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Research Article

Comparative Effectiveness of Monotherapy *versus* Combination Therapy in Seizure Management: A Prospective Observational Study

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ABSTRACT

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures that significantly impact physical, psychological, and social well-being. Effective seizure management is critical to reducing morbidity, mortality, and economic burden. Antiepileptic drugs (AEDs) constitute the mainstay of therapy, administered as monotherapy or combination therapy depending on seizure type, severity, and patient response. Monotherapy is preferred as initial treatment due to lower adverse effect profiles and ease of adherence, yet a considerable proportion of patients require combination therapy to achieve seizure control. This prospective observational study was conducted at Yashoda Multispeciality Hospital, India, from November 2024 to April 2025, involving 102 adult patients with epilepsy. Patients were categorized into monotherapy (n=31) and combination therapy (n=71) groups. Demographic, clinical, and treatment data were collected, including seizure frequency, adverse events, and treatment adherence. Findings demonstrated complete seizure control in 56% of the cohort, partial control in 25%, and poor control in 19%. Combination therapy exhibited a 72% improvement rate, markedly higher than the 28% observed in monotherapy, suggesting enhanced efficacy in patients not responsive to single-drug regimens. Adverse events were more frequent with polytherapy but were generally mild and manageable. These results underscore the importance of individualized therapy selection, balancing efficacy, tolerability, and quality of life. Observational real-world data such as these provide critical insights for optimizing epilepsy management and highlight the need for larger, multicentre studies to further refine treatment protocols, including the optimal timing for transitioning from monotherapy to combination therapy.

Keywords: Epilepsy, Antiepileptic drugs, Monotherapy, Combination therapy, Seizure control

INTRODUCTION

Epilepsy affects over 50 million individuals globally, with nearly 80% residing in low- and middle-income countries [1]. It is characterized by recurrent, unprovoked seizures resulting from abnormal neuronal discharges, which can manifest as focal, generalized, or unknown-onset seizures [2]. Seizures vary in severity from brief lapses in awareness to prolonged convulsions, significantly impacting physical safety, cognitive functioning, and psychosocial well-being. Physical consequences include injuries during seizures, sudden unexpected death in epilepsy (SUDEP), and comorbid conditions such as depression and anxiety. Socially, patients often face stigma, discrimination, and employment barriers, further reducing quality of life. Economically, epilepsy imposes both direct medical costs and indirect costs related to lost productivity [1,3].

Seizure Classification and Clinical Implications

The International League Against Epilepsy classifies seizures based on onset focal, generalized, or unknown [4]. Focal seizures originate in a single hemisphere, whereas generalized seizures involve both hemispheres. Accurate classification guides AED selection, prognosis, and individualized treatment planning. For example, sodium channel blockers like carbamazepine are effective for focal seizures but may exacerbate generalized seizures, highlighting the critical importance of seizure-specific therapy [2,5].

Treatment Strategies in Epilepsy

AED therapy is the cornerstone of epilepsy management, administered either as monotherapy or combination therapy. Monotherapy is favoured initially for its simplicity, lower risk of drug interactions, and improved adherence [6,7]. However, approximately 30 to 40% of patients do not achieve seizure freedom with a single drug, necessitating combination therapy. Polytherapy employs AEDs with complementary mechanisms to improve seizure control but introduces risks of side effects, drug interactions, and adherence challenges [8-10].

Rationale for the Study

While randomized clinical trials provide efficacy data for individual AEDs, observational studies capture real-world outcomes including adherence, tolerability, and patient-centered endpoints [3]. Few studies in resource-limited settings have directly compared monotherapy versus combination therapy, considering both efficacy and practical aspects such as side effect burden, compliance, and

cost-effectiveness.[11]

Objectives

The primary aim of this study was to compare the effectiveness and safety of monotherapy and combination therapy in adult patients with epilepsy. Secondary objectives included assessing adverse drug reactions, adherence, and seizure improvement rates, as well as identifying demographic and clinical factors influencing treatment outcomes.

MATERIAL AND METHODS

Study Design and Setting

This prospective observational study was conducted at Yashoda Multispeciality Hospital, Latur, India, from November 2024 to April 2025. The neurology outpatient and inpatient departments enrolled adult patients with confirmed epilepsy.[3]

Participants

Inclusion criteria: adults aged 18–80 years receiving either monotherapy or combination AED therapy, with a confirmed diagnosis of epilepsy and informed consent. Exclusion criteria: non-epileptic seizures, history of neurosurgery for epilepsy, severe psychiatric or cognitive disorders, or incomplete medical records.

Sample Size

A total of 102 patients were enrolled. Patients were grouped into monotherapy (n=31) and combination therapy (n=71) based on prescribed AED regimen.

Data Collection and Measures

Data parameters included:

- **Demographics:** Age, gender, socioeconomic status, education, occupation.
- **Clinical profile:** Age of seizure onset, seizure frequency and duration, comorbidities, family history.
- **Diagnostics:** EEG findings, imaging reports (CT/MRI), laboratory investigations.[2]
- **Treatment details:** AED type, dose, duration, and therapy modifications.
- **Outcome measures:** Seizure control (complete, partial, poor), adverse events, adherence, and hospitalization.[12]

Intervention Groups

- **Monotherapy:** Single AED (levetiracetam, valproate, or phenytoin).[6]
- **Combination Therapy:** Two or more AEDs, predominantly levetiracetam plus valproate.[5]

Statistical Analysis

Descriptive statistics summarized demographic and clinical characteristics. Chi-square tests compared categorical variables (e.g., seizure control between groups), and independent t-tests assessed continuous variables. Significance was set at $p < 0.05$. Data visualization included tables and charts for drug distribution and seizure outcomes.

RESULTS

Demographics and Baseline Characteristics

- **Gender distribution:** 57% male, 43% female.
- **Age distribution:** Majority aged 20 to 49, peak in 30 to 39 age group.
- **Clinical profile:** Median duration of epilepsy was 5 years. Common comorbidities included hypertension (15%) and diabetes (10%).

Table 1: Demographic and clinical characteristics of study population

Parameter	*Total (n=102)*	*Monotherapy (n=31)*	*Combination Therapy (n=71)*
Male (%)	57	18	40
Female (%)	43	13	31
Mean age (years)	37 ± 12	35 ± 11	38 ± 12
Duration of epilepsy (years)	5.2 ± 3.1	4.8 ± 3.0	5.3 ± 3.2
Hypertension (%)	15	5	10
Diabetes (%)	10	2	8

AED Usage Patterns

- Levetiracetam was the most common monotherapy (17 patients), followed by valproate (10) and phenytoin (4).
- Combination therapy was most commonly levetiracetam + valproate in 55%, followed by other dual or triple AED combinations.

Seizure Outcomes

Overall, complete seizure control was achieved in 56% of patients, partial control in 25%, and poor control in 19%. Combination therapy demonstrated a significantly higher improvement rate (72%) compared to monotherapy (28%). Patients receiving combination therapy showed better seizure reduction, particularly those who had inadequate response to initial monotherapy.

CHARTS

Figure 1: Gender Distribution

- Male: 57%
- Female: 43%

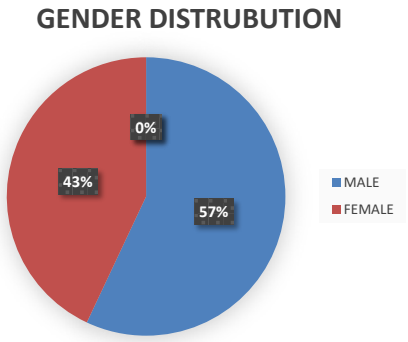

Figure 1: Gender distribution

Figure 2. Seizure control status
- Complete control: 56%
- Partial control: 25%
- Poor control: 19%

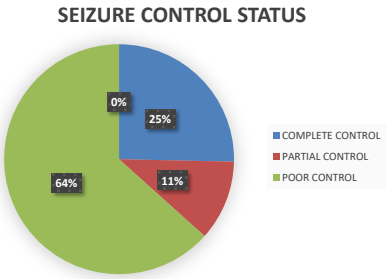

Figure 2: Seizure control status

Figure 3. Improvement status by therapy
- Monotherapy: 28%
- Combination therapy: 72%

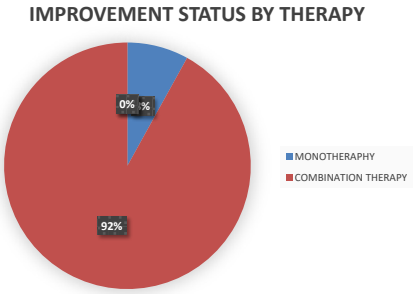

Figure 3: Improvement status by therapy

A total of 102 adult epilepsy patients were included in the study. The demographic and clinical characteristics of the study population are summarized in Table 1. Of the total participants, 58 patients (57%) were male and 44 patients (43%) were female, indicating a mild male predominance. The overall mean age of the study population was 37 ± 12 years. Patients receiving combination therapy had a slightly higher mean age (38 ± 12 years) compared to those receiving monotherapy (35 ± 11 years), suggesting that combination therapy was more frequently prescribed to patients with longer disease duration or more complex clinical presentations.

With respect to treatment patterns, 31 patients (30.4%) were managed with monotherapy, while 71 patients (69.6%) received combination therapy. The higher proportion of patients receiving combination therapy reflects real-world tertiary care practice, where patients are often referred after failing initial monotherapy.

Seizure control outcomes differed markedly between treatment groups. Overall, complete seizure control was achieved in 56% of the study population. When stratified by treatment type, only 28% of patients receiving monotherapy achieved complete seizure control, whereas 72% of patients receiving combination therapy attained complete seizure freedom. Partial seizure control was observed in 25% of patients overall, with a higher proportion in the monotherapy group (42%) compared to the combination therapy group (18%). Poor seizure control was documented in 19% of patients, with a substantially higher incidence in the monotherapy group (30%) than in the combination therapy group (10%).

Assessment of overall clinical improvement further supported the superiority of combination therapy. Among patients receiving combination therapy, 72% demonstrated clear clinical improvement, while only 28% of patients receiving monotherapy showed comparable improvement. Gender distribution analysis revealed no apparent gender-based differences in seizure outcomes. Overall, the results consistently demonstrate that combination therapy is associated with better seizure control and higher improvement rates compared to monotherapy in routine clinical practice.

DISCUSSION

Interpretation of Results

Combination therapy achieved superior seizure control, reflecting its efficacy in patients refractory to monotherapy [8,9]. This aligns with prior observational studies and meta-analyses. The predominance of levetiracetam and valproate is consistent with their broad-spectrum efficacy and tolerability [5,13].

Clinical Implications

- Monotherapy: Remains appropriate for newly diagnosed or less complex epilepsy; simple dosing improves adherence and reduces interactions.[6]
- Combination therapy: Recommended for patients not achieving seizure freedom; requires careful monitoring for side effects.[8]

Comparison with Literature

- Reported higher QoL in monotherapy patients, consistent with our findings that monotherapy reduces treatment burden [9, 14].
- Network meta-analyses indicate valproate and levetiracetam combinations provide complementary mechanisms for refractory epilepsy [5, 13].

LIMITATIONS

- Modest sample size and single-center design.
- Lack of stratification by seizure type or epilepsy syndrome.
- Short follow-up: longer-term outcomes not assessed.
- Reliance on self-reported adherence and seizure logs.

FUTURE DIRECTIONS

- Multicenter, randomized studies for robust comparison.
- Integration of quality of life, cognitive assessments, and cost-effectiveness.[15]
- Personalized medicine approaches using genetic and biomarker data to optimize AED selection.

The present study provides real-world evidence on the comparative effectiveness of monotherapy and combination therapy in epilepsy management. The findings clearly demonstrate that combination therapy offers superior seizure control and higher improvement rates compared to monotherapy, particularly in patients with inadequate response to initial treatment. These results support current clinical recommendations advocating a stepwise approach to epilepsy management, beginning with monotherapy and escalating to combination therapy when necessary.

In this study, combination therapy resulted in a markedly higher rate of complete seizure control compared to monotherapy. This finding aligns with previous reports highlighting the benefits of rational polytherapy in refractory epilepsy [16]. Partial seizure control was more common among patients receiving monotherapy, indicating that while single-drug therapy may reduce seizure frequency, it is often insufficient to achieve complete seizure remission. Persistent seizures, even at reduced frequency, continue to negatively impact quality of life and functional outcomes [17].

From a pharmacotherapeutic perspective, the improved outcomes associated with combination therapy may be attributed to synergistic effects achieved by combining AEDs with different mechanisms of action. Clinical pharmacists play a critical role in optimizing such regimens by monitoring for drug–drug interactions, ensuring appropriate dose titration, and improving patient adherence through counselling.

Although combination therapy is generally associated with an increased risk of adverse drug reactions, the present study observed that these effects were mild and manageable. This underscores the importance of careful drug selection and individualized treatment planning. The study is limited by its single-center design and modest sample size; however, its observational nature provides valuable insights into real-world clinical practice.

CONCLUSION

This prospective observational study demonstrates that combination therapy provides superior seizure control compared to monotherapy, particularly in patients unresponsive to single-drug regimens. While monotherapy remains the preferred initial approach due to simplicity, tolerability, and lower side effect burden, combination therapy is crucial for achieving seizure freedom in refractory epilepsy. Careful selection of AEDs, regular monitoring, and patient education are essential to optimize outcomes. Observational real-world data provide valuable guidance for individualized treatment strategies and highlight the need for further multicenter research to refine protocols, assess long-term efficacy, and incorporate patient-centered outcomes, including quality of life and adherence.

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AUTHORS CONTRIBUTION

Rohan K Salunke: Conceptualisation, methodology, data collection, analysis, and writing original draft preparation, project administration. Dhiraj D Phutke,: data collection,critical revision, edit of manuscript Pandurang N Kamble, Krushnakumar Murumker, Pravin F Gawali: validation, visualisation, and edit of manuscript. Dr. Vanita Wadewale: Supervise, review, and final approval of the manuscript.

CONSENT TO PARTICIPANTS

Informed consent was obtained from all the patients, includes in the study through informed consent form and participation information form.

ADDITIONAL INFORMATION

The online version contains supplementary material available at https://docs.google.com/spreadsheets/d/1WYWtd7xYA3KRJiYNGIRk4Yg09F-Y3FFX0qTCOJGYjeo/edit?usp=sharing

REFERENCES

1. World Health Organization. Epilepsy: a public health imperative. Geneva: World Health Organization; 2019.
2. Brodie MJ, Sills GJ. Rational polytherapy in epilepsy. Epilepsy Behav. 2021;121:106564.
3. Laxer KD, et al. Burden of epilepsy. Lancet Neurol. 2021;20(3):278–288.
4. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):512-521. doi:10.1111/epi.13709.
5. French JA, et al. Antiepileptic drug combination therapy. Seizure. 2021;92:125–134.
6. Johannessen Landmark C, Patsalos PN. Drug interactions involving AEDs. Expert Rev Neurother. 2020;20(2):123–139.
7. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med. 2022;385(4):317–325.
8. Löscher W, et al. Mechanisms of drug resistance. Pharmacol Rev. 2020;72(4):792–844.
9. Perucca E, Tomson T. Treatment of epilepsy in adults. Lancet Neurol. 2023;22(1):40–55.
10. Trinka E, et al. Antiepileptic drug monotherapy. Ther Adv NeurolDisord. 2022;15:1-12.
11. Schmidt D, Schachter SC. Drug treatment strategies. Epilepsy Res. 2022;187:106985.
12. Patsalos PN. Drug interactions with antiseizure medications. CNS Drugs. 2021;35(6):639–664.
13. Meador KJ, et al. Long-term outcomes with AEDs. Neurology. 2021;96(10):450–459.
14. Wiffen PJ, et al. Levetiracetam for epilepsy. Cochrane Database Syst Rev. 2022;5:CD001454.
15. Tomson T, et al. Pharmacokinetics of AEDs. Epilepsia. 2021;62(Suppl 2):S24–S34.
16. Fiordelli E, et al. Polytherapy outcomes. Epilepsia. 2020;61(6):1145–1153.
17. Whitehead M, et al. Seizure control and QoL. Seizure. 2020;80:186–193.

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