ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 05 | May - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PHYSICAL THERAPY INTERVENTION FOR PATIENT WITH EAST SYNDROME- A CASE STUDY.

Physiotherapy

Dr. Kinjal Bagthariya(M.P.T) Assistant Professor, Shri K. K. Sheth Physiotherapy College, Rajkot, Gujarat.

ABSTRACT

EAST syndrome is autosomal recessive disorder due to mutations in gene KCNJ10, a gene encoding a potassium channel expressed in the brain, eye, ear and kidney. It is characterized by four cardinal features; Epilepsy, Ataxia, Sensorineural deafness, and renal salt-wasting Tubulopathy, thus the acronym EAST syndrome. It was first described as a distinct clinical entity in 2009 by Bockenhauer and scholl, who named this condition EAST syndrome and SeSAME syndrome for Seizures, Sensorineural deafness, Ataxia, Mental retardation and Electrolyte imbalance respectively. Neurodevelopmental delay is evident in most patients with EAST syndrome that were old enough to be assessed; Thus, physiotherapy intervention also plays a vital role in EAST syndrome along with medical management. From physiotherapy perspective; symptomatic management to Improve overall health, wellbeing and motor control becomes ultimate goal in the patient with EAST syndrome. As there is no specific physical therapy treatment approach and no specific tool to evaluate function for children with EAST syndrome; for clinically presented delay development and ataxia, Neurodevelopment therapy (NDT) was utilized as treatment approach and Gross motor function measure (GMFM) & Gross motor performance measure (GMPM) were utilized for assessment in this case study to track progress on follow ups. Result showed marked improvement in GMFM and GMPM scores at follow ups and concluded that Physical therapy intervention improves the gross motor function as well as gross motor performance in patient with EAST syndrome.

KEYWORDS

EAST syndrome; SeSAME syndrome; Physiotherapy; NDT; GMFM; GMPM; Autosomal recessive; Ataxia

INTRODUCTION

EAST syndrome is autosomal recessive disorder due to mutations in gene KCNJ10, a gene encoding a potassium channel expressed in the brain, eye, ear and kidney. Gene KCNJ10 locates in the distal nephron's basolateral membrane and defective function of this potassium channel leads to impaired distal salt reabsorption; allowing potassium to flow into a cell rather than out. This condition is characterized by four cardinal features; Epilepsy, Ataxia, Sensorineural deafness, and renal salt-wasting Tubulopathy, thus the acronym EAST syndrome. It was first described as a distinct clinical entity in 2009 by Bockenhauer and scholl, who named this condition EAST syndrome and SeSAME syndrome for Seizures, Sensorineural deafness, Ataxia, Mental retardation and Electrolyte imbalance respectively.[1]

The neurological symptoms are generally non progressive in patients with EAST syndrome. The first symptom to be identified are Seizures typically, infantile in onset with the first seizure usually occurring between 3 to 9 months of age. Few reports of a possible episode in the neonatal period. These generalized seizures, which may be primary or secondary generalized seizures, were mostly easily controlled by a broad-spectrum anticonvulsant. In majority of cases initial clinical presentation of potassium channel defect leading to biochemical abnormalities, especially hypokalemic metabolic alkalosis along with hypomagnesaemia, hypocalciuria as well as activation of the renin angiotensin aldosterone axis and loss of urinary sodium, potassium, chloride and magnesium due to defective electrolyte transport in the distal convoluted tubule. Salt craving, polydipsia, polyuria and enuresis also present in patients with EAST syndrome suggestive of renal salt wasting.

Sensorineural deafness is a consistent feature found in patient with EAST syndrome. Severity of hearing impairment is variable from mild to severe, necessitating bilateral hearing aids. Another symptom is Ataxia; Ataxic gait, balance & coordination issues which are prominent features, evident only when patient learn to walk. Patient usually walk with broad-based ataxic gait, which resulted in unsteadiness and falls. Other signs of cerebellar dysfunction include intention tremor, dysdiadochokinesis, dysmetria, truncal ataxia, titubation and slurred and scanning (explosive) speech which may or may not be persistent.

Some form of neurodevelopmental delay is evident in most patients with EAST syndrome that were old enough to be assessed. Typically, there is delayed attainment of motor milestones with delays in head control, sitting unsupported, standing and walking aided or walking independently. EAST syndrome appears to be static or non-progressive in nature with no regression in attained milestones, however patients lose the ability to walk after a prolonged seizure as a result of brain hypoxia from the prolonged seizure and not directly due to the KCNJ10 mutation. Delayed onset of speech and language development, especially the ability to talk in full sentences is a common finding in patients with EAST syndrome along with slurred speech and scanning dysarthria indicative of cerebellar disease. Additional reported features are hypertonia, exaggerated deep tendon reflexes, ankle clonus and extensor plantar responses, dystonic posturing and nystagmus. There is no cure for EAST Syndrome and medical management is focused on controlling seizure activity and on salt supplementation.[1]

CASE REPORT:

Here reported case is of 2-year-old female, diagnosed with EAST syndrome. Here reported subject was relatively normal up to 5 months of age without any significant clinical signs of EAST syndrome. Her mother noticed her first epileptic attack at the age of 5 months which was controlled with medical management in the form of anticonvulsant medications. At the age of 7 months her parents noticed delay development in her as she has not achieved supported sitting. In gross Motor milestone; head control, turning from supine to prone and prone to supine (rolling over) was achieved.

At the age of 7 months; patient had frequent episodes of seizure at brief intervals; she required hospitalization in NICU and further investigation procedures due to prolonged seizure. Out of investigations done; serum electrolyte investigations were suggestive of renal tubulopathy with significant reduced sodium, potassium, chloride and magnesium levels in serum along with elevated plasma renin activity (PRA) and aldosterone. After that her parents had consulted Pediatric-Neurologist for the same and she was diagnosed having EAST syndrome with reports of molecular genetic DNA analysis. Her DNA analysis showed homozygous KCNJ10 gene variant c.611G>A(p.Arg204His) on Exon 2 suggestive of EAST syndrome. Medical management was started for the same in the form of anticonvulsant and oral sodium, potassium or magnesium supplementation.

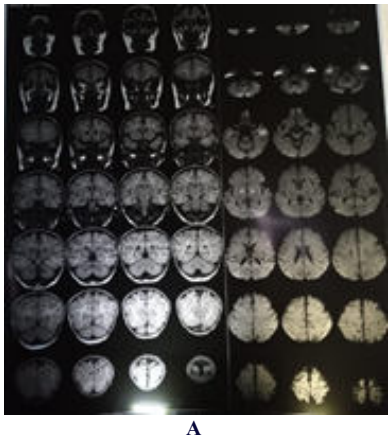
As the time progressed, the episodes of seizures at brief interval continued with her. After another prolonged seizure; her mother noticed difficulty in movement of right upper limb and lower limb in her; while apparently there was no any difficulty in movement of left upper limb and lower limb. Her mother noticed weakness of right side of body in her as she was unable to turn on her right side and on Neuro-pediatrician consultation; she was advised for physical therapy intervention for delay development.

The patient reported to physical therapy department at the age of 8 months with 5.8 kg of weight, normal head and chest circumference. No history of any prenatal abnormality with mother or birth asphyxia. She is born of a non-consanguineous marriage, through vaginal delivery at full term & normal birthweight (2.9 kg); with clinical indications of global developmental delay, hypotonia, dystonia,

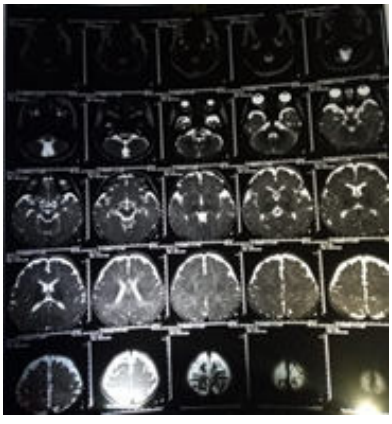
hypokalemia, renal tubular acidosis and early onset of epilepsy. She had multiple attacks of epilepsy starting from 5 months of age. She had approximately 25-30 attacks of epilepsy within last 3 months. Her multiple epileptic attacks (seizures) were generally of 5-30 minutes except few prolonged seizures for hours or day in which she required hospitalization. Epileptic attack usually starts with crying, continuous eye blinking, lip smacking and tonic-clonic movements of body followed by drowsiness or sleep. She has achieved head control and turning over at 5 months of age; social smile at 3 months of age; recognition of mother and stranger anxiety at 6 months of age.

The Brain MRI of her show bilateral basal ganglia (globus pallidus) hyperintensities. The Electroencephalography (EEG) report showed normal drowsy and sleep EEG. BERA analysis showed moderate elevation of hearing threshold, which could be conductive. With independent stimulation of right and left ears at 105 dbnHL alternating clicks, markedly prolonged absolute latencies and some prolongation of interpeak latencies along with 70 dbnHL threshold for wave V bilaterally found in BERA analysis.

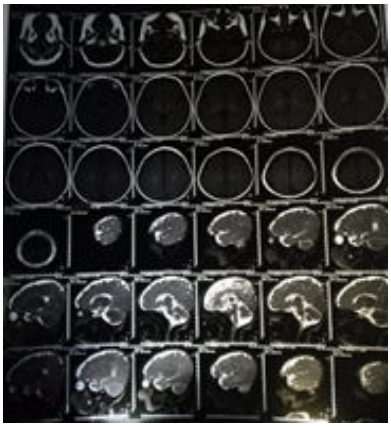
Picture A, B, & C shows MRI report showing basal ganglia changes in her brain.



A



B



C

On examination of developmental milestones; Head control, turning from supine to prone and prone to supine (rolling over) was achieved in gross motor milestone. In fine motor milestone; Unidextrous reach (reaching out for objects/toys with one hand) & transfer of objects between both the hands achieved but unable to hold the object properly with her right hand. In social and adaptive milestones; she was having social smile, recognizes mother and strangers, having stranger anxiety. In visual milestones; she was able to fix the vision & follow the objects of her interest. In hearing milestone; she was alert to sound but unable to localize the source of sound by head turning. In language milestones; she was alert to sound, only producing musical vowels(cooing). On developmental analysis; her chronological age was 8 months & developmental age was near 5 months.[2] She momentarily holds supported sitting for few seconds but represent titubation and involuntary movements in that position. She was also having weakness of right side of body; presented features of right-side hemiparesis.

On electrophysiological analysis; Bilateral sural SNAPs are normal; however right sural amplitude appears to be reduced as compared to left. Distal motor latencies, CMAP amplitude, motor nerve conduction velocities, and F waves are normal in bilateral median, ulnar, radial and tibial nerves. Bilateral tibial H reflexes are of small amplitude but present. Distal motor latencies, CMAP amplitude, motor nerve conduction velocities are normal in bilateral peroneal nerves; absent F waves are seen in left peroneal and not well-formed F wave in right peroneal nerve. Posterior tibial SSEP (Somatosensory evoked potential) analysis showed evidence of a severe disturbance above the level of lumber spinal cord; on independent stimulation of tibial nerves with recording over lumber region and central scalp, N21 was normal & no clear-cut potentials were noted consistently from scalp on either side.

PHYSIOTHERAPY ASSESSMENT:

After taking written consent by her parents; analysis of gross motor function and gross motor performance was done. The gross motor function of the subject in this case was assessed by gross motor function assessment (GMFM).[3,4,5] The GMFM-88 is an observational clinical tool designed to assess changes in gross motor function of children with developmental delay and cerebral palsy range from 5 months to 16 years. The GMFM-88 assesses five domains: (1) lie and roll; (2) crawling and kneeling; (3) sitting; (4) standing and (5) walk-jump-run. The GMFM-88 provides an overall percentage scores as well as each of the five-dimension scores. The gross motor performance of subject was assessed by gross motor performance measurement (GMPM).[6,7] The GMPM was developed to evaluate quality of movement and change over time in children with cerebral palsy & delay development range from 5 months to 12 years.

As there is no specific outcome measure/tool designed to assess function in patient with EAST syndrome. The GMFM and GMPM have been utilized in this case study for assessment and to track progress on follow ups.

PHYSIOTHERAPY INTERVENTION:

As there is no cure of EAST syndrome, thus physiotherapy treatment focuses on symptom management based to address patient's goals and impairment; preventing other disabilities & comorbidities. Physical therapy exercises with aim of acquiring motor control & skills that focus on sustaining and regaining control of proximal muscles of trunk, shoulder and pelvic girdle; improve postural control and balance (static & dynamic); stretching and mobility exercises to improve or maintain range of motion and bone density; task specific exercises to improve fine motor skills and dexterity along with the strategies to compensate underlying impairment like use of splints & walking aids, that can improve or restore function by increasing weight bearing control in patient with EAST syndrome.

Physiotherapy management of the patient started when patient was 8 months old and continued for 5 days per week according to neurodevelopmental therapy (NDT) approach. As the subject was unable to bare weight on her legs and unable to hold sitting position; Exercises started in the form of mat exercises for goal specific movements and postures in different weight bearing positions like supported sitting; quadruped position; kneeling and standing. Sensory integration, Balance and coordination exercises for transition in different postures were done using vestibular ball, wedge board & Balance board to facilitate normal postural alignment and movement

patterns. Balance exercises were done with adaptive chairs and positioners to reduce impact of ataxic movements. Physiotherapy intervention was performed for total of 16 months and follow ups were taken at every 4-month interval; at the age of 12;16;20 & 24 months of age with evaluation by GMFM & GMPM scores. Medical management, dietary supplements and oral supplements of sodium, potassium & magnesium were continued throughout the physiotherapy intervention duration according to Neuro-pediatric opinion.

On examination of developmental milestones at the age of 2 years; she was able to sit independently and walk with wide base of support, able to take few steps with support though ataxic movements were present in gross motor milestone. Pincer grasp achieved in fine motor milestone. In social and adaptive milestones; she comes when called, plays simple games with ball/toys, pull people to show toys and ask for food. In visual milestones; she was able to follow rapidly moving objects and able to recognize the toys. In hearing milestone; she was able to localize the source of the sound. In language milestones; she was able to laugh loud, momentarily monosyllabic ah-goo sounds present.

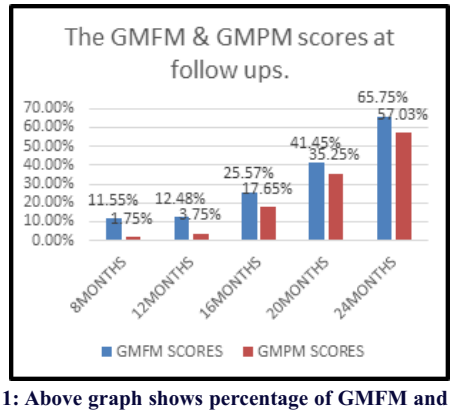
THE PRE & POST DATA OF GMFM-88 AND GMPM:

At the age of 8 months: the percentage of GMFM and GMPM scores were 11.55% and 1.75% respectively. The percentage of GMFM scores in follow ups at the age of 12;16;20 & 24 months were 12.48%, 25.57%, 41.45% and 65.75% respectively. The percentage of GMPM scores in follow ups at the age of 12;16;20 & 24 months were 3.75%, 17.65%, 35.25% and 57.03% respectively.

In this case, subject's gross motor function and gross motor performance markedly improved in follow ups at 2 year of age.

Table 1: Above table shows percentage of GMFM and GMPM scores in follow ups.

AGE IN MONTHS	8 MONTHS	12 MONTHS	16 MONTHS	20 MONTHS	24 MONTHS
GMFM SCORES	11.55%	12.48%	25.57%	41.45%	65.75%
GMPM SCORES	1.75%	3.75%	17.65%	35.25%	57.03%



Graph 1: Above graph shows percentage of GMFM and GMPM scores in follow ups.

DISCUSSION:

The EAST syndrome characterized by constellation of epilepsy, ataxia, sensorineural deafness and salt wasting secondary to renal tubulopathy; which is due to mutations in the KCNJ10 gene, located on chromosome 1 and has an autosomal recessive mode of inheritance. The key to diagnose this disease is molecular genetic analysis, serum electrolytes and MRI scanning. There are 14 different KCNJ10 mutations have been published by many researchers on molecular genetic analysis which either directly affect the potassium channel function or may lead to mislocalisation.

The course and clinical features of the disease is variable in subjects with EAST syndrome. According to M Severino (2018); MRI scanning in the EAST syndrome represent unusual white matter involvement associated with KCNJ10 mutations.[8] The MRI study of the subject in this case only represent bilateral basal ganglia hyperintensities. Sensorineural deafness is a consistent feature found with EAST syndrome. Severity of hearing impairment is variable from mild to severe; here BERA analysis of patient showed moderate elevation of hearing threshold, which could be conductive. EAST syndrome appears to be static or non-progressive in nature with no regression in neurological symptoms; it was non-progressive in nature in this subject but M Celmina (2019) noted a progressive course of EAST syndrome in terms of hearing impairment and neurological deficit and concluded that future research should concentrate on recognizing the lesions in central nervous system to evaluate more potential diagnostic criteria and on formally evaluating intellectual disability.[9]

From physiotherapy perspective; symptomatic management to Improve overall health, wellbeing and motor control of the patient becomes ultimate goal in the patient with EAST syndrome. According to A YAKASAI (2016); Exercise releases "feel good" hormone into the brain; helps to keep muscle active, increases oxygen flow to brain and increases the bone density which can help to prevent bone pathologies. The person with epilepsy may not feel like doing exercise due to tiredness because of seizures or antiepileptic medication; but even gentle exercises can boost the energy levels. The positive effects of exercises by improving overall health and wellbeing may help to reduce seizures in some patients with epilepsy. The neuroprotective and antiepileptogenic actions of exercise also helps as a complementary nonpharmacological management of epilepsy.[10]

As there is no specific physical therapy treatment approach for children with EAST syndrome; in this case, Neurodevelopment therapy(NDT) was utilized as a treatment approach for clinically presented delay development and ataxia.[11,12] Neurodevelopmental therapy was developed by Berta Bobath and Karel Bobath. It is client centered, hands on, problem solving approach; used for management of children having disorders of function, movement or postural control because of damage in central nervous system. It is based on the premise that the presence of normal postural reflex mechanisms is fundamental to a motor skill's performance. The normal postural reflex mechanisms consist of righting and equilibrium reactions, reciprocal intervention, and coordination patterns. NDT interventions aimed to stop abnormal postures and movements by holding child in fixed postures that were supposed to inhibit abnormal primitive/postural reflexes. The key elements of NDT are; facilitation (use of sensory inputs to improve motor behavior), management of contemporary motor behaviors & an overall management strategy (by 24-hour interdisciplinary management approach). Other treatment approaches include sensory integration therapy, task-oriented strategies, process-oriented therapies, speech-language therapy and occupational therapy.[13,14]

CONCLUSION:

Physical therapy intervention improves the gross motor function as well as gross motor performance in patient with EAST syndrome.

ACKNOWLEDGMENT:

I would like to thank my parents and family for their enormous support; also thankful to patient's parents for their consent & support in this study.

CONFLICT OF INTEREST: There was no conflict of interest at personal or institutional level.

SOURCE OF FUNDING: Not required

REFERENCES

1. Ola Abdelhadi, Daniela Iancu, Horia Stanescu, Robert Kleta, Detlef Bockenhauer. EAST syndrome: Clinical, pathophysiological, and genetic aspects of mutations in KCNJ10. Rare diseases. 2016;4(1):e1195043.
2. O P Ghai,Vinod K Paul, Arvind Bagga. GHAI ESSENTIAL PAEDIATRICS: Development(p.42-62). Eighth edition. Delhi; CBS Publishers & Distributors Pvt Ltd: 2013.
3. Russell D, Rosenbaum P, Gowland C. Gross motor function measure manual. Second edition Hamilton, Ontario: McMaster University; 1993.
4. Russell DJ, Rosenbaum PL, Avery LM, Lane M. Gross motor function measure (GMFM-66 and GMFM-88) user's manual. London, United Kingdom: Mac Keith Press: 2002.
5. Jooyeon Ko, Minyoung Kim. Reliability and Responsiveness of the gross motor function measure-88 in children with cerebral palsy. Journal of physical therapy 2012;93(3):393-400.
6. The gross motor performance measure: validity and responsiveness of a measure of quality of movement.physical Therapy 1995;75(7):603-13.
7. Gowland C, Boyre WF, Wright V et al. Reliability of gross motor performance measure. Physical therapy 1995;75:597-602.
8. Mariasavina Severino et al. Unusual white matter involvement in EAST syndrome associated with novel KCNJ10 mutations. J Neurol. 2018;265(6):1419-1425.
9. YAKASAI AM. The role of physical therapy in the management of children with epilepsy. 2016.(numss.com)

10. M Celmina et al. EAST/SeSAME syndrome: Review of the literature and introduction of four new lavian patients. Clin Genet 2019;95(1):63-78.
11. Helen Hartley, Elizabeth Cassidy, Bennie Carter. Exercise and physical therapy interventions for children with ataxia: a systemic review. Cerebellum (London,England) 2019; 18(5):951-968.
12. Kyoung Hwan Lee, Jin Woo Park, Bum Sun Kwon. Efficacy of intensive neurodevelopmental treatment for children with developmental delay, with or without cerebral palsy. Annals of rehabilitation medicine 2017; 41(1): 90-96.
13. Bouwien CM et al. Efficacy of interventions to improve motor performance in children with developmental coordination disorder: a combined systemic review and meta analysis. Developmental medicine and science neurology 2012;55(3):229-237.
14. Barbara R Lucas et al. Interventions to improve gross motor performance in children with neurodevelopmental disorders: a meta analysis. BMC Paediatrics 2016;16(1):193.