EFFICACY AND TOLERABILITY OF PULSE STEROID AS AN ADD-ON THERAPY IN MANAGEMENT OF REFRACTORY CHILDHOOD EPILEPSY

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ABSTRACT

Background*: Epilepsy is one of the commonest neurological conditions, with an estimated prevalence of 0.5%–1% in developed countries. Steroids have been used for the treatment of certain epilepsy types, such as infantile spasms; however, the use in the treatment of other intractable epilepsies has received limited studies.*

Objectives*: We aimed to evaluate efficacy and adverse effects of high dose intravenous methylprednisolone (pulse steroid therapy) as an add-on therapy for refractory childhood epilepsy and its impact on both clinical and electroencephalographic aspects.*

Patients and Methods: *This interventional comparative study was carried out on 30 patients with refractory epilepsy, at PICU and Pediatric Neurology Unit of Al-Hussein University Hospital, during the period from December 2017 to November 2018. They were divided into two groups: Group A (intervention group) and group B (control group). All patients were aged from 2 months up to 18 years and of both genders. Patients with infantile spasms, autoimmune disorders, or progressive degenerative or metabolic disorders were excluded. History-taking, complete clinical examination and laboratory investigations were registered. Electroencephalography was done on admission and post-control therapy. Adequate rationals of AED polytherapy were given. For the intervention group (group A), intravenous methylprednisolone was added at 30 mg/kg once daily, for 3 consecutive days, followed by oral prednisolone 2 mg/kg/day, in 3 divided doses, for 2 weeks then gradually tapered over 4 weeks.*

Results: *There were no significant differences between the study groups regarding age, gender and onset of seizures. Two main etiologies were recorded among the study groups; Lennox-Gastaut Syndrome (LGS) and idiopathic epilepsy. All patients among group A (100%) had daily seizures while among group B 80% had daily seizures and 20% had weekly seizures. The seizures-type among the study groups was comparable; with 2 main types were recorded, Generalized Tonic Clonic (GTC) and multiple seizures-type. Follow up of all patients for 6 months after start of treatment revealed a significant improvement regarding EEG findings among group A more than among group B. After treatment among group A, 9 patients showed full improvement (normal EEG), 4 patients showed fair control (less frequent spikes on EEG) and 2 patients*

showed no improvement (same EEG abnormalities). There was no statistically significant difference, before and after treatment, among group B. After treatment among group B, 3 patients showed full improvement (normal EEG), 2 patients showed fair control (less frequent spikes on EEG) and 10 patients showed no improvement (same EEG abnormalities). A significant seizures-reduction was recorded among group A more than among group B after treatment, 66.67% seizures-reduction among group A vs 20% seizures-reduction among group B. Adverse effects of steroids were infrequent, mild and transient with no major adverse effects.

Conclusion: *Intravenous methylprednisolone as an add-on therapy for refractory childhood epilepsy is effective on both clinical (frequency of seizures) and electroencephalographic aspects.*

Key Words: *Methylprednisolone, Child, Intractable, Epilepsies, Seizures.*

INTRODUCTION

Epilepsy is one of the commonest neurological conditions, with an estimated prevalence of 0.5%–1% in developed countries **(Dalic and Cook, 2016)**.

Despite the fact that new epileptic drugs are designed every year, seizures in about 20–40% of patients still remain uncontrolled **(Kasprzyk et al., 2014)**.

Drug resistance can be defined as ‘failure of adequate trials of two tolerated, appropriately chosen and used anti-epileptic drug schedules, whether as monotherapy or in-combination, to achieve a sustained seizure-freedom **(Kwan et al., 2010)**.

The international league against epilepsy (ILAE) current definition of intractability is failure of two appropriate medications **(Mikati and Hani, 2015)**.

Therapeutic options for children with epilepsy refractory to antiepileptic drug therapy are limited. Steroids have been used for the treatment of certain epilepsy types, such as infantile spasms; however, their use in the treatment of other intractable epilepsies has received limited study **(Almaabdi et al., 2014)**.

Add-on steroid treatment for children with intractable epilepsy is safe and may be effective in some children when used in a short course. Clinical improvement was accompanied by the disappearance of epileptiform discharges on follow-up electroencephalography. No major side effects were noted, specifically hypertension and glucosuria **(Almaabdi et al., 2014)**.

Intravenous pulse methylprednisolone may be a useful addition in the treatment of some children with refractory epilepsy. The absence of pharmacokinetic interactions facilitates its use in individuals who are already taking multiple antiepileptic drugs. This treatment represents a safe and potentially effective option for treating children with high seizure frequency unresponsive to standard antiepileptic drugs **(Almaabdi et al., 2014)**.

AIM OF THE WORK

The aim of this study was to evaluate efficacy and adverse effects of high dose intravenous methylprednisolone (pulse steroid therapy) as an add-on therapy for refractory childhood epilepsy and its impact on both clinical and electroencephalograghic aspects.

PATIENT AND METHODS

This interventional comparative study was carried out on 30 patients with refractory epilepsy, at PICU and Pediatric Neurology Unit of Al-Hussein University Hospital, during the period from December 2017 to November 2018, and divided into two groups: Group A (intervention group) and group B (control group).

Inclusion Criteria:

- Age, from 2 months up to 18 years, and both genders were included.
- Children with refractory epilepsy, defined as 'failure of adequate trials of two tolerated, appropriately chosen and used, anti-epileptic drug schedules, whether as monotherapy or in-combination, to achieve a sustained seizure-freedom **(Kwan et al., 2010)**.

Exclusion Criteria:

- Acute CNS disorders (e.g. infection, stroke, and tumours).
- Patients with infantile spasms, autoimmune disorders, or progressive degenerative or metabolic disorders.

Plan of the Study:

All patients were subjected to the following:

A. Thorough history-taking.

B. Thorough clinical examination.

C. Laboratory investigations:

1. Complete blood counts.
2. Liver function tests.
3. C-reactive protein, albumin, urea, creatinine and serum electrolytes (Na, K, calcium, phosphorous, magnesium, alkaline phosphatase).

D. Electroencephalography (EEG):

(EEG) was done, on admission and post-control therapy, by the pediatric neurologist using (E-Series-EEG 64 Control module, S/N 5840, Compumedics, Australia).

E. Adequate rational of AED polytherapy.

F. For the intervention group (group A), the following was added:

Intravenous methylprednisolone 30 mg/kg once daily, for 3 consecutive days, followed by oral prednisolone 2 mg/kg/day, in 3 divided doses, for 2 weeks then gradually tapered over 4 weeks.

Follow up were performed by:

1. Pediatric neurologist to document therapeutic response and occurrence of side effects.
2. Therapeutic response was recorded as: complete (seizure-freedom), good (>50% seizure reduction), fair (<50% seizure reduction), or none (no response).
3. Seizure outcome was assessed based on seizure-diaries prepared by the parents, during follow-up at Al-Hussein Pediatric Neurology Unit for 6 months.

Ethical Considerations:

1. Approval of ethical committee, Faculty of Medicine, Al-Azhar University.
2. Written consents from the parents of the patients.
3. The patients have the right to withdraw from the study at any time.
4. All the obtained data are confidential and the patients have the right to keep them.
5. The authors declare that there is no any financial conflict regarding the research and publication.
6. No conflict of interest regarding the study and publication.

Statistical Analysis:

The data were collected, tabulated, and analyzed by SPSS (Statistical Package for Social Science) computer software program version 19.

Two types of statistics were done:

- Descriptive statistics {e.g. percentage (%), mean (x) and standard deviation (SD)},
- Analytical statistics: which include the following tests:

- Student (t) test: was used to study statistical significance between two quantitative variables.
- Chi-square test (x2): was used to study statistical significance between two qualitative variables.
- P-value of < 0.05 was considered statistically significant.

RESULTS

Table (1): Demographic Data of the Study Groups

	Group A (n=15)	**Group B (n=15)**	**P value**
Age (yr):			
Mean ± SD	5.16 ± 2.742	5.9 ± 3.19	0.5133^
Range	4 mo – 10 yr	4 mo – 11 yr	
Gender: n (%)			
Male	10 (66.67%)	7 (46.67%)	0.269#
Female	5 (33.33%)	8 (53.33%)	
Age of onset of seizures (yr):			
Mean ± SD	2.45 ± 2.739	3.2 ± 2.873	0.4855^
Range	2 mo – 9 yr	2 mo – 10 yr	

There was no statistically significant difference between the study groups regarding age, gender and onset of seizures, denoting that both groups are comparable with no risk of bias.

Table (2): Etiology of Seizures among the Study Groups

	Group A		Group B	
	n	**%**	**n**	**%**
Brain atrophy	1	6.67%	0	0%
Focal cortical dysplasia	1	6.67%	0	0%
Mitochondrial disorder	1	6.67%	1	6.67%
Post-encephalitis	1	6.67%	1	6.67%
Post-meningitis	1	6.67%	2	13.33%
Hydrocephalus	0	0%	2	13.33%
HIE	2	13.33%	1	6.67%
LKS	1	6.67%	1	6.67%
LGS	4	26.67%	3	20%
Idiopathic	3	20%	4	26.67%
P value	0.814#			

HIE: Hypoxic Ischemic Encephalopathy, LGS: Lennox-Gastaut syndrome, LKS: Landau–Kleffner syndrome

Our patients had different etiologies of their seizures, with 2 main etiologies were recorded among the study groups, LGS and idiopathic epilepsy, with no statistically significant difference between both groups.

Table (3): Number of Anti-epileptic Drugs Used among the Study Groups

	Group A		Group B	
	n	**%**	**n**	**%**
2 Drugs	3	20%	7	47%
3 Drugs	11	73%	8	53%
4 Drugs	1	7%	0	0%
P value	0.215 #			

There was no statistically significant difference between the studies groups regarding number of anti-epileptic drugs, with most of the patients were on 2 or 3 drugs.

Table (4): Seizure-Types among the Study Groups

	Group A		Group B	
	n	%	n	%
GTC**	5	33.33%	4	26.67%
Focal +secondary generalization	2	13.33%	4	26.67%
Atypical absence seizures	2	13.33%	1	6.66%
Multiple-seizures type	6	40%	6	40%
P value	0.774 #			

**GTC: Generalized Tonic Clonic

Seizure-types among the study groups were comparable, with 2 main types were recorded, GTC and multiple seizures-type, with no statistically significant difference between both groups.

Table (5): EEG-Findings among the Study Groups, before Treatment

	Group A		Group B	
	n	%	n	%
Normal	1	6.67%	2	13.33%
Abnormal	14	93.33%	13	86.67%
P value	0.543 #			

There was no statistically significant difference between the study groups regarding EEG-findings, before treatment.

Table (6): EEG-Findings among the Study Groups, after treatment

	Group A (AED+ pulse therapy)		Group B (AED)	
	n	%	n	%
Normal	9	60%	3	20%
Abnormal	6	40%	12	80%
P value	0.025* #			

There was a statistically significant EEG improvement (normal EEG) among group A more than among group B, after treatment.

Table (7): EEG-Findings among Group A, before and after Treatment

	Group A (before treatment)		Group A (after treatment)	
	n	%	n	%
Normal	1	6.67%	9	60%
Abnormal	14	93.33%	6	40%
P value	0.005* #			

There was a statistically significant EEG improvement (normal EEG) among group A, after treatment.

Table (8): Therapeutic Response (EEG Findings) among Group A

	n	%
Normal	9	60%
Fair control	4	26.67%
No improvement	2	13.33%

After treatment among group A, 9 patients showed full improvement (normal EEG), 4 patients showed fair control (less frequent spikes on EEG) and 2 patients showed no improvement (same abnormalities).

Table (9): EEG-Findings among Group B, before and after treatment

	Group B (before treatment)		Group B (after treatment)	
	n	%	n	%
Normal	2	13.33%	3	20%
Abnormal	13	86.67%	12	80%
P value	0.624 #			

There was no statistically significant EEG improvement after treatment among group B.

Table (10): Therapeutic Response (EEG Findings) among Group B

	n	%
Normal	3	20%
Fair control	2	13.33%
No improvement	10	66.67%

After treatment among group B, 3 patients showed full improvement (normal EEG), 2 patients showed fair control (less frequent spikes on EEG) and 10 patients showed no improvement (Abnormal EEG).

Table (11): Frequency of Seizures among the Study Groups, before Treatment

	Group A		Group B	
	n	%	n	%
Daily	15	100%	12	80%
Weekly	0	0%	3	20%
P value	0.068 #			

There was no statistically significant difference between the study groups regarding frequency of seizures before treatment.

Table (12): Frequency of Seizures among the Study Groups, after Treatment

	Group A		Group B	
	n	%	n	%
Daily	4	26.67%	10	66.67%
Weekly	3	20%	2	13.33%
Monthly	2	13.33%	2	13.33%
None	6	40%	1	6.67%
P value	0.036* #			

There was a statistically significant reduction of frequency of seizures after treatment among group A more than among group B.

Table (13): Frequency of Seizures among Group A, before and after Treatment

	Group A (before treatment)		Group A (after treatment)	
	n	**%**	**n**	**%**
Daily	15	100%	4	26.67%
Weekly	0	0%	3	20%
Monthly	0	0%	2	13.33%
None	0	0%	6	40%
P value	0.0006* #			

There was a statistically significant reduction of seizures among group A after treatment.

Table (14): Frequency of Seizures among Group B, before and after Treatment

	Group B (before treatment)		Group B (after treatment)	
	n	**%**	**n**	**%**
Daily	12	80%	10	67%
Weekly	3	20%	2	13%
Monthly	0	0%	2	13%
None	0	0%	1	7%
P value	0.3359 #			

There was no statistically significant reduction of seizures before and after treatment, among group B.

Table (15): Percentage of Seizures-Reduction among the Study Groups, after Treatment

	Group A		Group B	
	n	**%**	**n**	**%**
100 % Reduction	6	40%	1	7%
>50% Reduction	4	26.67%	2	13%
<50% Reduction	4	26.67%	2	13%
No response	1	6.66%	10	67%
P value	0.007* #			

There was a statistically significant seizures-reduction among group A more than among group B after treatment, (66.67% seizures-reduction among group A vs 20% seizures-reduction among group B, with P value=0.0011*).

Table (16): Adverse Effects of Methylprednisolone among Group A

	n	%
Clinical:		
Weight gain	4	26.67%
GIT upset	3	20%
Irritability	3	20%
Laboratory:		
Hyperglycemia (Transient)	1	6.67%

Adverse effects of steroids were infrequent, mild and transient with no major adverse effects.

DISCUSSION

This interventional comparative study was carried out on 30 patients with refractory epilepsy at PICU and Pediatric Neurology Unit of Al-Hussein University Hospital during the period from December 2017 to November 2018. The aim of this study was to evaluate efficacy and adverse effects of high dose intravenous methylprednisolone as an add-on therapy for refractory childhood epilepsy and its impact on both clinical and electroencephalographic aspects. They were divided into two groups: Group A (intervention group) and group B (control group).

Children from 2 months up to 18 years and of both genders with refractory epilepsy, defined as 'failure of adequate trials of two tolerated, appropriately chosen and used anti-epileptic drug schedules, whether as monotherapy or in-combination, to achieve a sustained seizure-freedom, were included **(Kwan et al., 2010)**.

Patients with infantile spasms, autoimmune disorders, or progressive degenerative or metabolic disorders were excluded.

For both groups the following were carried out: Thorough history-taking and physical examination, laboratory

investigations, EEG on admission and post-control therapy, general supportive care and conventional antiepileptic drugs.

For the intervention group (group A): Intravenous methylprednisolone 30 mg/kg once daily, for 3 consecutive days, followed by oral prednisolone 2 mg/kg/day, in 3 divided doses, for 2 weeks then gradually tapered over 4 weeks.

There was no statistically significant difference between the study groups regarding age, sex and onset of seizures.

Our patients had different etiologies of their seizures with the main etiology was idiopathic epilepsy; (3 cases among group A (20%) and 4 cases among group B (26.67%) and LGS; (4 cases among group A (26.67%) and 3 cases among group B (20%). Seizure-Types among the study groups were comparable with 2 main types were recorded, GTC and multiple-seizures type, table (2). There was no statistically significant difference between the study groups regarding number of anti-epileptic drugs with most of patients were on 2 or 3 drugs, Table (3).

As regard EEG findings, there was no statistically significant difference between the study groups. There was statistically significant improvement regarding EEG findings after treatment among group A more than among group B. There was statistically significant improvement EEG-findings among group A before and after treatment. After treatment among group A, 9 patients showed full improvement (normal EEG), 4 patients showed fair control (less frequent spikes on EEG) and 2 patients showed no improvement (same EEG abnormalities). There was no statistically significant difference, before and after treatment among group B. After treatment among group B, 3 patients showed full improvement (normal EEG), 2 patients showed fair control (less frequent spikes on EEG) and 10 patients showed no improvement (same EEG abnormalities), Table (8, 10).

In agreement with our study, **(Pera et al., 2015)** reported that 11 children with epileptic encephalopathy were administered 1 cycle of intravenous methylprednisolone (15-30 mg/kg/day for 3 consecutive days, once a month for 4 months) in addition to constant dosages of their regular antiepileptic drug. That treatment resulted in statistically significant reductions of generalized slow spike-and-

wave discharges (p=0.0028), which persisted even after methylprednisolone pulse therapy was stopped.

Also, **(Almaabdi et al., 2014)** showed that follow-up EEG recordings, performed 4-6 months after treatment, revealed no epileptiform discharges in 7 (41%) children, all of whom had a favorable therapeutic response. In their study, 17 children with severe drug-resistant epilepsy (having failed multiple antiepileptic drug trials) were included. Most children (88%) had ongoing daily seizures and 13 (76%) had been admitted previously with status epilepticus. IV methylprednisolone was given at 15 mg/kg per day followed by a weaning dose of oral prednisolone for 2-8 weeks (mean 3 weeks).

Also, **(Bast et al., 2014)** found that after four pulses of methylprednisolone therapy, 30 of 54 (56%) patients were responders, according to several clinical and electroencephalography criteria. A response was not correlated with any epilepsy-related clinical factor. The treatment consisted of four pulses with single doses of 20 mg/kg/day methylprednisolone (MPR), administered every week on 3 consecutive days. After this initial phase, the intervals between the pulses were increased based on individual factors. MPR pulses were administered exclusively orally in 39 patients and 7.8% of all pulses were applied intravenously. The patients received a median of eight MPR pulses (range, 1–52), and the median duration of the therapy was 11 weeks.

Moreover, **(Verhelst et al., 2005)** found that a positive effect on EEG recordings (normalization, decrease in epileptiform activity, and/or improvement of background activity) was noticed among 15 out of the 36 treatment courses and in all the 13 responders. Among the 19 patients without reduction in seizure frequency, improvement of EEG was only noticed among 2. In their study, 32 pediatric patients (16 boys, 16 girls) who were treated with steroids for intractable epilepsy at the Ghent University Hospital, Epilepsy and Rehabilitation Center Pulderbos and the Academic Hospital of Brussels between 1993 and 2003 were included. Patients with West syndrome and patients who received a single dose for status epilepticus were excluded.

As regard frequency of seizures, there was no statistically significant difference between the study groups regarding frequency of seizures before treatment. There

was statistically significant decrease among group A more than among group B regarding frequency of seizures after treatment. There was statistically significant decrease in frequency of seizures after treatment among group A. After treatment among group A, 6 patients showed full improvement (100 % seizure-reduction), 4 patients showed good control (<50% seizure-reduction), 4 patients showed fair control (>50% seizure-reduction), and 1 patient showed no improvement (no change in frequency). There was no statistically significant difference among group B, before and after treatment, table (14, 15).

After treatment among group B, 1 patient showed full improvement (100 % seizure-reduction), 2 patients showed good control (<50% seizure-reduction), 2 patients showed fair control (>50% seizure-reduction), and 10 patients showed no improvement (no change in frequency), table (15).

There was statistically significant seizure reduction after treatment among group A more than among group B, (66.67% seizure-reduction among group A vs 20% seizure-reduction among group B with P value = 0.0011*), table (14).

In agreement with our study, **(Pera et al., 2015)** who showed that the treatment resulted in statistically significant reductions of seizure frequency (p=0.013), which persisted even after methylprednisolone pulse therapy was stopped. A globally positive outcome was noted in 9/11 patients (81.8%).

Also, **(Almaabdi et al., 2014)** found that after pulse steroid therapy, 6 (35%) children became completely seizure free; however, 3 of them later recurred. The timing and frequency of clinical follow-up varied among patients, but all had follow-up at 6 months. Most of those with favorable response (7 of 10) did so in the initial 2 weeks of therapy. Patients with mixed seizures were more likely to have a favorable response when compared with those with one seizure type (49% vs 31%, P = 0.02). No beneficial response was noted in 7 (41%) children; however, none had seizure worsening.

Also, **(Bast et al., 2014)** showed that the response was maintained in 19 of 30 (63%) patients, and 3 of 24 (13%) without initial response became seizure-free (total responder rate at the end of the therapy 22/54 [41%]).

Moreover, **(Sevilla-Castillo et al., 2009)** found that the frequency of epileptic seizures was reduced by more than 50 % in 12/14 patients during methylprednisolone treatment. The median number of seizures before treatment with methylprednisolone was 8, 8, and 7; during the treatment: 1, 1, and 1; and after treatment: 2, 2, and 3 ($p < 0.001$). In their study, 14 children with refractory epilepsy (all were receiving two antiepileptic drugs having different mechanisms of action. For 5 consecutively days, each patient received methylprednisolone by intravenous administration at a dosage of 15 mg/kg/day each 8 hr, once a month for 3 months.

Moreover, **(Verhelst et al., 2005)** showed that of the total of 36 treatment courses, 17 (47%) lead to a clinically significant response and 19 did not. 13 (36%) patients were responders of whom 9 (25%) became seizure free and 4 (11%) had a reduction in seizure frequency > 50%. Another 4 (11%) had a reduction in seizure frequency of < 50%. Of the 9 patients with seizure freedom during therapy, 3 remained seizure free after long-term follow up (28 months to 4 years), and 6 patients relapsed, 1 after 10 months and 5 during the first month after stop steroids. However, 4 of the 6 patients with relapse seizures still had a residual seizure control > 50% at the end of follow-up (1—8 year). Of the overall group of 13 responders, 8 had still a seizure frequency reduction > 50%, of which 3 were seizure free, at the end of the study (1-8 years follow-up). Also, they found that the only factor that correlates with becoming seizure free was a longer duration of treatment, independently of the type of steroid. Of the 19 patients without any clinically significant response, 13 patients were treated for < 4 weeks, 2 between 4 weeks and 6 months and only 4 patients > 6 months. Although, it should be mentioned that in 2 patients steroid therapy was stopped after 4 weeks because of lack of response.

Regarding adverse effects of steroids, our study showed that they were infrequent, mild and transient with no major side effects. Weight gain (26.67%), GIT upset (20%), irritability (20%) and transient hyperglycemia (6.67%) were reported, table (16).

(Pera et al., 2015) found that no significant or persistent side effects were noted, only a modest transient hyperglycemia in the 24 hours after infusion in 1 patient and a modest weight gain in 1/11 patient (9.1%) (this patient had

introduced valproic acid therapy one month before the start of the pulse therapy).

(Almaabdi et al., 2014) reported no major side effects were noted, specifically hypertension or glucosuria, six (35%) of the parents reported improvements in their child's level of alertness and appetite. This may be related to seizure reduction rather than a direct drug effect.

(Bast et al., 2014) reported that most patients experienced adverse effects that were typically mild and transient in 38 (70%) children. unspecific symptoms, such as tiredness, irritability, or mood alteration in 18 cases. At least 1 infection occurred in 19 children, 6 children developed a transient cushingoid appearance, 2 children presented with repetitive abnormal blood glucose levels (maximum 172 mg/dl), and blood pressure showed mildly elevated values in 2 children. In an 8-month-old girl, nephrocalcinosis and mild cardiac septal hypertrophy without functional deficit were observed and returned normal. Transient sinus bradycardia during sleep was noticed in 3 children.

(Sevilla-Castillo et al., 2009) reported that one patient had a mild increase in blood pressure (130/95) and another patient complained of muscle cramps in the lower limbs during treatment with methylprednisolone, but it was not necessary to stop treatment because they resolved spontaneously.

(Verhelst et al., 2005) reported that side effects were noticed in 23 of the 36 treatment courses and included obesity (6), increased weight (5) or improved appetite (3), Cushing syndrome (7), behavioural disturbance (4), hypertension (3), hypokalaemia (1), femur fracture (1) and cardiac decompensation (1). A positive correlation between duration of treatment and side effects was found. No correlation was seen between type of steroid and number and severity of side effects.

Limitation of the Study

1. Limited number of cases of refractory epilepsy.
2. Uncompliance of treatment in some patients
3. Withdrawal of some patients from the study
4. Refuse of pulse steroid therapy by some patients

CONCLUSION

From our study we concluded that intravenous methylprednisolone as an add-on therapy for refractory childhood epilepsy is effective on both

clinical (frequency of seizures) and electroencephalographic aspects. Adverse effects of methylprednisolone were infrequent, mild and transient with no major side effects.

RECOMMENDATIONS

From our study we recommend that:

- Intravenous pulse methylprednisolone therapy is a reasonable option in pediatric patients with refractory epilepsy.
- Intravenous methylprednisolone 30 mg/kg once daily, for 3 consecutive days, followed by oral prednisolone 2 mg/kg/day for 2 weeks then gradually tapered over 4 weeks.
- Follow up of these patients should include clinical and electroencephalograghic criteria with monitoring of adverse effects.

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كفاءة وقابلية التحمل للكورتيزون المكثف كعلاج إضافى فى مرضى الصرع المقاوم للادوية المضادة للصرع

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الهدف : نهدف الى تقييم الفاعلية والآثار الناتجة لإستخدام دواء الميثيل بريدنيزولون عن طريق الوريد كعلاج إضافى للأطفال الذين لايستجيبون لأدويه الصرع التقليدية (اثنان دواء أو اكثر) فى وحدة العناية المركزة للأطفال ووحدة الأمراض العصبية للأطفال فى مستشفى الحسين الجامعي وأثرها على الجوانب الإكلينيكية والكهربائية الدماغية.

المنهجية: أجريت هذه الدراسة على 30 مريضاً يعانون من الصرع المقاوم للأدوية المضادة للصرع ، في وحدة العناية المركزة للأطفال ووحدة الأمراض العصبية للأطفال فى مستشفى الحسين الجامعي ، خلال الفترة من ديسمبر 2017 إلى نوفمبر 2018 ، وقسمت إلى مجموعتين: المجموعة (أ) (مجموعة الدراسة) والمجموعة (ب) (مجموعة المراقبة). شملت جميع المرضى الذين تتراوح أعمارهم بين شهرين حتى 18 سنة من كلا الجنسين. تم استبعاد المرضى الذين يعانون

من تشنجات الرضع ، واضطرابات المناعة الذاتية ، أو الاضطرابات التنكسية أو الأيض التدريجي. تم أخذ التاريخ المرضي وإجراء الفحص السريري الكامل وتم إجراء الاختبارات المعملية في المستشفي السابقة. تم إجراء رسم المخ الكهربائى أثناء وبعد أخذ العلاج، تم إعطاء ميثيل بريدنيزولون الوريدي عند (30ملجم/كجم) مرة واحدة يومياً ، لمدة (3) أيام متتالية ، يليه بريدنيزولون عن طريق الفم (2 ملجم/كجم/ يوم) ، على (3) جرعات مقسمة ، لمدة أسبوعين ثم سحبه تدريجيًا على مدى (4) أسابيع.

النتائج: أظهرت النتائج عدم وجود فرق بين مجموعات الدراسة فيما يتعلق بالعمر والجنس وبداية النوبات. أظهرت الدراسة أن إثنين من المسببات الرئيسية تم تسجيلها بين مجموعات الدراسة، متلازمة لينوكس غاستو والصرع المجهول السبب.

جميع الأطفال بين المجموعة (أ) (100٪) لديهم نوبات يومية ، وبين المجموعة (ب) (80٪) لديهم نوبات يومية و (20٪) لديهم نوبات أسبوعية. وتبين الدراسة أن أنواع التشنجات بين مجموعات الدراسة كانت متقاربة ، مع وجود نوعين رئيسيين تم تسجيلهما، تشنجات عامة وتشنجات متعددة، بعد 6 اشهر من بدء العلاج أظهرت النتائج تحسن فى رسم المخ الكهربائى للمجموعة (أ) أكثر من المجموعة (ب) حيث اظهرت تحسن بعد العلاج فى المجموعة (أ) (9) أطفال (رسم المخ الكهربائي طبيعي) ، وتحسن جزئى لـ(4) أطفال ولم

يستجب عدد اثنين من الأطفال (لم يتغير رسم المخ الكهربائى).

لم يكن هناك دلالة إحصائية بين المجموعة (ب) قبل وبعد العلاج ، حيث ظهر بعد العلاج تحسن كامل لـ(3) أطفال (رسم المخ الكهربائي طبيعي) وتحسن جزئي لـ (2) من الأطفال بينما (10) أطفال لم يتغير رسم المخ الكهربائى لديهم.بالنسبه لمعدل حدوث التشنجات كان هناك انخفاض ذو دلاله احصائيه فى المجموعه (أ)اكثر من المجموعه (ب) انخفاض بنسبه(26.67%) فى المجموعه (أ) مقابل (20%) انخفاض فى المجموعه (ب).

اظهرت النتائج ان الآثار الجانبية لإستخدام الكورتيزون المكثف هى آثار منخفضة ومعتدلة وعابرة ولم يحدث أى آثار جانبية رئيسية.