Revisiting Perampanel: A Literature-Based review on its Role as a first add-on in Focal Seizure Management

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Introduction

Epilepsy[1]

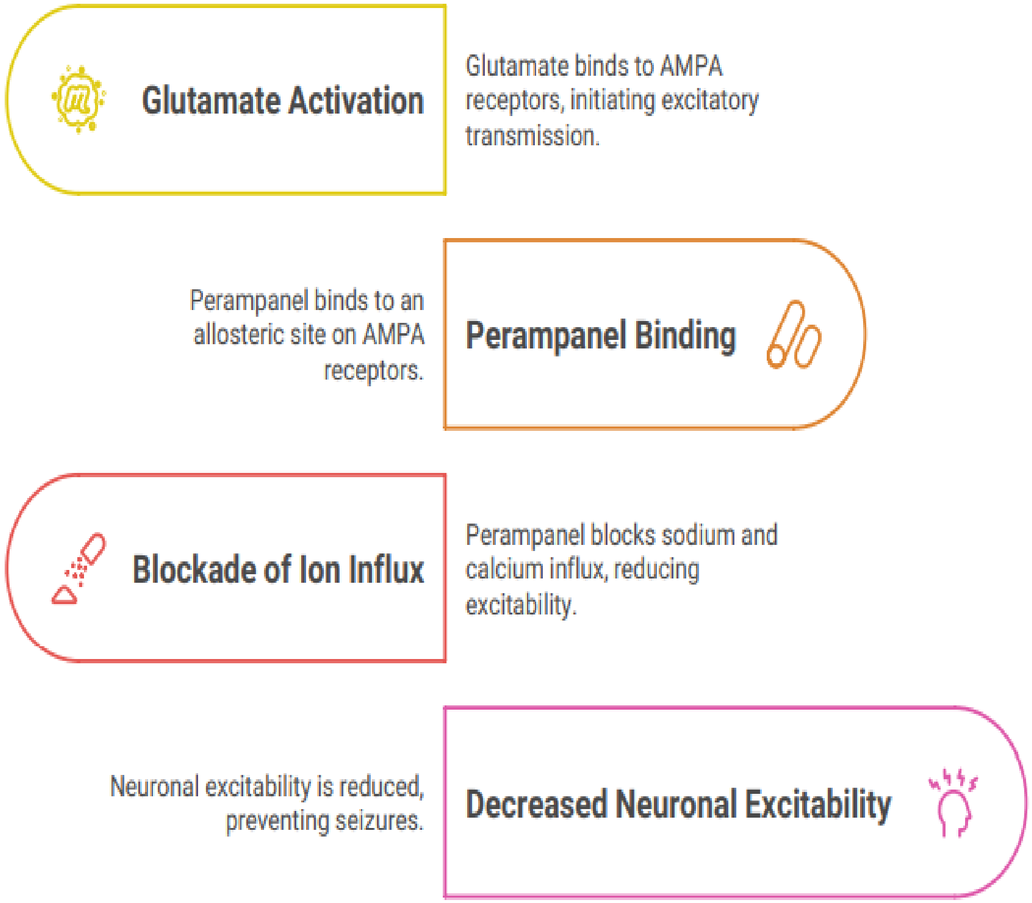
- India has an estimated epilepsy prevalence ranging from 3.0-11.9 per 1,000 individuals, with approximately 12 million individuals affected nationwide and almost half of them suffering from focal seizures

Challenges faced

- Globally, around 20–30% of persons with epilepsy have drug-resistant epilepsy (DRE)[2]
- An Indian study showed **40-50%** failed to respond to first-line AED monotherapy[3]
- Some monotherapy AEDs cause side effects that lead to treatment withdrawal

Perampanel (AMPA antagonist)

- Perampanel, a highly selective, and non-competitive antagonist of AMPA receptor, approved for adjunctive treatment of partial-onset seizures, with or without secondarily generalized seizures in patients aged ≥12 year
- It's once-daily oral dosing, predictable pharmacology and dose-response (allows gradual up-titration to balance efficacy and neuropsychiatric/coordination AEs), and synergy observed in some combinations make it convenient to introduce as a first add-on[4]



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2 Clinical Neurology and Neurosurgery,Volume 256,2025,109009,.
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4. Hanada, T. (2014). The discovery and development of perampanel for the treatment of epilepsy. Expert Opinion on Drug Discovery, 9(4), 449–458

Materials and Methods

Existing literature from 2017-2024 was screened to evaluate the role of perampanel as first add-on in management of partial onset seizures

Primary research articles were obtained from PubMed and Google Scholar.

Keywords included Perampanel, AMPA receptor antagonist, Focal onset seizures, Adjunctive therapy / Add-on therapy , seizure freedom

Aim

To highlight role of perampanel as first add-on in management of partial onset seizures as assessed by seizure freedom rate

Results of Perampanel as first add on

	Study name	Baseline	3 months	6 months	1 year	> 1 year
1	Zhang et al (2021) N=56, Observational Prospective	20 (no. of FOS)	Seizure freedom – 8%	Seizure freedom – 15.8%		
			≥50% reduction rate – 52%	≥50% reduction rate – 55.3%		
2	Seo et al (2019) N=85, Prospective Interventional	85		Seizure freedom – 80%		
				≥50% reduction rate – 47.1%		
3	Takahashi et al (2019) N=51, Observational Retrospective	13		Seizure freedom – 29%	Seizure freedom – 28%	
				≥50% reduction rate – 85%	≥50% reduction rate – 80%	
4	Stavropoulos, et al. (2019) N=181, Observational retrospective	134	Seizure freedom – 4.2%	Seizure freedom – 5.6%	Seizure freedom – 5.6%	
			≥50% reduction rate – 16.14%	≥50% reduction rate – 19.2%	≥50% reduction rate – 20.2%	
5	Santamarina et al. (2020) N=149, Observational Retrospective	113			Seizure freedom – 40.7%	
					≥50% reduction rate – 82.3%	
6	Gasparini et al (2022) N=503, Observational Restrospective	155	Seizure freedom – 42%	Seizure freedom – 50%	Seizure freedom – 48%	
			≥50% reduction rate – 66%	≥50% reduction rate – 88%	≥50% reduction rate – 83%	
7	Punia et al (2024) N=54, Phase IV	30			Seizure freedom – 26.7%	
					≥50% reduction rate – 77.8%	
8	Lee et al (2021) N=106, Extension study	96			Seizure freedom – 43.6%	Seizure freedom 2 years – 50%, 3 years – 58.7%
					≥50% reduction rate – 76.4%	≥50% reduction rate 2 years – 79.2%, 3 years – 84.8
9	Kim et al (2022) N=106, Post hoc	79		Seizure freedom – 50.6%		
				≥50% reduction rate – 83.5%		

Adverse effects

Studies have shown the most common AEs were dizziness (33.8%), somnolence (5.4%), anger (4.1%), and irritability (4.1%). No significant cardiac or metabolic adverse effects were reported.

1. Zhang R, Qiao S, Fang X, Wang K, Shi Y, Du Q, Yang T and Liu X (2021) Efficacy and Tolerability of Perampanel as Adjunctive Therapy in Chinese Patients With Focal-Onset Seizures: An Observational, Prospective Study. Front. Neurol. 12:731566. .
2. Takahashi S, Shimizu K, Inaji M, Hashimoto S, Yamamoto S, Maehara T. Effectiveness of perampanel as a first add-on antiepileptic drug for the treatment of partial epilepsy. Epilepsy Behav. 2019 Nov;100(Pt A):106492
3. Stavropoulos I, Louden W, Queally C, Adcock J, Tristram M, Neale M, Moran N, Flores L L, Nashef L, Richardson MP, Bell C, Slaght S, Aram J, Rayner N, Powell R, Mead A, Sen A, Elwes R. Perampanel for the treatment of epilepsy; Longitudinal actuarial analysis and dose responses based on monthly outcomes. Seizure. 2019 Jul;69:125-132.
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6. . Kim JH, Kim DW, Lee SK, Seo DW, Lee JW, Park HJ, Lee SA. First add-on perampanel for focal-onset seizures: An open-label, prospective study. Acta Neurol Scand. 2020 Feb;141(2):132-140

Conclusion

- Evidence has shown perampanel being reliable option in focal seizure management with seizure freedom ranging from 8%- 58% and ≥50% reduction rate from 16%-84% with duration between 3 months- 3 years .
- A desirable feature of perampanel which is relevant to add-on use is its unique mechanism, which facilitates use in combination with any antiseizure medication.
- No significant cardiac or metabolic adverse effects were reported, supporting long-term safety.
- It’s role as add-on is useful in polytherapy settings due to low-interaction potential.
- Overall, perampanel showed significant efficacy and safety as first add-on in patients with focal seizures

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