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ORIGINAL ARTICLE

Outcome of Acute Transverse Myelitis in Children with Use of Intravenous Methylprednisolone

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ABSTRACT

Objective: The main objective of this study is to analyze the outcome of acute transverse myelitis in children with use of intravenous methylprednisolone

Study Design: Clinical study

Place and Duration of Study: This study was conducted at the Neurology Department of Children's Hospital and the Institute of Child Health, Lahore from 02-02-2016 to 01-08-2016.

Material and Methods: Total 75 children were included and IVMP for five days and tablet Prednisolone for 15 days was given. The outcome was monitored using Medical research council scale

Results: We had 40% (n=30) patients between 1-10 years of age, the mean of which was 11.75 ± 4.31 years. A total of 53.33% (n=40) were males and 46.67% (n=35) females. The outcome after use of IVMP was recorded with 32% (n=24) having a complete recovery, 38.67% (n=29) partial recovery and the rest with no recovery.

Conclusion: The use of IVMP has shown substantially good results in pediatric cases of ATM. A lot of further research work is needed to be done to have a more precise line of management.

Key Words: *Children, Acute transverse myelitis, Intravenous methylprednisolone, Outcome*

INTRODUCTION

Acute transverse myelitis (ATM), name of a severely debilitating condition and a disorder of motor and sensory tract of the spinal cord, is often explained as a localized form of demyelinating acute encephalomyelitis.[1–3] An annual incidence of two million cases of acute transverse myelitis has been recorded in the United Kingdom and Canada.[4] ATM is rare in the pediatric population and interestingly, there is a bimodal distribution of affected population which is greater in those <5 years and also the ones >10 years of age. Overall, when age distribution was evaluated, 20% of the TM cases have been reported in the pediatric population.[5] It can be described as an inflammatory, demyelinating, and immune-mediated disorder of the central nervous system, with typical characteristics of motor, sensory and autonomic involvement.[3,4,6,7]

Transverse myelitis (TM) is usually due to an unknown cause (idiopathic ATM) and is believed to be postinfectious while it can also manifest as a part of metabolic, autoimmune, or vascular disorders like arteriovenous malformation, multiple sclerosis, and/or Neuromyelitis Optica.[5,8,9] Idiopathic TM typically has an acute to subacute course, a hyperacute or chronic course of the disease instantaneously points towards other

associated. Thorough clinical history and neurological assessment are the first stepping stones toward the diagnosis of the disease, followed by exclusion of other etiologies, aided with radiological, hematological and other investigations.[4,8] The progression of the disease from the time of symptomatic onset to the maximum exacerbation varies, and depends on the severity and etiology, ranging from four hours up to 21 days.[10] Clinically, the disease presents with a range of crippling symptoms like pain, paraesthesia, weakness (quadriplegia or paraplegia), numbness, and bowel or/and bladder dysfunction. In the acute phase of the disease, deep tendon reflexes and muscle tone may get decreased or weakened in the affected limb periphery which is overturned with an increase in tone and hyperreflexia (courtesy of the involvement of corticospinal tract) in the later stages of the disease.[8]

As far as the treatment is concerned, a study published in 2016 states that due to the lack of literature, statistical data and clinical trials, the United States Food and Drug administration authority has approved no treatment for acute transverse myelitis.[4] However, according to the guidelines released by American Academy of neurology there are only class IV evidence in support of using corticosteroids in the treatment of acute transverse myelitis, while on the contrary in clinical practice, corticosteroids are the first tool to be operated in the line of treatment and is assumed to have very low level of risk factors involved in their usage. Typically the treatment regimen of corticosteroid comprises daily doses of intravenous Methylprednisolone (IVMP) of 30mg/kg (up to 1000mg) for 3-5 days. Other forms of usable corticosteroid include Dexamethasone, oral high-dose prednisone or prednisolone.[8] Several other forms of treatment are also is the notation like Plasmapheris or Plasma exchange (PLEX) and the use of cyclophosphamide. PLEX is basically considered in those cases which do not respond to the orthodox IVMP therapy after 24-48 hours while cyclophosphamide producesa better outcome in TM patients with Systemic lupus erythematosus.[11,12] Cerebrospinal fluid (CSF) studies are also used as a way for assessing infectious myelitis, but it has to be noted that there should be no delay in the initiation of intravenous corticosteroid due to the evaluation. Since corticosteroids even help to improve the outcome of conditions mimicking ATM, it is preferred to start the treatment without waiting for definitive diagnosis because of the unfolded benefits.[4,8]

In the pediatric population, the onset of acute transverse myelitis imparts a negative impact physically and emotionally. More clarity in mode and impact of therapy is the need of the hour. No study is available showing the outcome of ATM with the use of IVMP in pediatric age group. This study is an effort for the assessment and evaluation of the impact of corticosteroid or more precisely IVMP therapy in pediatric cases of transverse myelitis so that it can be used more confidently.

MATERIALS AND METHODS

Here, a prospective interventional study was conducted at the Neurology Department of Children's Hospital and the Institute of Child Health, Lahore for a period of six months from 02-02-2016 to 01-08-2016. By using the World Health organization's sample size calculator, estimating prevalence of no improvement (Medical Research Council grade 0-2) as 19.4%, i.e. least among all the outcome variables of IVMP in children with ATM, the sample size came out to be 75.[13]

After approval of the ethical committee, children of age between 1 and 18 years, irrespective of gender, and presenting within one month of onset of symptoms were included. Patients with Hypokalemia (serum potassium <3.5), those with progression to a nadir of clinical deficits <4 hours from symptom on setor progression >21 days from symptom onset were excluded. Patients with a history of radiation to the spine within the last 10 years, clinical deficit due to anterior spinal artery thrombosis or spinal cord arteriovenous malformations (seen on Magnetic Resonance Imaging), or clinically apparent Optic neuritis were also excluded.

A total of 75 children admitted to through Outpatient and emergency department with ATM, fulfilling the inclusion and exclusion criteria were enrolled in the study after taking informed consent from their parents or guardians. A detailed history and clinical examination were performed on every patient. IVMP 24-hourly for five days followed by tablet Prednisolone 2 mg/kg/day orally once daily

for 15 days was given. Complete neurological examination was done at admission and then at four weeks of initiation of treatment and outcome was monitored using Medical research council (MRC) scale as: complete recovery or minimal residual deficit (MRC grade 5-4); partial recovery with moderate disability (MRC grade 3); and no improvement or severe disability (MRC grade 0-2).[14] Data was documented on a structured proforma containing the bio-data of the patient. Complete recovery with a minimal residual deficit, partial recovery and no improvement or severe disability was recorded as per operational definition.

The collected data were analyzed statistically by using SPSS version 23.0. Quantitative variables like age and duration of ATM were presented in the form of mean ± standard deviation. Qualitative variables like gender and outcome were presented in the form of frequency and percentage. Data were stratified for age, gender, duration of ATM, MRC grade at presentation to deal with effect modifiers. A post-stratification Chi-square test was applied and p-value ≤0.05 was considered significant.

RESULTS

We distributed all the patients (n=75) according to their which showed that 40% (n=30) were between 1-10 years of age while 60% (n=45) were between 11-18 years of age. The mean age came out to be 11.75 ± 4.31 years. We had 53.33% (n=40) males and 46.67% (n=35) females.

The outcome of acute transverse myelitis in children with the use of IVMP was recorded with 32% (n=24) having a complete recovery as shown in fig 1.

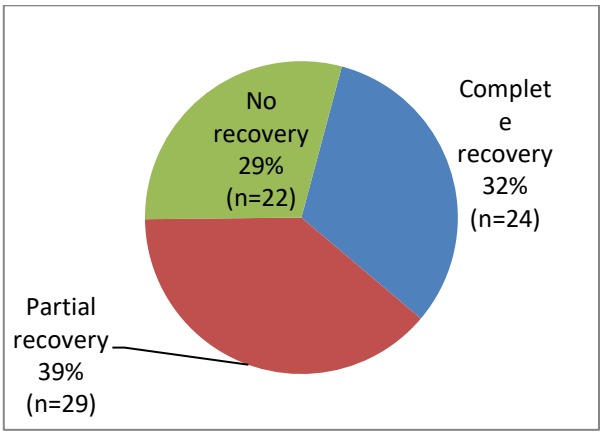

Fig 1: Outcome of acute transverse myelitis in children with the use of intravenous methylprednisolone (n=75)

The data were stratified for age, gender, duration of ATM, and MRC grade at presentation where significant results came out for age (p=0.02).

Table 1: Stratification for the outcome of acute transverse myelitis with regards to age, gender, duration, and medical research council grade at presentation (n=75)

	Outcome			Total	P-Value
	Complete recovery (n=24)	Partial recovery (n=29)	No recovery (n=22)		
Age groups					
1-10 years	08	08	14	30	0.02
11-18 years	16	21	08	45	
Gender					
Male	13	15	12	40	0.97
Female	11	14	10	35	
Duration of acute transverse myelitis					0.99
1-2 weeks	15	18	14	47	
3-4 weeks	09	11	08	28	
Medical research council grade at presentation					0.44
0	13	12	08	33	
1	11	17	14	42	

DISCUSSION

It is believed that the treatment of ATM with high dose steroids holds the progression of neurological symptoms up to six months, in cases of different isolated demyelinating syndromes. However, its efficacy can get decreased with the passage of time.[15] Factually, the disease has a poor outcome in infants, while interestingly ATM has shown good prognosis in children, as it is reported that almost 50% of the children are fully recovered after two years of treatment.[3,4,16] According to a study published 2001, related to the treatment efficacy and outcome of IVMP it has been reported that 66% of people treated with IVMP walked independently after one month and 75% had normal recovery after one year post-treatment, which represents a very positive outcome when compared and analyzed with the results of the control population (not on IVMP treatment).[1] These findings which are aligned with the substantial impact of therapy outcome of using IVMP in the treatment of TM also correlates with the statistical data of our study as in the reference of recovery of the disease where a larger group of the participants showed complete (32.00%, n=24) or partial recovery (38.67%, n=29). MRC grading system was applied in our study which is considered as one of the most reliable in terms of inter-rater and intra-rater evaluation of muscle.[17]

The majority of our study population (60%, n=45) was between 11-18 years of age (60%) while the rest were ≤10 years. In the pediatric population, under the age of 5 and over 10 years of age, most frequently reported number of cases of ATM were found to be idiopathic.[18] We found male preponderance at a percentage of 53.3 (n=45). Existing literature showed ATM to be more common in males with a ratio of male : female as 1-1.6:1 in pre-pubertal age, perfectly contrasting with the data in post-pubertal age in which females are seen to be dominating, especially in those cases where TM has a symptomatic manifestation similar to multiple sclerosis or Neuromyelitis Optica.[8]

The results of this study demonstrated that most of the patients had duration of disease of around 1-2 weeks. The time of the start of the therapy might have a role in this regard as the average duration between the onset of symptoms in TM and the use of IVMP has been reported as 8.1 days (range 1-21 days).[1]

There is a limitation that can be reviewed in the future researches that there is only a single form of therapy studied and evaluated in our study while there are also some other forms of therapies that can be studied, having variable potencies and outcomes.[19] For instance, the use of Cyclophosphamide therapy has produced better outcomes in ATM patients with SLE, while the same is for therapeutic PLEX in patients having ATM with Neuromyelitis Optica.[4,11,16] Moreover, in severe cases, or those refractory to IVMP, the treatment strategy is modified towards the usage of PLEX, impacting very effectively in the acute management of ATM, especially in those cases where the pathology is supposed to be centrally mediated by antibody.[8] This PLEX therapy is also reported to be safe and potent in children.[20] However, the benefits offered by PLEX in those cases of TM resistant to default treatment strategy of IVMP have not been statistically analyzed and/or reported.[21] Lastly, intravenous immunoglobulin can be used, alone or in combination with IVMP.[22] Further studies comprising of a placebo or control group along with adequate randomization are required.

CONCLUSION

Transverse myelitis is a very crippling condition especially if it happens in the earlier phase of life. A proper diagnosis and management are of cardinal importance. In light of the aforementioned studies, the use of methylprednisolone has shown substantially good results in pediatric cases of transverse myelitis. A lot of further research work is needed to be done in this regard in order to have a more precise line of management of the disease.

Conflict of interest: Nil

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