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RESEARCH ARTICLE

EVALUATION OF EFFICACY, SAFETY AND TOLERABILITY OF NEWER ANTIEPILEPTIC DRUGS IN PATIENTS OF EPILEPSY

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ABSTRACT

Introduction: Epilepsy is the most common neurological disorder. The conventional anti-epileptic drugs (AEDs), used as first line agents, control seizures successfully in 70-80% of individuals. Several new AEDs have been approved for epilepsy with the aim of improving seizure control, tolerability and quality of life.

Objective: To evaluate the efficacy and safety of newer AEDs in epileptic patients.

Material and methods: A prospective study where 100 epileptic patients who were on treatment since one year reporting to neurology OPD were included in the study.
Seizure freedom for minimum one year and >50% reduction in seizure frequency within one year after initiating the treatment were taken as criteria for the efficacy of the AEDs. Appropriate statistical tests were applied and p value ≤ 0.05 considered to be statistically significant.

Results: Carbamazepine & oxcarbazepine were the most commonly used conventional & newer monotherapy respectively. Valproic acid & topiramate were most commonly used conventional & newer AED respectively as a part of combination therapy.
We found more seizure freedom and >50% reduction in seizure frequency in patients on newer monotherapy as compared to conventional monotherapy. In combination therapy, number of patients with seizure freedom in conventional plus newer combination group were significantly more as compared to conventional plus conventional combination group.
Though adverse drug reactions were little more with conventional AEDs, overall they were well tolerated. While newer AEDs were almost 2 to 2.5 times costly as compared to conventional monotherapy.

Conclusion: Newer AEDs can be considered for the treatment of epilepsy as they found to be more effective, safe and better tolerable when used alone or in combination.

INTRODUCTION

Epilepsy is the most common neurological disorder. The conventional anti-epileptic drugs (AEDs), used as first line agents, control seizures successfully in 70-80% of individuals. Remaining patients continue to have uncontrolled seizures despite the use of anti-epileptic drugs either alone or in combination.[1] This has substantial deleterious effects on individual health and heavy burden on society.[2]Also, these conventional AEDs are associated with neurological and systemic adverse effects, effects on hormonal patterns in women, teratogenicity and various drug interactions.[3] Several new AEDs have been approved for epilepsy therapy with the aim of broadening treatment options, improve seizure control, tolerability and quality of life.[4,5] The randomized trials of new AEDs conducted as a part of regulatory approval did not provide data to address the issues like 100% control of seizure, long-term safety and improvement in quality of life.[6] Evaluation of AEDs usage pattern can provide valuable information on safety and efficacy of AEDs as well as address the issues like cost effectiveness and quality of life associated with use of AEDs.

Aim and Objectives

Aim: -To evaluate the efficacy and safety of newer AEDs in epileptic patient's refractory to conventional AEDs.

Objectives

1. To evaluate the efficacy of newer AEDs in epileptic patients refractory to conventional AEDs
2. To evaluate the safety and tolerability of newer AEDs.

3. To assess the Quality of Life and cost effectiveness of newer AEDs.

MATERIAL AND METHODS

This was a prospective study carried out at Dr. D. Y. Patil Medical College, Pune and Nobel Hospital, Pune. 100 epileptic patients reporting in neurology OPD were included in study. Itwas initiated after obtaining permission from Institutional Ethics Committee; Dr. D. Y. Patil Medical College, Pimpri, Pune. Appropriate statistical tests were applied and p value ≤ 0.05 considered to be statistically significant.

Inclusion Criteria

- Patients of all age and either sex
- Diagnosed cases of epilepsy (as per ILAE classification)
- Patients on AEDs for at least one year
- Patients giving informed consent

Exclusion Criteria

- Patients with other neurological and systemic disorder
- Patients with alcohol withdrawal, drug abuse
- Patient with febrile convulsion.

Statistical analysis

Statistical analysis was done using Fischer's exact test.

RESULTS

Out of 100 patients, 31 patients were on conventional monotherapy, 10 on newer monotherapy and 59 on combination therapy (23 on conventional+conventional and 36 on conventional+newer).

Carbamazepine was the most commonly used conventional AED as monotherapy followed by valproic acid. Valproic acid was most commonly used conventional AED as a part of combination therapy. Oxcarbazepine was most commonly used newer antiepileptic as a monotherapy. Topiramate was most commonly used newer antiepileptic in a combination therapy.

Patients on conventional monotherapy	**31**
Patients on newer monotherapy	10
Patients receiving conventional+conventional AEDs	23
Patients receiving conventional + newer AEDs	36
Commonly used conventional AED as monotherapy	Carbamazepine
Commonly used conventionalAED for combination therapy	Valproic acid
Commonly used newer AED as monotherapy	Oxcarbazepine
Commonly used newer AED for combination therapy	Topiramate

Seizure freedom (patients who don't have seizures for a minimum one year of receiving the same dose of AEDs) and >50% reduction in seizure frequency (reduction in 50% of seizure frequency within one year of receiving same dose of AEDs) were taken as criteria for the efficacy of the AEDs.We found more seizure freedom and >50% reduction in seizure frequency in patients on newer monotherapy as compared to conventional monotherapy, though the difference was not statistically significant.

Reduction in seizure frequency	**Conventional Monotherapy**	**Newer Monotherapy**	**P Value**
Seizure freedom	8**(25.80%)**	3**(30%)**	0.799
>50% Seizure reduction	23**(74.19%)**	7**(70%)**	
Total	31	10	

Comparison of seizure freedom using Fischer exact test

In combination therapy, number of patients with seizure freedom in conventional plus newer combination group were significantly more as compared to conventional plus conventional combination group. This could be due to different mechanism of action, broad spectrum activity and lack of enzyme induction with newer AEDs.

Reduction in seizure frequency	**Conventional+ Conventional**	**Conventional+ Newer**	**P Value**
Seizure freedom	3**(13.04%)**	15**(41.66%)**	**0.02***
Seizure reduction	20**(86.95%)**	21**(58.33%)**	
Total	23	36	

Comparison of seizure freedom using Fischer exact test
*statistically significant seizure freedom in Newer + Conventional group

As far as cost effectiveness is concerned Newer AEDs were almost 2 to 2.5 times costly as compared to conventional monotherapy.

Drug Therapy	**Cost of treatment Rs/month**
Conventional Monotherapy	305
Newer Monotherapy	760

The overall incidence of adverse events though was not very high in our study; they were mostly seen with the conventional AEDs. Drowsiness was most common ADR seen with carbamazepine and valproic acid. Among newer AEDs, ADRs like weight loss and decreased appetite were observed in patient receiving topiramate. Overall, the AEDs were well tolerated.

Significant improvement in overall quality of life was seen after the onset of treatment in patients. However, no statistical significance was seen when compared between the different groups.

DISCUSSION

Many new AEDs have been introduced in recent years to improve seizure control in epileptic patients. Randomized control trials among patients with refractory epilepsy have shown efficacy of these drugs compared to placebo.[7,8] This study described the pattern of AEDs utilizationin 100 patients with epilepsy.

In our study, carbamazepine was commonly used conventional AED as monotherapy. Valproic acid was mostly used conventional AED in combination therapy. In a Hyderabad study, phenytoin was the commonest AED prescribed.[9] But our observation corroborate with Ludhiana study where carbamazepine was the most commonly used AED followed by valproic acid.[10]

In our study, oxcarbazepine was most commonly used newer AED as monotherapy. Topiramate was the most commonly used newer AED in combination therapy. Hyderabad study supports our findings where topiramate was the most commonly used newer AED as an adjuvant.[9] But in Ludhiana study, clobazam and clonazepam were the most commonly used newer AEDs as add on therapy.[10]

In a Delhi study, there was significant increase in seizure freedom among the group receiving combination with newer AEDs[11] which corroborates with our study. We found that statistically significant number of patients had seizure freedom in conventional plus newer combination group as compared to

those receiving conventional plus conventional AEDs. Topiramate was the most commonly used newer AED in our study which is similar to the findings of the study done in Delhi.

The reason for higher number of patient responding to combination of conventional plus newer AEDs can be attributed to:

1. Different mechanism of action of newer AEDs
2. Broad spectrum activity of newer AEDs
3. less drug interactions with newer AEDs

In our study, drowsiness was the most commonly reported ADR by patients receiving conventional AEDs, which is same as reported by a study in Hyderabad[9].

A study in Delhi showed that addition of newer AEDs to the conventional therapy significantly increase the cost of treatment, which is supported by our study.[11] However, a study in Singapore found that addition of one newer AED in a two drug combination increases the cost by four times.[12]

CONCLUSION

The newer AEDs are safe, well tolerable and effective when used alone or in combination to control seizures in patients with refractory epilepsy. Despite being relatively costly than conventional AEDs they provide good quality of life in patients with refractory epilepsy. Hence, newer AEDs can be considered for the treatment of refractory epilepsy in patients who can afford it.

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