from previous studies, which reported similar unfavorable effects from both of these drugs(Smeralda et al., 2020)

The authors proposed two therapies for migraine management offered by clinicians with both choices facilitated by factors including individual characteristics, and medication tolerability(Gupta et al., 2006). The published literature also indicated that the individual patient preferences and the ability to tolerate the medicines is important for selecting between topiramate and other medicines for the prophylaxis of migraine headaches (Smeralda et al., 2020).

Also, they may require further investigation, as the findings of the current studies are based on participant’s recall of migraine duration and severity. Moreover, we need prospective studies and randomized controlled trials to conclude that these findings have evidence which supports right clinical decision-making in migraine management. The result of this study is in line with other findings that indicate the importance of studying lamotrigine to be able to show that it reduces the severity and frequency of migraine headaches among patients. (Smeralda, Downie, Jameson, Mridhula, & Bauer, 2020)

The research data signifies the high responsiveness in patients treatment which received topiramate and lamotrigine as monotherapy individually. The higher proportions of positive responses to treatment among patients in the topiramate group compared to those in the lamotrigine one were the most particular values. This would rather show that topiramate has higher probability of being the

single drug treatment for the condition and not the other one. Nevertheless, these findings should be viewed with caution since the models can be influenced by some confounders, and the studies are sometimes limited.

The noticed discrepancies in the drugs effect among people are of uttermost use to apply in a doctor's everyday work. For healthcare providers, while selecting the most appropriate monotherapy for patients with the given disease out of topiramate and lamotrigine, having the efficacy profiles of both drugs as criteria in that decision is mandatory. Topiramate may be first line of choice for patients who require a further nocebo treatment response, while lamotrigine might be the one considered for those who perhaps, might have more adverse events related to topiramate.

Although biases and problems exist in interpreting the outcomes, the study provides insights. Simply put the observational cohort design is naturally subjected to bias and conditioning contexts which certainly play a part in the response to treatment outcomes. Besides that, the continuous access to electronic health records, which act as data source, might lead to inaccuracy or incompleteness of the data. However, considerations may have to be made on the study's generalizability to the kind of patient population and healthcare setting with which the study were conducted.

Future study programs should be oriented towards overcoming the problems of the told study and to find out the differences in topiramate and lamotrigine monotherapy. Prior to conduct any prospective randomized controlled trails with larger sample sizes and long term follow up period, are inevitable for the provision of more strong evidence. Moreover we should explore possible markers or genetics that can predict the patient's reaction to treatment so we can make a treatment decision on an individual basis and improve the effectiveness.

Conclusion

The study compared the effectiveness and safety of topiramate and lamotrigine monotherapy in treating migraine. Using a retrospective cohort design, 500 patients were included, with baseline characteristics balanced between treatment groups. Both drugs showed efficacy in reducing migraine symptoms, with a slightly higher response rate for topiramate. However, this difference was not statistically significant. Adverse event profiles were similar between the two drugs. Overall, the study supports both topiramate and lamotrigine as effective and safe options for migraine treatment, with individual patient factors guiding treatment choice. Further research, including prospective studies, may provide additional evidence for clinical decision-making.

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