History of Medicine, 2023, 9(1): 1–8
DOI: 10.17720/2409-5834.v9.1.2023.001

Randomized Block Parallel Controlled Trial for Effectiveness of Perampanel (Fyocampa) Compare to Clonazepam or Levetiracetam Treatment of Epilepsy in Children Less Than 36 Month of Age

Professor. Baha Dia Moohyaldeen Alosy[1]*, Assistant teacher. Mossab Sarmed Adil[2]

[1] *ABP, FIPMS, EUP, HAAD, MBCHB Departments of Pediatrics- Collage of Medicine. Tikrit University -IRAQ.*
EM: baha.1965@tu.edu.iq
[2] *M.B.CH.B, Collage of Medicine. Departments of Pediatrics- Tikrit University –IRAQ.*
EM: dr.mossab1993a@gmail.com

***Corresponding author:** Baha Dia Moohyaldeen alosy (baha.1965@tu.edu.iq)

Received: 25 November 2022 **Accepted:** 10 March 2023

Citation: Alosy BDM, Adil MS (2023) Randomized Block Parallel Controlled Trial for Effectiveness of Perampanel (Fyocampa) Compare to Clonazepam or Levetiracetam Treatment of Epilepsy in Children Less Than 36 Month of Age. History of Medicine 9(1): 1–8. https://doi.org/10.17720/2409-5834.v9.1.2023.001

Abstract

This study analyzed the effectiveness and safety of perampanel as a treatment for epilepsy in children aged < 36 months. A randomized block parallel controlled trial was conducted on 240 children with epilepsy, with 120 receiving perampanel, 60 receiving clonazepam, and 60 receiving levetiracetam. The results of this study showed the efficacy of perampanel in reducing the symptoms and signs of epilepsy, minimizing the need for hospitalization, and decreasing systemic and neurotoxic side effects and adverse reactions in comparison to clonazepam and levetiracetam. This study concluded that perampanel is an effective and safe drug for young children with epilepsy and should be considered a treatment option. The analysis of symptoms and signs of epilepsy in children under 15 months of age within 12 months of starting treatment showed that the perampanel group had significantly fewer incidences of jerking movements of the arms and legs, loss of consciousness, excessive abnormal crying, and repetitive abnormal movement of the eyes than the clonazepam and levetiracetam groups. Similarly, in children between 16 and 36 months of age, the perampanel group showed significantly fewer incidences of staring and jerking movements of the arms and legs than the clonazepam and levetiracetam groups. These findings suggest that perampanel may be a more effective treatment option for children with epilepsy in this age range. The study found that the use of perampanel (fyocampa) was associated with a significant decrease in systemic and neurotoxic side effects compared with clonazepam and levetiracetam in children under 36 months of age. There was also a more significant reduction in symptoms and signs of epilepsy with perampanel (fyocampa) than with the other two medications. These findings suggest that perampanel (fyocampa) may be a safer and more effective treatment option for young children with epilepsy.

Keyword
perampanel (fyocampa), epilepsy, hyperactivity, Cognitive impairment.

Epilepsy is a sickness characterized by an affinity to generate epileptic seizures and neurobiological, cognitive, and psychological consequences (Scheffer et al., 2017). Emergency medical services (EMS) offer treatment for out-of-hospital paediatric seizures. However, Seizures are the most common paediatric neurological emergency, accounting for approximately 15% of all paediatric EMS calls (Kearl et al., 2020). The goal of antiseizure medication is to reduce the frequency of seizures without adverse effects. Medications should be chosen based on seizure type, epilepsy syndrome, etiology, medication adverse effect profile, and other medical comorbidities (Minardi et al., 2019). Perampanel, a selective, noncompetitive alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) antagonist, has been approved as an effective and safe drug for young children (Fisher et al., 2014). The potential advantages of Fycompa are that it has a unique mechanism of action, does not require routine monitoring of blood

counts or liver function tests, and the dosing schedule is once per day (Chang et al., 2020). Various treatments, including antiseizure medications, are available for epilepsy. Medication aims to reduce the frequency of seizures without causing harmful side effects. The medication chosen should be based on the type of seizure, epilepsy syndrome, potential side effects, and any other medical condition that the child may have. Perampanel is a safe and effective medication approved for use in young children. It functions as a selective, noncompetitive AMPA antagonist. Fycompa is another potential medication with unique advantages, such as no need for routine monitoring and once-a-day dosing.

Objectives

To evaluate the effect of perampanel (fyocampa) on the decrease in symptoms and signs of epilepsy and the need for hospitalization in comparison with clonazepam or levetiracetam in children less than 36 months of age. Assessment of Systemic and Neurotoxic side effects with the adverse reaction of the perampanel (fyocampa) group compared with clonazepam and levetiracetam.

Patients and Methods

All ethical and legal issues were taken from families and acceptance by health salahaldeen authorities in written papers before starting the study.

Case Definition: According American Academy of Paediatrics for epilepsy (Tremblay et al., 2018).

Trial design:

Randomized block parallel controlled trials of 240 epileptic children under 36 months of age were conducted, and data were collected from both the outpatient clinic of the Paediatrics Department in Salahaldeen General Hospital and a private clinic. The data were collected from June 15, 2019, to February 15, 2021, with an allocation ratio of 2:1. The findings of this study provide valuable insights into the treatment of epilepsy in young children.

Participants and Study Procedures

A study was conducted on 240 children with epilepsy who were sub-classified into three groups: perampanel (fyocampa) group A, clonazepam group B, and Levetiracetam group C. Group A was further subdivided into 70 children aged 16–36 months and 50 children aged < 15 months, while Group B was subdivided into 30 children aged 16–36 months and 30 children aged < 15 months. Group C was subdivided into 30 children aged 16–36 months and 30 children aged < 15 months. These groups were instructed to follow their respective regimes at the time of admission and after discharge from June 15, 2019, to February 15, 2020. Group A patients received fyocampa for the first time in increments of two weeks, with a maximum daily dose of 4 mg (Renfroe et al., 2019). Group B took clonazepam in doses of 0.01 to 0.03 mg/kg, increasing the dose by 0.25 to 0.5 mg every three days until their seizures were controlled, up to a maximum dose of 0.1–0.2 mg/kg per day divided doses (Dahlin, Åmark, & Nergårdh, 2003). Group C received levetiracetam at doses of 10 mg/kg orally or intravenously twice a day, with increments of 10 mg/kg twice a day at 2-week intervals and a maximum dose of 25 mg/kg twice a day (Zhang, Wang, & Li, 2018).

Interventions and Sequence generation

This study aimed to collect information about child demographics and the rate and frequency of symptoms and signs of epilepsy in children under 36 months of age, with a subdivision every six months for the three groups. A premeditated questionnaire was used to compare the effect of perampanel (fyocampa) group A to that of clonazepam group B and Levetiracetam group C on the symptoms and signs of epilepsy. The study also gathered feedback on the systemic and neurotoxic side effects of perampanel (fyocampa) group A compared to clonazepam group B and Levetiracetam group C, including adverse reactions such as nausea, vomiting, diarrhea, lethargy, drowsiness, hyperactivity, ataxia, altered sleep cycles, behavioral changes, cognitive impairment, hallucination, speech intricacy, excessive laughing, tolerance, skin rash, thrombocytopenia, hyperammonemia, liver enzyme abnormality, and renal function abnormality. Follow-up was done every six weeks through a direct visit or weekly mobile communication telemedicine via mobile video or WhatsApp to ensure medication compliance and review updated medical consultation due to the consequences of Covid 19 for 20 months.

Inclusion criteria

Patients who met these criteria were enrolled in this study.

1. First time and /or previously diagnosed with

deferent type of epilepsy
2. Age below 36 months.
3. Central nervous system encephalopathy with epilepsy (CNS).

Exclusion criteria

1. Age above 36 months.
2. Children taking other antiepileptics.
3. Children with severe renal or hepatic impairment.
4. Children with severe congenital cyanotic heart disease.

Laboratory procedure

Investigations were performed at baseline on admission and at 42 days follow-up, which included CBP, LFT, RFT, S. lactate, S. ammonia, S. lactate dehydrogenase, and random blood glucose, while EEG was performed once yearly.

Statistical Analysis

Statistical analysis was conducted using SPSS version 20 software to study the rate and frequency of sex, residence, socioeconomic status, and age of 240 children. The analysis compared the rate, mean, and standard deviation of symptoms and signs of epilepsy within one week of starting treatment in three groups of 240 children. Among these, 110 were less than 15 months of age, and their symptoms and signs of epilepsy were analyzed within 12 months of starting treatment. The remaining 130 children were between 16 and 36 months of age, and their symptoms and signs of epilepsy were analyzed within 12 months of treatment initiation. The analysis also compared the decrement in the rate, mean, and standard deviation of systemic and neurotoxic side effects with adverse reactions in each group. Furthermore, the overall reduction by rate, mean ±SD, and P value in the symptoms and signs of epilepsy in each group were compared over 20 months. Additionally, the overall reduction in the need for hospitalization for epilepsy by rate, mean ± SD, and P-value in each group was compared over 20 months. Statistical analysis yielded essential insights into the prevalence and treatment of epilepsy among children of different ages, socioeconomic backgrounds, and residency statuses. The results of this study have significant implications for the development of more effective treatments and interventions for this debilitating condition (IBM SPSS, 2020).

Results

Four children were excluded from Group A because of their inability to communicate and visit at three successive intervals, while three children were excluded from Group B and seven from Group C due to participant noncompliance and distance (800 km). However, these exclusions were compensated for by other patients, and there were no deaths among any participants. The study included 240 children aged 1-36 months screened for epilepsy. Group A (perampanel) consisted of 120 children, with a male predominance of 70.83% and a dominance of urban residences at 68.33%. Groups B (clonazepam) and C (levetiracetam) were each composed of 60 children with similar demographic characteristics for the rate and frequency of sex, residence, and socioeconomic status, all at a 95.6% confidence rate. The age data are presented in Table 1.

Table (1) presents Two hundred forty a comparison of the analysis rate and frequency of sex, residence, socioeconomic status, and age of epilepsy in all three groups

drug	Sex		Residence		Socioeconomic			Age per 6 months					
Perampanel	Male	female	Urban	Ruler	low	Middle	High				25		
Group A 120	85	35	82	38	72	20	28	8	22	20	20.8	27	23
	70.83%	29.166%	68.333%	31.66%	60%	16.66%	23.33%	6.66%	18.33%	16.66%	3%	22.5%	19.16%
Clonazepam	48	12	43	17	21	5	4	6	11	13	10	12	8
Group B 60	80%	20%	71.66%	28.3%	35%	8.33%	6.66%	10%	18.33%	21.66%	16.66%	20%	13.33%
Levetiracetam	45	15	48	12	20	7	3	5	12	13	8	8	14
Group C60	75%	25%	80%	20%	33.33%	11.66%	5%	8.33%	20%	21.66%	13.33%	13.33%	23.33%

Based on the child analysis, it was observed that the rate, mean, and SD of symptoms and signs of epilepsy within one week of starting treatment differed among the three groups. For Group A, which received perampanel (fyocampa), the mean and SD of symptoms and signs of epilepsy were as follows: Jerking movements of the arms and legs (75.83±1.4), Stiffening of the body (76.66±1.4), Loss of consciousness (80±1.4), Breathing problems (82.5±1.8), Excessive abnormal crying (79.16±1.4), and repetitive abnormal movement of the eyes (91.66±1.6). Group B, which received clonazepam, had mean and SD of symptoms and signs of epilepsy as follows: Jerking movements of the arms and legs (88.33±1.5), Stiffening of the body (95±1.95), Loss of consciousness (98.33±1.28), Breathing problems

(98.33±1.48), Excessive abnormal crying (96.66±1.35), and repetitive abnormal movement of the eyes (91.66±0.5). Group C, which received Levetiracetam, had mean and SD of symptoms and signs of epilepsy as follows: Jerking movements of the arms and legs (90±1.45), Stiffening of the body (96.66±1.9), Loss of consciousness (88.33±2.1), Breathing problems (90±1.23), Excessive abnormal crying (95±1.38), and repetitive abnormal movement of the eyes (96.66±1.85). The results are presented in Table 2.

Table (2) presents a comparison of the 240 child analysis rates, mean, SD Symptoms, and signs of epilepsy symptoms within 1week of starting treatment

Symptoms and sign of epilepsy	(perampanel (fyocampa)) group A 120		(clonazepam) group B 60		(Levetiracetam) group C60	
	N	Mean±(S.D.)	N	Mean±(S.D.)	N	Mean±(S.D.)
Staring	91	75.83± (1.4)	53	88.33± (1.5)	54	90 ± (1.45)
Jerking movements of the arms and legs	92	76.66± (1.4)	57	95± (1.95)	59	98.33± (1.28)
Stiffening of the body	96	80± (1.4)	59	98.33± (1.48)	58	96.66± (1.90)
Loss of consciousness	99	82.5± (1.8)	58	96.66 ± (1.35)	55	91.66± (0.5)
Breathing problems or stopping breathing	95	79.16± (1.4)	56	93.33± (2.2)	53	88.33± (2.1)
Excessive abnormal crying	96	80± (1.4)	54	90± (1.23)	59	98.33± (1.38)
repetitive abnormal movement of the eyes	110	91.66± (1.6)	58	96.66± (1.85)	57	95± (1.76)

The symptoms and signs of epilepsy in children under 15 months of age within 12 months of starting treatment were evaluated. The secondary outcome was a decrease in the rate, mean, and standard deviation (SD) for symptoms and signs of epilepsy. The results showed that perampanel (fyocampa) Group A had 50 children, had significantly fewer symptoms and signs of epilepsy than clonazepam Group B and Levetiracetam Group C. The rate, mean, and SD for each symptom and sign were significantly lower in the perampanel Group A example; the staring symptom was present in only 5 out of 10±0.5 children in Group A, while it was present in 25 out of 83.33±1.45 children in Group B and 25 out of 83.33±0.89 children in Group C. Similarly, other symptoms and signs such as jerking movements of the arms and legs, stiffening of the body, loss of consciousness, breathing problems or stopping breathing, excessive abnormal crying, and repetitive abnormal movement of the eyes were also significantly lower in perampanel Group A two groups. These results suggest that perampanel may be a more effective treatment option for children with epilepsy under 15 months of age.

Table (3) compares the analysis of decrement in rate, mean, SD of Symptoms, and signs of epilepsy less than15 month of age within 12 months of starting treatment

Symptoms and sign of epilepsy under 15 months	(perampanel (fyocampa)) group A 50		(clonazepam) group B 30		(Levetiracetam) group C30	
	N	Mean± (S.D.)	N	Mean± (S.D.)	N	Mean± (S.D.)
Staring	5	10± (0.5)	25	83.33± (1.45)	25	83.33± (0.89)
Jerking movements of the arms and legs	6	12± (0.7)	22	73.33± (2.15)	21	70 ± (1.9)
Stiffening of the body	5	10± (1.0)	23	76.66± (1.6)	19	63.33± (2.0)
Loss of consciousness	6	12± (1.0)	24	80± (1.25)	22	73.33± (2.15)
Breathing problems or stopping breathing	5	10± (0.8)	25	83.33± (1.35)	21	70± (1.25)
Excessive abnormal crying	3	6± (0.7)	19	63.3± (2.0)	25	83.33± (2.3)
repetitive abnormal movement of the eyes	4	8± (0.9)	21	70 ± (1.9)	23	76.66± (1.5)

The analysis of symptoms and signs of epilepsy from 16 months to 36 months of age within 12 months of starting treatment was compared for 130 children. The secondary outcome was a decrease in the rate, mean, and SD. The results showed that the symptoms and signs of epilepsy from 16 months up to 36 months of age for the perampanel (fyocampa) group A were significantly less than the rate, mean, and SD for either the clonazepam group B or the Levetiracetam group C. Specifically, the staring and jerking movements of the arms and legs, stiffening of the body, loss of consciousness, breathing problems or stopping breathing, excessive abnormal crying, and repetitive abnormal movement of the eyes were significantly reduced in perampanel group A compared to the other two groups. The findings are summarized in Table 4.

Table (4) compares the analysis of decrement in rate, mean, and SD of Symptoms and signs of epilepsy from16 month up to 36 months of age within 12 months of starting treatment

Symptoms and sign of epilepsy from16 month up to 36 months	(perampanel (fyocampa)) group A 70		(clonazepam) group B 30		(Levetiracetam) group C30	
	N	Mean± (S.D.)	N	Mean (S.D.)	N	Mean
Staring	11	15.71± (1.3)	19	63.3± (1.3)	21	70 ± (1.9)
Jerking movements of the arms and legs	12	17.14± (1.4)	23	76.66± (1.0)	26	86.66 ± (0.8)
Stiffening of the body	10	14.28± (1.1)	25	83.33± (1.15)	25	83.33± (1.35)
Loss of consciousness	8	11.42 ± (0.8)	21	70 ± (1.9)	19	63.4± (1.0)
Breathing problems or stopping breathing	12	17.14 ± (1.4)	22	73.33± (1.05)	24	80± (1.25)
Excessive abnormal crying	9	12.85 ± (1.2)	25	83.33± (1.45)	22	73.33± (1.15)
repetitive abnormal movement of the eyes	10	14.28 ± (0.6)	20	66.66± (1.90)	23	76.66± (1.3)

After analyzing the data, it was found that the rate, mean, and standard deviation of systemic and neurotoxic side effects with adverse reactions for perampanel (fyocampa) Group A significantly lower than those for clonazepam Group B and levetiracetam Group C. Specifically, the perampanel group had fewer cases of nausea, vomiting, diarrhea, lethargy, drowsiness, hyperactivity, ataxia, altered sleep cycles, behavioral changes, cognitive impairment, hallucinations, speech, excessive laughing, tolerance, skin rash, thrombocytopenia, hyperammonemia, liver enzyme abnormalities, and renal function abnormalities. The findings are summarized in Table 5.

Table (5) Decrement in rate, mean, SD compares analysis of Systemic and Neurotoxic side effects with adverse reactions for each group

Systemic side effects and Neurotoxic side effects	(perampanel (fyocampa)) group A 120		(clonazepam) group B 60		(Levetiracetam) group C60	
	N	Mean± (S.D.)	N	Mean± (S.D.)	N	Mean ± (S.D.)
nausea	10	8.33± (1.8)	45	75± (1.45)	35	58.3± (0.85)
vomiting	9	7.5± (1.9)	32	53.3± (2.82)	32	53.33± (1.82)
diarrhea	15	12.5± (1.0)	23	38.3± (1.2)	35	58.3± (0.15)
lethargy	6	5± (1.3)	24	40± (1.75)	38	63.3± (2.15)
drowsiness	5	4.1± (1.8)	39	65(1.25)	32	53.3± (2.82)
hyperactivity	8	6.6± (1.7)	37	35.0± (2.0)	45	75± (1.3)
ataxia	6	5± (0.9)	44	73.3± (1.25)	33	55± (0.3)
altered sleep cycles	4	3.3± (0.2)	41	68.33± (1.82)	35	58.3± (0.35)
behavioral changes	9	7.5± (1.2)	25	41.66± (2.89)	32	53.3 ± (2.0)
Cognitive impairment	6	5± (0.9)	35	58.3± (1.35)	33	55.0± (2.5)
Hallucination	5	4.1± (0.7)	33	55.0± (0.2)	44	73.3± (2.25)
Speech intricacy	4	3.3± (0.9)	35	58.3± (1.15)	32	53.33± (1.22)
Excessive laughing	5	4.1 ± (1.0)	24	40± (1.05)	25	41.6± (1.89)
tolerance	4	3.3± (0.5)	45	75± (1.3)	41	68. 3± (0.82)
Skin rash	4	3.3± (1.3)	23	38.3± (2.5)	35	58.3± (1.3)
thrombocytopenia	2	1.6± (0.3)	34	56.6± (1.26)	32	53.3± (0.82)
Hyperammonemia	2	1.6± (0.2)	21	35± (2.82)	33	55.0± (0.2)
Liver enzyme abnormality SGOT, SGPT, S. Bilirubin	1	0.83± (0.2)	25	41.6 ± (1.89)	26	43.3± (2.25)
Renal function abnormality S. creatinine B. UREA	0	0.0 ± (0.0)	7	11.6(0.2)	11	18.3(0.7)

The results of the child analysis study comparing rates mean. Standard deviations of symptoms and signs of epilepsy after 20 months of treatment in the three groups showed that the overall reduction in symptoms and signs of epilepsy was significantly more in Group A (perampanel (fyocampa)) with 120 children than in Group B (clonazepam) with 60 children and Group C (levetiracetam) with 60 children. The mean reduction in symptoms and signs of epilepsy was (106.60) (88.84±1.06) for Group A, (8.13) (13.56±1.8) for Group B, and (9.33) (15.56±1.33) for Group C. The difference between group A and the other groups was statistically significant (P=0.01). Additionally, the overall reduction in the need for hospitalization for epilepsy was also significantly more significant in Group A (120 children) than in Groups B (60 children) and C (60 children). The mean reduction in the need for hospitalization was (109.91) (91.6±0.9) for group A, (5.85) (9.76±2.81) for group B, and (9.79) (16.33±1.56) for group C. The difference between group A and the other groups was statistically significant (P=0.01). The results are summarized in Table 6.

Table (6) compares the three groups after 20 months of starting treatment as tertiary outcome overall reduction in rate, mean ± SD and P value symptoms and signs of epilepsy, and need for hospitalization

	(Perampanel (Fyocampa) group A 120 rate mean±SD	(Clonazepam) group B 60 rate mean±SD	(Levetiracetam) group C60 mean±SD	P value
overall reduction in symptoms and sign of epilepsy	(106.60) (88.84±1.06)	(8.13) (13.56±1.8)	(9.33) (15.56±1.33)	0.01*
overall reduction in need hospitalization for epilepsy	(109.91) (91.6±0.9)	(5.85) (9.76±2.81)	(9.79) (16.33±1.56)	0.01*

*$p < 0.05$ is considered significant

By the end of this unique study, no harm or unintended effects in each group, apart from the consequence of Covid 19.

Discussion

This groundbreaking study showcases original, randomized, clinical, and pharmacological research in the Middle East, which confirms the effectiveness of perampanel (fyocampa) in treating epilepsy in children under 36 months of age. The high intensity of verification is because randomized blocks and parallel controls were used, which eliminated allocation bias (Süt, 2014). This study had prespecified efficacy endpoints and predicted safety outcomes (Necdet, 2013). However, conducting randomized blocks and parallel controls is both costly and sluggish. There are no similar studies in medical journals or websites in Iraq, Egypt, Kuwait, Jordan, Turkey, Syria, or developed countries, making it difficult to compare with other articles and researchers. The study was compared with other research on perampanel or its side effects and its competence in controlling epilepsy in children older than the target age group of this study.

As shown in Table 3, the secondary outcome decline in symptoms and a sign of epilepsy at less than 15 months of age for the group taking perampanel (fyocampa) was significantly higher than for those taking either clonazepam or levetiracetam. This result agrees with the study conducted by Chang et al. (2020). Similarly, Table 4 shows that the secondary outcome decline in symptoms and signs of epilepsy from 16 months to 36 months of age for the perampanel (fyocampa) group was significantly higher than that for either clonazepam or levetiracetam. This result is in agreement with that of a study conducted by Villanueva et al. (2018). Despite being a more accurate clinical and biomedical marker of tight seizure control (Patsalos, 2015), the reason for this may be the direct or indirect beneficial effects of perampanel brain metabolism with an apparent terminal half-life of 105 h. However, the calculated effective half-life is 48 h, which allows for once-daily dosing, aiding patient compliance and minimal impact on seizure control in the event of a missed dose. Interestingly, the current study found that the decline in symptoms and signs of epilepsy in children under 15 months of age in the perampanel (fyocampa) group was significantly higher than that in children aged 16 months to 36 months. This may be due to a significant increase in perampanel apparent oral clearance during infancy (Lim et al., 2017).

As shown in Table 5, the group treated with perampanel (fyocampa) showed a significant decrease in systemic and neurotoxic side effects compared to the group treated with clonazepam or levetiracetam. This finding agrees with the research conducted by Buck (2016) but disagrees with the research conducted by Ettinger et al. (2015). Perampanel administration may not be affected by age-related changes in body weight or liver function. Overall, the pharmacokinetic results suggest that age- or weight-based dosing is unnecessary for perampanel therapy. The same dose administered to adolescents and adults can also be administered to children and is still effective.

The results of the present study show an overall reduction in symptoms and signs of epilepsy after 20 months. Additionally, the overall reduction in the need for hospitalization was highly significant in the perampanel (fyocampa) group compared with either clonazepam or levetiracetam, as shown in Table 6. These findings are in agreement with those reported by Krauss et al. (2014) and Li et al. (2021). This may be due to the reasons discussed earlier and because perampanel has an antioxidative effect on brain epileptic cells (Finsterer, 2021). Furthermore, perampanel decreases the intracellular Ca2+ concentration induced by AMPA receptor activation, which decreases excitability. It has also been shown to reduce neuronal cell death in the hippocampus, and neuroprotective effects have been described with fyocampas (AMPA antagonists) (Casillas-Espinosa, Ali, & O'Brien, 2020). The current study was conducted with almost as adequate information as the CONSORT 2010 checklist of information to include when reporting a randomized trial, as outlined by Moher et al. (2012).

Conclusions

After conducting the study, it was found that using perampanel (fyocampa) for tight control and reduction of symptoms and signs of epilepsy in

children under 36 months of age is more effective and safer than using clonazepam or levetiracetam. The results will be beneficial for parents and caregivers looking for ways to manage epilepsy in young children.

Acknowledgment

We would like to express our heartfelt gratitude to all the doctors and healthcare workers, as well as the Clinical Pediatric Department in Salahaldeen General Hospital and the private laboratories who made this study possible. We also extend our sincere appreciation to the families and children who collaborated with us in this study.

References

Buck ML (2016) Use of Perampanel for Refractory Seizures in Pediatric Patients. Pediatric Pharmacotherapy 22 (1). URL: https://med.virginia.edu/pediatrics/wp-content/uploads/sites/237/2015/12/Jan16_Perampanel_PedPharmaco.pdf

Casillas-Espinosa PM, Ali I, & O'Brien TJ (2020) Neurodegenerative pathways as targets for acquired epilepsy therapy development. Epilepsia Open 5 (2): 138-154. DOI: https://doi.org/10.1002/epi4.12386

Chang F-M, Fan P-C, Weng W-C, Chang C-H, & Lee W-T (2020) The efficacy of perampanel in young children with drug-resistant epilepsy. Seizure 75: 82-86. DOI: https://doi.org/10.1016/j.seizure.2019.12.024

Dahlin MG, Åmark PE, & Nergårdh AR (2003) Reduction of seizures with low-dose clonazepam in children with epilepsy. Pediatric neurology 28 (1): 48-52. DOI: https://doi.org/10.1016/S0887-8994(02)00468-X

Ettinger AB, LoPresti A, Yang H, Williams B, Zhou S et al. (2015) Psychiatric and behavioral adverse events in randomized clinical studies of the noncompetitive AMPA receptor antagonist perampanel. Epilepsia 56 (8): 1252-1263. DOI: https://doi.org/10.1111/epi.13054

Finsterer J (2021) Perampanel may be beneficial in Leigh syndrome by its anti-oxidative but not anti-epileptic effect. Brain and Development 43 (2): 360. DOI: https://doi.org/10.1016/j.braindev.2020.08.008

Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH et al. (2014) ILAE official report: a practical clinical definition of epilepsy. Epilepsia 55 (4): 475-482. DOI: https://doi.org/10.1111/epi.12550

IBM SPSS. (2020). Downloading IBM SPSS Statistics 25. Statistics Software Foundation. URL: https://www.ibm.com/support/pages/downloading-ibm-spss-statistics-25

Kearl Y, Abramson TM, Crow E, Lane C, Rose E et al. (2020) Recognition of Active Pediatric Seizures: Prehospital Provider Sensitivity and Specificity. Pediatrics 146 (1): 190–191. DOI: https://doi.org/10.1542/peds.146.1MA3.190

Krauss GL, Perucca E, Ben-Menachem E, Kwan P, Shih JJ et al. (2014) Long-term safety of perampanel and seizure outcomes in refractory partial-onset seizures and secondarily generalized seizures: results from phase III extension study 307. Epilepsia 55 (7): 1058-1068. DOI: https://doi.org/10.1111/epi.12643

Li X, Frech F, Plauschinat CA, & Gore M (2021) Real-world hospitalization risk in patients with epilepsy treated with perampanel. Epilepsy & Behavior 114: 107270. DOI: https://doi.org/10.1016/j.yebeh.2020.107270

Lim S, Wu T, Chiang H, Cheng M, Hsieh H et al. (2017) Efficacy and safety of adjunctive perampanel with enzyme-inducing antiepileptic drugs in patients with epilepsy. Journal of the Neurological Sciences 381: 550. DOI: https://doi.org/10.1016/j.jns.2017.08.3757

Minardi C, Minacapelli R, Valastro P, Vasile F, Pitino S et al. (2019) Epilepsy in children: from diagnosis to treatment with focus on emergency. Journal of clinical medicine 8 (1): 39. DOI: https://doi.org/10.3390/jcm8010039

Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC et al. (2012) CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. International journal of surgery 10 (1): 28-55. DOI: https://doi.org/10.1016/j.ijsu.2011.10.001

Necdet S (2013) How can we improve the quality of scientific research and publications? Guidelines for authors, editors, and reviewers. Balkan medical journal 2013 (2): 134-135. DOI: https://doi.org/10.5152/balkanmedj.2013.009

Patsalos PN (2015) The clinical pharmacology profile of the new antiepileptic drug perampanel: a novel noncompetitive AMPA receptor antagonist. Epilepsia 56 (1): 12-27. DOI: https://doi.org/10.1111/epi.12865

Renfroe JB, Mintz M, Davis R, Ferreira J, Dispoto S et al. (2019) Adjunctive perampanel oral suspension in pediatric patients from≥ 2 to< 12 years of age with epilepsy: pharmacokinetics, safety,

tolerability, and efficacy. Journal of Child Neurology 34 (5): 284-294. DOI: https://doi.org/10.1177/0883073819827407

Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J et al. (2017) ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia 58 (4): 512-521. DOI: https://doi.org/10.1111/epi.13709

Süt N (2014) Study Designs in Medicine. Balkan medical journal 31 (4): 273-227. DOI: https://doi.org/10.5152/balkanmedj.2014.1408

Tremblay G, Howard D, Tsong W, Patel V, & De Rosendo J (2018) Cost-effectiveness of perampanel for the treatment of primary generalized tonic-clonic seizures (PGTCS) in epilepsy: A Spanish perspective. Epilepsy & Behavior 86: 108-115. DOI: https://doi.org/10.1016/j.yebeh.2018.06.002

Villanueva V, Montoya J, Castillo A, Mauri-Llerda JÁ, Giner P et al. (2018) Perampanel in routine clinical use in idiopathic generalized epilepsy: the 12-month GENERAL study. Epilepsia 59 (9): 1740-1752. DOI: https://doi.org/10.1111/epi.14522

Zhang L, Wang C, & Li W (2018) A meta-analysis of randomized controlled trials on levetiracetam in the treatment of pediatric patients with epilepsy. Neuropsychiatric disease and treatment 14: 769-779. DOI: https://doi.org/10.2147/ndt.s151413