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Intravenous Immunoglobulin versus Methylprednisolone in Children with Acute Disseminated Encephalomyelitis: A Randomized Control Trial

Running Title: Which one is better?-IVIG or Methylprednisolone in children with ADEM

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Abstract: ***Background**: Acute disseminated encephalomyelitis (ADEM) is an immune-mediated, demyelinating disease of the central nervous system (CNS) affecting children and young adults after an infection or vaccination. Because of its heterogeneity in both clinical presentation and course, challenges remain in establishing the most appropriate therapeutic approach in each patient. The present study is a randomised controlled trial with the objective of assessing the neurological recovery in children with ADEM at intervals after completion of treatment with IVIG using IV methylprednisolone as a control. The secondary objectives were to assess the duration of hospital stay, residual neurologic deficits including mortality and other adverse reactions in the two treatment groups. **Methods**: A randomised controlled trial was conducted in the Department of Pediatrics, IMS, BHU comprising of 22 children aged 0-18 years with diagnosis of ADEM randomly allocated to Group I (12 children, received IV Methylprednisolone) and Group II (10 children, received Intravenous immunoglobulin) and assessed for neurological recovery using modified Rankin scale at 1 week, 1 month and 3 months after treatment completion. Duration of hospital stay, mortality and adverse reactions of drugs were also compared in both the groups. **Results**: Neurological recovery at 1weekis comparable between both groups however, in long term (at 3 months) both the groups had 3 patients (25% of group I and 30% of group II) with neurological deficit. The mean duration of hospital stay was comparable in two groups. Two (9.09%) patients of group I expired during treatment. In methylprednisolone group, 25% subjects developed hyperglycemia and hypertension whereas in IVIg group, 10% children developed hypersensitivity reaction and 20% developed fever and back pain. **Conclusion**: Intravenous immunoglobulin hastens the clinical recovery in children with ADEM as compared to IV methylprednisolone but the overall morbidity, long term neurological sequel is similar with both the drugs.***

CTRI/2017/11/010618 [Registered with Clinical Trial Registry India on 23/11/2017]

Keywords: ADEM, children, IVIg, Methylprednisolone, treatment, outcomes, safety, efficacy

1. Introduction

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated demyelinating CNS disorder with predilection to early childhood. ADEM is generally considered a monophasic disease. It principally involves the white matter tracts of the cerebral hemispheres, brainstem, optic nerves, and spinal cord.

The main bacterial infection, which has been implicated with the occurrence of ADEM, is mycoplasma. Currently, postimmunisation encephalomyelitis is most commonly associated with measles, mumps, and rubella vaccinations. Population-based studies show the incidence of ADEM to be 0.3–0.6 per 100, 000 per year[1, 2]. The median age at presentation of ADEM is 5–8 years, with male predominance.

ADEM is defined as a first clinical event with acute or subacute onset that affects multifocal areas and the clinical presentation must be polysymptomatic and must include unexplained encephalopathy along with focal or multifocal lesions, predominantly involving white matter, without radiologic evidence of previous destructive white matter changes:

Demyelinating lesions of ADEM are better visualised by MRI. The pathological hallmark of ADEM is perivenular inflammation with limited ‘‘sleeves of demyelination[4, 5]. ”Serial MRIs play an important role to confirm the ADEM diagnosis retrospectively.

Systemic symptoms like fever, malaise, myalgias, headache, nausea, and vomiting begin 4–21 days after the insult and often precede the neurological symptoms of ADEM which progress rapidly with peak dysfunction in several days. In childhood ADEM, long lasting fever and headaches occur more frequently, but in adult cases, motor and sensory deficits predominate[6].

Cerebrospinal fluid changes include increased pressure, lymphocytic pleocytosis (up to 1000/ mm3), and raised protein (usually <1.0 g/l). Rarely, in cerebrospinal fluid oligoclonal band of IgG may be demonstrated which disappears as the patient improves[7-8]. Electroencephalographic abnormalities are common but are usually non-specific[9].

Corticosteroids are generally considered as first-line therapy (class IV) [10, 11]. IVIg is an option for second-line treatment or if contraindications to corticosteroids exist (class IV) [12, 13]. Acute therapy for ADEM has not been studied rigorously, either in pediatric or in adult patients. Although the experience with intravenous immunoglobulin in either adults or children with severe acute encephalomyelitis is scarcer, it has also proven efficacious, especially when high-dose methylprednisolone initially failed[14-18].

Recovery occurs over the course of weeks or months. The mortality varies between 10% and 30%, with complete recovery in 50%[19-24]. Poor prognosis is correlated with severity and abruptness of onset of the clinical syndrome. Longterm cognitive deficits have been observed, affecting attention, executive function, verbal processing, and behaviour, as well as IQ scores, specifically in children with ADEM before age 5 years[25, 26]. Relapse occurs at the interval of 6-22 months, mean 6 months[24].

Plasmapheresis has been effective as a mode of therapy for ADEM who failed to improve on steroids[27, 28].

We conducted a prospective randomized trial using IV methylprednisolone as a control to address the efficacy and safety of IVIg in the treatment of ADEM.

2. Materials and Methods

This randomised control study was conducted in Department of Paediatrics, Institute of Medical sciences, Banaras Hindu University, Varanasi. The period of study was October 2016 to June 2018. The Ethics Committee of Institute has approved the study protocol. CTRI registration also done.

Design of the study: Randomized control trial

Research hypothesis: Intravenous immunoglobulin is as effective as intravenous methylprednisolone, in patients of Acute Disseminated Encephalomyelitis in terms of recovery.

Research Question: In hospitalized ADEM children (**P),** what is the effect of Intravenous immunoglobulin (**I),** compared with Intravenous methylprednisolone **(C),** on neurological recovery (**O)** at discharge and 3 months follow up (**T).**

Inclusion criteria: The study included all children 0-18 years admitted in emergency paediatric ward with clinical features of any focal neurological deficit/s with normal cerebrospinal fluid studies and suggestive MR imaging i. e. increased signal intensity on T2 weighted image & fluid attenuated inversion recovery sequence (FLAIR) as large, globular, multiple and asymmetric lesion. Imaging criteria is mentioned in **Table-1**.

Exclusion criteria: Children with acute bacterial and tubercular meningitis, intracranial space occupying lesion, underlying known autoimmune and connective tissue disorder was excluded from the study.

Randomization: After inclusion into the study children were randomly assigned to intravenous immunoglobulin group and methylprednisolone group using computer generated block randomization sequence of variable block sizes (4, 6 or 8). Allocation concealment was ensured by placing the sequence in serially numbered opaque and sealed envelopes.

Primary outcome:
1) Neurological recovery at 1 week, 1 month and 3 months.

Secondary outcomes:
1) Residual neurological deficit in follow up,
2) Duration of hospital stay and mortality due to the disease,
3) Adverse reactions of both treatment groups.

All included patients were classified in two groups:

Group I: Intravenous methylprednisolone is given at a dosage of 30 mg/kg per day (maximum 1 g/day) for 5 days, followed by an oral corticosteroids in tapering dose over 4 to 6 weeks.

Group II: Intravenous immunoglobulin G (IVIg) is given at a dosage of 2 g/kg divided over 2 days, followed by oral corticosteroids in tapering dose over 4 to 6 weeks.

The residual neurological deficit is measured by **The Modified Rankin Scale (mRS)** at admission, at 1 week, at 1 month and at 3 months and if possible thereafter also. The scale runs from 0 to 6, ranging from perfect state without symptom to death.

- 0-No symptom.
- 1-No significant disability, able to carry out all usual activities, despite some symptoms.
- 2-Slight disability, able to look after own affairs without assistance. But unable to carry out all previous activities.
- 3-Moderate disability requires some help, but able to walk unassisted.
- 4-Moderately severe disability, unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5-Severe disability, requires constant nursing care and attention, bedridden, incontinent.
- 6-Dead.

Laboratory workup: Other laboratory work up like complete blood count, renal function test, liver function test, serum electrolytes, arterial blood gas cerebrospinal fluid analysis were done in all cases.

Diagnostic criteria for ADEM:

International Pediatric MS Study Group-Consensus Definitions (Diagnostic criteria) [29, 30]

Monophasic ADEM

A first clinical event with a presumed inflammatory or demyelinating cause, with acute or subacute onset that affects multifocal areas of the CNS; the clinical presentation must be polysymptomatic and must include encephalopathy, which is defined as one or more of the following:

- Behavioral change, e. g., confusion, excessive irritability.
- Alteration in consciousness, e. g., lethargy, coma.
- Event should be followed by improvement, clinically, on MRI, or both, but there may be residual deficits.
- Patient has no history of clinical episode with features of a prior demyelinating event.
- No other etiologies can explain the event.
- New or fluctuating symptoms, signs, or MRI findings occurring within 3 months of the inciting ADEM event are considered part of the acute event.
- Brain MRI, with FLAIR or T2-weighted images, reveal large (>1 to 2 cm) lesions that are multifocal, hyperintense, and located in the supratentorial or infratentorial white matter regions; gray matter, especially basal ganglia and thalamus, without radiologic evidence of previous destructive white matter changes on FLAIR sequence (**Figure iA** &**ii).**
- Spinal cord MRI may show confluent intramedullary lesion (s) with variable enhancement, in addition to abnormal brain MRI findings specified previously **(Figure iB).**

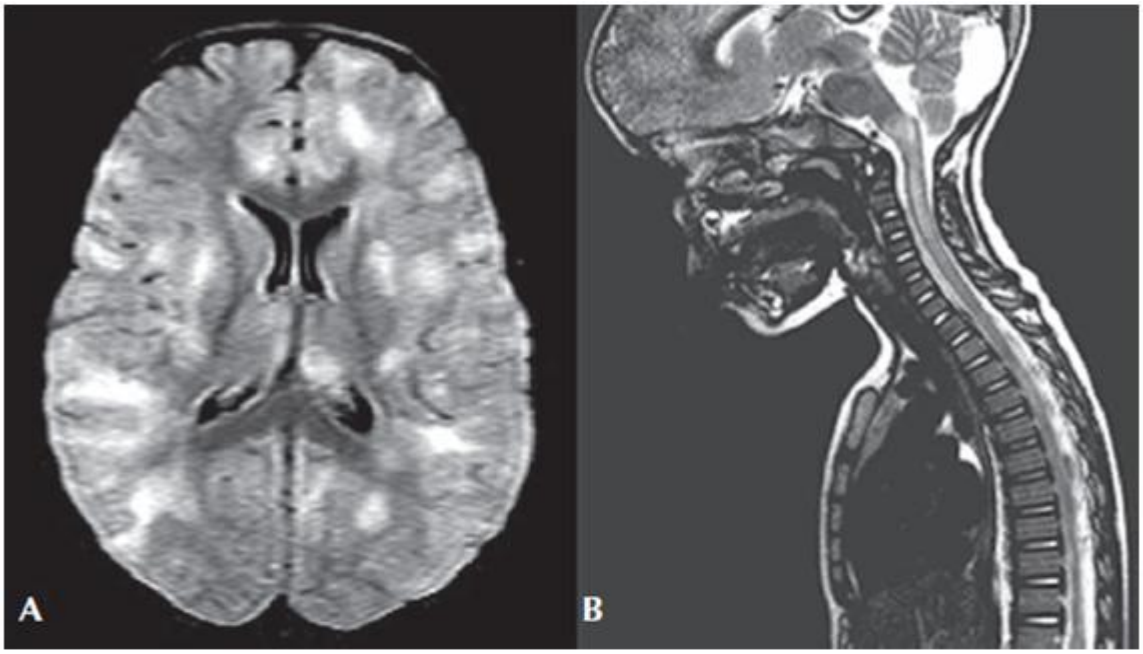

Figure i (A) and i (B)

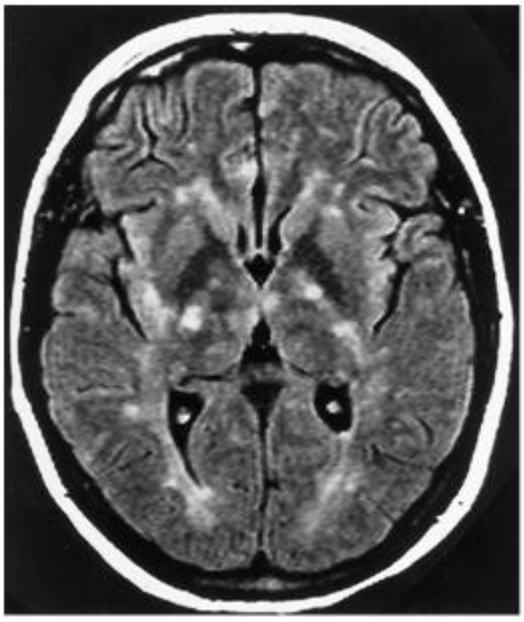

Figure (ii)

Statistical Analysis

The statistical program SPSS version 20.0 was used for data entry and analysis. Independent samples T-test, Mann Whitney U test, Chi-Square test and Fisher exact test were used to compare continuous and categorical variables between groups. One way analysis of variance (ANOVA) test and *post hoc* Bonferroni test were used to find out the significant difference among multiple groups. A P value of <0.05 was considered statistically significant.

3. Results

The present study included 22 cases of acute disseminated encephalomyelitis (ADEM) admitted in our Paediatric ward and ICU, Institute of Medical Sciences, Banaras Hindu University, Varanasi from September 2016 to June 2018.

Out of 22 cases of ADEM, 12 (54.54%) children were in Group I i.e. methylprednisolone group and 10 (46.46%) children were in Group II i. e. Intravenous Immunoglobulin group. In both the groups 6-10 years constitute the majority (50% of patients). In IVIg group majority were male i. e.6

(60%) and female were 4 (40%). Among 22 cases of ADEM fever was most common clinical symptom. In neurological examination, among 22 patients most common clinical sign was presence of Babinisky sign. Among lab parameters 5 patients were anaemic, 2 (16.7%) in group I and 3 (30%) in group II but none of them were severely anemic. In CSF study among enrolled children with ADEM, CSF glucose was normal. CSF protein was raised in group I (mean 50.83 mg/dl) in respect to group II (mean 19.9 mg/dl), but the value is statistically insignificant. Among MRI changes all the patients had patchy areas of increased signal intensity, most commonly observed either in brain or in brain and spine. The baseline characteristics of enrolled subjects are enlisted in **Table 1**.

Table 1: Baseline characteristics of the subjects enrolled in the treatment groups

Parameters	Group-I (n=12)	Group-II (n=10)
Age		
-0 to5 yr	2 (16.6%)	2 (20%)
-5 to10yr	5 (41.7%)	6 (60%)
->10 yr	5 (41.7%)	2 (20%)
Sex		
Male	6 (50%)	6 (60%)
Female	6 (50%)	4 (40%)
Symptoms		
-Fever	9 (75%)	8 (80%)
-Headache	6 (50%)	4 (40%)
-Vomiting	4 (33.33%)	6 (60%)
-Rash	2 (16.6%)	1 (10%)
-Diarrhoea	0 (0%)	2 (20%)
-URTI	2 (16.6%)	5 (50%)
-Joint pain	1 (8.33%)	1 (10%)
-Seizure	6 (50%)	3 (30%)
-Altered sensorium	8 (66.6%)	6 (60%)
-Bowel/ Bladder involvement	9 (75%)	6 (60%)
-Psychiatric manifestation	1 (8.33%)	0 (0%)
Signs		
-Tone abnormalities	7 (58.33%)	5 (50%)
-Cranial nerve involvement	0 (0 %)	2 (20%)
-Extensor planter present	8 (66.7%)	7 (70%)
-Sensory involvement	1 (8.33%)	1 (10%)
-Meningeal signs present	1 (8.33%)	1 (10%)
-Autonomic involvement	1 (8.33%)	0 (0%)
CSF findings		
-Total cell count	10+20.7	5.4±4.8
-Total protein (mg/dl)	50.83±70.09	19.9±11.31
MRI changes		
1) Patchy areas of increased signal intensity		
-Brain	7 (58.3%)	3 (30%)
-Spine	0 (0%)	4 (40%)
-both	5 (41.7%)	3 (30%)
2) Contrast enhanced lesions	10 (83.3%)	8 (80%)
3) Perifocal oedema present	3 (25%)	3 (30%)
4) Gray matter involvement	8 (66.7%)	4 (40%)
Blood parameters		
-Total leucocyte count (cumm.)	13070.83 ± 9234.06	12676 ± 3677.55
-Serum creatinine (mg/dl)	0.55± 0.138	0.48±0.155
-Serum sodium (mEq/L)	139.87±4.42	138.74±1.95
-Blood glucose (mg/dl)	119.5±39.25	97.5±30.57

Recovery at 1wk after discharge is comparable between both the groups. Most of the patients who received IVIg improved at 1month as compared to patients receiving methylprednisolone, 5 (50%) patients in group II had mRS score 0, whereas only 2 (16.7%) patients in group I had mRS score 0 at 1 month follow up but the values are not statistically significant. Most of the patients recovered at 3 months follow up. Seven (70%) patients of group II and 8 (66.7%) patients of group I recovered completely at 3 months. Two (16.7%) patients of group I and of group II had mild symptom without any significant disability at the end of 3 months (mRS 1). One patient in group II did not improve even after 3 months and required plasmapheresis. Recovery was measured by modified Rankin scale. Mean duration of hospital stay was 9.8 days in group I and 9.9 days in group II, which is not statistically significant. (**Table 2** and **Figure 2)**

Table 2: Outcomes of enrolled children with ADEM on basis of mRS

Outcome	Group I	Group II	t-value	P-value
mRS at				
1 wk	3.5±1.625	3.9±0.738	-0.718	0.481
1m	2.33±1.923	1.40±1.713	1.19	0.248
3m	1.25±2.261	0.6±1.265	0.808	0.429
Duration of hospital stay (days)	9.83 ± 3.46	9.90 ± 2.132	-0.053	0.958

Abbreviations: mRS; modified Rankin Scale

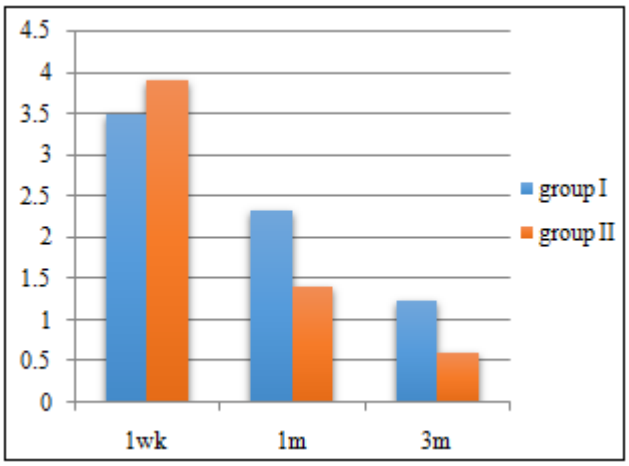

Figure 2: Outcomes of enrolled children with ADEM on basis of mRS

In follow up at 1 month total 13 (59.09%) patients had neurological deficit, among which 8 (66.67%) patients belongs to group I and 5 (50%) belongs to group II. At 3months after treatment total 6 (27.27%) patients had neurological deficit, 3 (25%) from group I and 3 (30%) from group II.2 (9.09%) patients expired during treatment, both of them belongs to group I. One patient expired after 11 days and other expired after 4 days of admission. (**Table 3** and **Figure 3).**

Table 3: Follow up neurological deficit &death among enrolled children with ADEM

	Group I (n=12)	Group II (n = 10)	Total (n=22)	Chi-Square value	P-value
Follow up neurological deficit					
1 month	8 (66.67%)	5 (50%)	13 (59.09%)	1.147	0.284
3 month	3 (25%)	3 (30%)	6 (27.27%)	0.019	0.890
Death	2 (16.67%)	0 (0%)	2 (9.09%)	1.833	0.176

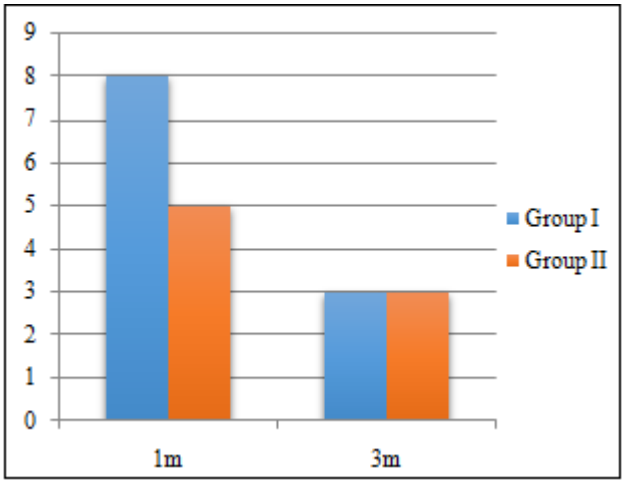

Figure 3: Follow up neurological deficit among enrolled children with ADEM

Among 22 patients, 3 (13.63%) patients developed hyperglycemia after drug transfusion, all belongs to group I (25% of group I). Four (18.18%) patients developed hypertension among which 3 (25%) from group I and 1 (10%) from group II. One (10%) patient of group II (4.54% of total) developed hypersensitivity reaction in the form of fever, itching, and flushing of face and 2 (20%) patients of group II (9.09% of total) developed fever and back pain after drug transfusion. (**Table 4** and **Figure 4).**

Table 4: Adverse reactions in enrolled children with ADEM after drug transfusion

Adverse reactions	Group I (n=12)	Group II (n=10)	Total (n=22)	Chi-Square value	P-value
Hyperglycemia	3 (25%)	0 (0%)	3 (13.63%)	2.895	0.089
Hypertension	3 (25%)	1 (10%)	4 (18.18%)	0.825	0.364
Hypersensitivity reaction (fever, itching, flushing)	0 (0%)	1 (10%)	1 (4.54%)	1.257	0.262

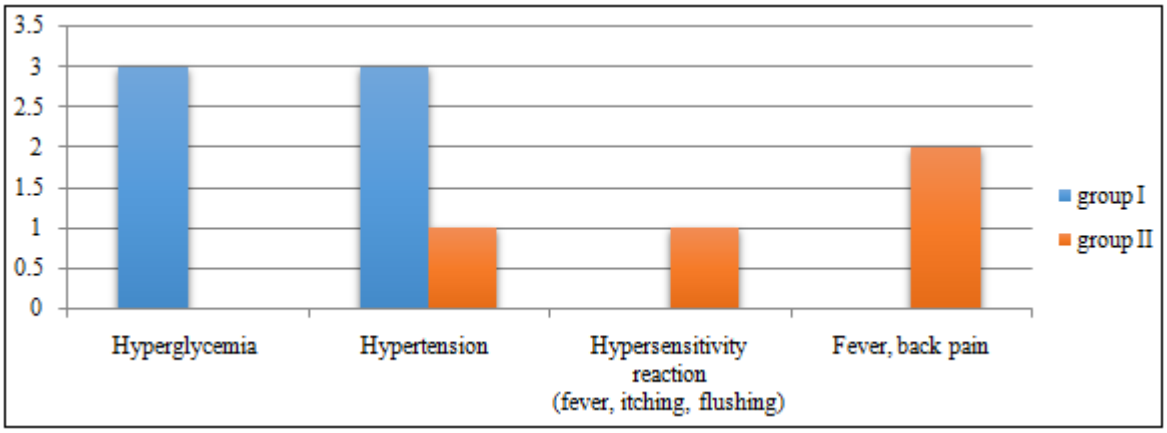

Figure 4: Adverse reactions in enrolled children with ADEM after drug transfusion

4. Discussion

In our study, subjects who received IVIg had early recovery as measured by modified Rankin scale (mRS) than those who received methylprednisolone. At1month follow-up, 8 (66.67%) patients of group I and 5 (50%) patients of group II had neurological deficit however, at 3 months follow up, proportion of subjects showing residual deficits were similar in both groups with group I having more severe neurological deficit. Duration of hospital stay was comparable in both the groups (9.83 days in group I and 9.9 days in group II). One patient who received IVIg did not improve and required plasmapheresis in follow up. Two patients receiving methylprednisolone expired during hospital stay, one after 4 days of treatment and other after 11 days of hospital admission. None of the patients receiving IVIg expired.

Pre and post transfusion vital parameters were comparable in both the groups except in group I where mean blood glucose level increased after drug transfusion (from 100.75 mg/dl to 129 mg/dl). There was also increase in systolic and diastolic blood pressure in group I after drug transfusion. Rests of the vital parameters were mostly unchanged in both the groups. We also observed for any adverse drug reaction among these two groups. There were 13.63% incidence of hyperglycemia, all belonged to methylprednisolone group (25% patients of group I develop hyperglycemia). Incidence of hypertension was 18.18% among which 3 (25%) belonged to group I and 1 (10%) belonged to group II. Among patients receiving IVIg, 1 (10%) patient developed hypersensitivity reaction like fever, itching, flushing. Two (20%) patients of group II developed fever with back pain.

In our study, the most common age group affected was 5-10 yrs similar to the finding noted by Banwell et al. who reported that children with ADEM were more likely to be younger than 10 years ($p<0.001$) [31]. Among enrolled children males were slightly predominant (54.54%) similar to studies reported in literature[22, 32].

Symptoms	Present study	Hynson et al., (2001)	Leake et al., (2004)
Fever	77.27%	52%	67%
Headache	45.45%	45%	57%
Vomiting	45.45%	35%	41%
Rash	13.6%	-	7%
Diarrhoea	9.09%	-	14%
URTI	31.81%	37%	53%
Joint pain	9.09%	-	0%
Seizure	40.9%	13%	19%
Altered sensorium	63.63%	68%	-
Bowel/ Bladder involvement	68.18%	-	-
Psychiatric manifestation	4.54%	-	0%

The following table summarizes the clinical manifestations of present study compared to other previously reported studies[33-40].

Table 5: Comparison of clinical symptoms of the subjects with other studies

Clinical examination showed upper motor neuron type of lesion and patchy, focal involvement. Most of the patients had hypertonia (31.8%) and 22.7% patient had hypotonia. Cranial nerve involvement was observed in 9.09% patients. Deep tendon reflex was brisk in most of the cases (36%). DTR was absent more in lower limb (36.4%) as compared to upper limb (31.8%). Planter was extensor in most of the cases (68.2%). Two (9.09%) patients had positive meningeal sign, 9.09% patients had sensory deficit, and only 4.5% patient had autonomic involvement. These findings are similar to Murthy et al., where they observed patients presented most commonly with motor deficits (77%) and secondly with altered consciousness (45%) [38]. International Pediatric MS Study Group—Consensus Definitions (Diagnostic criteria) also defines monophasic ADEM first clinical event aspoly symptomaticwhich must include encephalopathy. But Elhassanien et al. and Jayakrishnan et al. observed motor deficits and convulsions as the presenting signs. In their study, altered sensorium was not much common[10, 41]. Tenembaum et al. also reported unilateral or bilateral long tract signs (85%), acute hemiparesis (76%), changes in mental status (69%), and ataxia (50%), isolated or in combination, as the most prominent initial findings. Consciousness impairment was observed in 69% cases. Seizures (35%) were mainly present as partial motor status epilepticus. But they observed meningeal reaction in 43% cases and cranial nerve palsy in 44% patients unlike our study findings[21].

On CSF examination most of the patients had cell count less than 15. Mean CSF cell count was 10 and 5.4 in group I and group II respectively. Cells were mainly lymphocytes and mean CSF glucose was 73 in both the groups and protein was 50.8 and 19.9 in group I and group II respectively. Murthy et al. and Hollinger et al. reported almost similar findings in CSF study[9, 38]. Tenembaum et al., (2012) observed CSF abnormalities in 28% children with either lymphocyte pleocytosis (<180 cells/mm3) or mildly elevated protein (<1 g/dL) [21].

In our study we confirmed all the cases by MRI, so 100% of patients had some MRI changes. The following table summarizes the comparison of MRI findings of our study with others.

Table 6: Comparison of MRI findings of the subjects with other studies

MRI changes	Present study	Hynson et al.3 (2001)	Leake et al.3 (2004)	Schwarz et al.4 (2001)
Patchy areas of increased signal intensity				
Brain	45.5%	90%	40%	92%
Spine	18.2%	16%	-	65%
Both	36.4%	-	40%	-
Contrast enhancement present	81.1%	29%	7%	-
Perifocal oedema present	27.3%	-	-	-
Gray matter involved	54.5%	61%	70%	46%

Amongst laboratory parameters, mild leucocytosis was seen in both groups. As ADEM is precipitated by preceding infections, hence TLC increased. Similar finding was observed by Jayakrishnan et al and Elhassanien et al[10, 41]. Ionised calcium and blood sugar level were within normal range in both the groups. These were performed to rule out other causes of seizure and altered sensorium. King et al. in 2013 reported hyperglycemia in a 63 years old patient with ADEM. But no such association is reported in pediatric age group[43].

Singh-Grewal et al. in a prospective study observed the most common immediate reactions after IVIg transfusion were headache, pain at the infusion site, and vertigo[44]. Sherer et al. reported low-grade fever, chills as the most common adverse events in patients transfused with IVIg similar to our study[45]. Lyons et al. observed hyperglycemia in 4.6% of patients treated with intravenous methylprednisolone while our study reported hyperglycemia in 25% patients treated with steroids for ADEM[46]. Klein-Gitelman et al. in 1998 observed in their prospective study that 4.2% patients transfused with high dose IV methylprednisolone was associated with the incidence of vital sign changes including hypertension (n=5), hypotension (n=2), and tachycardia (n=2) [47]. Heidrich et al., (2013) observed in their retrospective study of 74 children (aged 5 to 17 years) receiving IV methylprednisolone, after the first dose, vital signs (heart rate and blood pressure) fluctuated, with a majority had greater than 10% changes from baseline as increment, decrement, or both. Time of initial 10% change in vital signs ranged from immediately after the dose to 135.5 hours later[48]. Our study reported vital sign changes mostly hypertension and tachycardia in subjects receiving iv methylprednisolone after the first dose.

In our study, subjects who received IVIg had early recovery as measured by modified Rankin scale (mRS) than those who received methylprednisolone. Jayakrishnan et al., (2010) observed 14 children treated with intravenous methyl prednisolone, 10 (71%) children had total remission of symptoms within one week of starting steroids while 4 (29%) children had residual symptoms at the end of steroid therapy[10]. Tenembaum et al., (2002) observed clinical response to corticosteroid therapy was usually evident within hours of initiation of treatment, particularly after pulsed IV corticosteroids[21].

In our study, at1month follow-up, 8 (66.67%) patients of group I and 5 (50%) patients of group II had neurological deficit however, at 3 months follow up, proportion of

subjects showing residual deficits were similar in both groups with group I having more severe neurological deficit. Tenembaum et al., (2002) conducted a study where children were treated with either PO or IV corticosteroid therapy, depending on severity of neurologic involvement.28% patients had neurological deficit in follow up (follow-up period ranged from 1 to 19 years). None of the patient expired[21].

Maramattom et al., in a follow up study observed that [duration of follow up was approximately 2.5 years] 7 patients (15%) had a modified Rankin score (mRS) of 0 and had gone back to work. Residual deficits were present in 9% of patients who were able to work (MRS of 1). There were fifteen patients (33%) who had an MRS of two and were ambulant but unable to work. MRS was three (moderate disability requiring some help, but able to walk without assistance) was the outcome score for 13% of patients. There were eleven patients (24%) who were severely disabled and dependent for all activities (MRS of 5). ADEM was associated with a low mortality (4%). In their study all the patients were treated by IV methylprednisolone[49].

Murthy et al., (2002) in their 6 yrs retrospective study observed 15 (83.3%) patients had neurological deficit at discharge. But only 5 (27.7%) patients had neurological deficit at 3 month follow up. On 5 years follow up, only 3 cases had persistent deficit, among which one had relapse 9 months after completion of treatment. Eleven patients (61%) were treated with corticosteroids, and 2 were treated with intravenous immunoglobulins. All patients survived[38].

In our study, two patients receiving methylprednisolone expired during hospital stay. None of the patients on IVIg expired. Schwarz et al., (2001) observed out of 26 patients with the final diagnosis of ADEM on iv methylprednisolone, two patients had died, nine had minor deficits, three had moderate deficits, and 12 patients had no remaining symptoms in follow up[42].

Our study is one of the very few studies in children with ADEM in which a head to head comparison of IVIg and iv Methylprednisolone was done in terms of efficacy, side effects, residual neurological defects and time to full functional recovery. But, at the same time, our study had it's limitations: sample size was small considering the low prevalence of the disease and follow-up duration was not too long. Also, we did not characterize the types of residual neurological deficits post treatment in the two groups.

5. Conclusion

In our study, Intravenous immunoglobulin was found to hasten the clinical recovery in children with ADEM but the overall morbidity, long term neurological sequelae was similar with both the used drugs. Our study implicates that IVIg may be used as the 1st line therapy in children with ADEM replacing steroids owing to its comparable efficacy and better safety profile.

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