International Journal of Orthopaedics Research
www.orthopaedicsjournal.in
E-ISSN: 2663-0923, P-ISSN: 2663-0915
Received: 15-10-2020, Accepted: 30-10-2020; Published: 18-11-2020
Volume 2; Issue 4; 2020; Page No. 57-61

Is intraoperative neuromonitoring (IONM) a reliable tool for scoliosis correction in patients with friedreich's ataxia?

Muaz Alghadir[1], Justin Arockiaraj[2*], Muhammad Tariq Imtiaz[3]
[1,] Senior consultant, Department of Spine surgery, National Neurosciences Institute, King Fahad Medical City, Riyadh, Saudi Arabia.
[2] Assistant consultant, Department of Spine surgery, National Neurosciences Institute, King Fahad Medical City, Riyadh, Saudi Arabia.
[3] Senior consultant, Department of Neurophysiology, National Neurosciences Institute, King Fahad Medical City, Riyadh, Saudi Arabia

Abstract
Objective: Our objective is to report the role of IONM in our patients with Freidrich's ataxia in order to create awareness among Spine surgeons.
Methods: This is a retrospective analysis of three patients with Freidrich's ataxia who required surgery for severe scoliosis were included in the study. All three of them had clinical features and neurophysiological evidence of Freidrich's ataxia with truncal imbalance. Two of them were wheel chair bound and one had ataxic gait. Scoliosis correction was done using pedicle screw instrumentation under multi-modality neuromonitoring.
Results: There was minimal response in Motor evoked potential in the child who was walking. No reproducible or replicable baseline response was present in all the modalities of IONM in spite of supramaximal stimulation in the other two patients. Post operatively, one patient developed grade 1 reduction in neurology compared to the pre-operative status. All three of them had good correction and good sitting balance after surgical correction.
Conclusion: Intra-operative neuromonitoring in patients with Freidreich's ataxia remains a challenge. The good old 'Stagnara wake-up' test will be a better alternative to assess integrity of the spinal cord in these patients. Awareness among Spine surgeons is needed regarding this rare disease.

Keywords: neuromonitoring; friedreich's ataxia; spine; scoliosis

Introduction

Friedreich's ataxia (FRDA) is a progressive, autosomal recessive neurodegenerative disorder, named after Dr. Nikolaus Friedreich [1], a German physician who first described it in 1863. The prevalence is approximately 1 in every 40,000 individuals. It is more prevalent in Europe, Middle East, India and North Africa. Friedreich's ataxia has been described as one among the rare diseases under the NORD (National organization for rare disorders) [2]. FRDA is due to insufficient levels of frataxin (FXN) caused by expanded guanine-adenosine adenosine (GAA) sequencing repeats in the FXN gene [3]. Typically, patients with FRDA manifest with ataxia, neurologic impairment, musculo-skeletal manifestations, hypertrophic cardiomyopathy and diabetes mellitus [4]. Scoliosis, pes cavus, talipes equino varus are the common musculoskeletal manifestations of which Scoliosis is the commonest. Surgery for correction of scoliosis is indicated usually in those patients with progressive scoliosis (> 50degrees) and truncal imbalance. Multi-modal neuromonitoring plays a vital role in Scoliosis surgery in assessing the integrity of the spinal cord. We have reported the role and pattern of IONM during scoliosis correction in our patients with Friedreich's ataxia and to create awareness among the Spine surgeons.

Materials and methods

Three adolescent children diagnosed to have Freidreich's ataxia based on clinical and neurophysiological features were included in the study. All of them had history of frequent falls and initially developed difficulty in walking. Two of them were wheel chair bound within 10 years of onset of symptoms. Their birth history, mile stones and intellect were within normal limits. All of them were born to consanguineous parents and had a positive family history of siblings with similar presentation (Table 1). Clinical examination revealed positive cerebellar signs, absent deep tendon reflexes and motor weakness (2-3/5 MRC grade) in all three of them. Neurophysiological evidence of axonal type of severe sensory neuropathy was present (Table 2). All the patients had normal glucose and Vitamin E levels. All three had progressive scoliosis with loss of sitting balance and hence underwent corrective surgery for Scoliosis using pedicle screw instrumentation. Multi-modality intra operative neuromonitoring (Cadwell Cascade Elite – 32 channels and 64 inputs – Cadwell Industries Inc. 2015. Kennewick, WA, USA.) using Transcranial Motor evoked potential, Somatosensory evoked potential and EMG.

Table 1: Demography, Clinical presentation and physical examination

Features	Patient 1	Patient 2	Patient 3
History			
Age	13	24	16
Gender	Girl	Male	Male
Presenting Complaints	Frequent falls, unsteady gait for the past 7 years Gradually progressive deformity over her back for the past 7 years increased in the last year	At 11 years – Unsteadiness while walking. He was able to walk independently. At 15 years – frequent falls, Can walk only with assistance, and slurred speech. At 19 years – Wheel chair bound	He was normal till the age of 10 years. He developed difficulty in walking, slurring of speech and weakness of upper and lower limbs. At 16 years – He is Wheel chair bound.
Family History	One cousin with cerebellar atrophy	Brothers have similar problems	His sister with difficulty in walking and scoliosis
Parents – Consangunity	Second degree	First degree	First degree
Birth History, Mile Stones	Normal	Normal	Normal
Performance in School	Good	Good	Good
Scoliosis	Progressive deformity	Progressive deformity Loss of sitting balance	Progressive deformity Difficulty in sitting in the bed or wheel chair
Physical Examination:			
Dysmorphic features	No	No	No
Gait	Broad based, Ataxic gait	Wheel chair bound	Wheel chair bound
Ocular anomalies	Bilateral mild horizontal nystagmus at the lateral gaze	Horizontal Nystagmus present	No Nystagmus
Hearing	Normal	Normal	Normal
Speech	Fluent and Coherent	Dysarthria	Dysarthria
Spasticity	Normal tone	Spastic with knee contracture	Normal tone
Spine	Kyphoscoliosis present with left lumbar and right thoracic scoliosis	Scoliosis with trunk imbalance Costo pelvic impingement present on the right side	Scoliosis with trunk imbalance Costo pelvic impingement present on the left side
Motor examination	Decreased bulk Normal tone. No contractures. Distal muscle weakness in both upper and lower limbs – MRC grade 2/5 No fasciculations.	Spasticity was seen in all four limbs. Distal muscle weakness in both upper and lower limbs – MRC grade 2/5 Bilateral foot drop	Decreased bulk Normal tone. No contractures. Distal muscle weakness in both upper and lower limbs – MRC grade 2/5 Tongue fasciculations present.
Sensory examination	Normal in both upper and lower limbs	Distally grade ½	Normal
Vibration & Proprioception	Poor in the all four limbs	Absent	Absent
Reflexes – Patellar, Ankle	Absent	Absent	Absent
Cerebellar signs	Rhomberg sign positive Dysmetria on finger to nose test Abnormal heel and shin test. Unable to perform Tandem Gait	Severe dysmetria on Finger nose test Truncal ataxia Dysdiadokinesia present	Dysmetria on finger to nose test Abnormal heel and shin test.

Table 2: Investigations, Neuromonitoring and Management

Features	Patient 1	Patient 2	Patient 3
Investigations			
Radiology	Thoraco lumbar scoliosis Right Thoracic Scoliosis – 52.3 degrees Left Lumbar – 51 degrees 70 degrees of kyphosis	Right Thoracic Scoliosis – 71.7 degrees Left Lumbar – 75.2 degrees (Figure 2) Right Costo pelvic impingement	Left Thoracic Scoliosis – 83.1 degrees Left Costo-pelvic impingement
MRI spine	Normal. Spinal cord is normal in calibre and it ends at the upper border of L2.	Atrophic appearance of the spinal cord along the mid and lower thoracic spine	Normal
MRI brain	Normal No structural abnormality. No evidence of atrophy of the white matter. Normal myelination pattern.	Vermian atrophy with cortical cerebellar atrophy in conjunction with the lateral temporal and frontal atrophy. There was prominent prepontine CSF cistern with atrophy in the mid brain and brain stem.	Normal No structural abnormality. No evidence of atrophy of the white matter. Normal myelination pattern.
Neurophysiology	Severe sensory polyneuropathy, Axonal type.	Severe sensory axonal polyneuropathy involving both upper and lower limbs. Some motor conduction slowing were noted but motor CMAP s are well preserved. No demyelinating features.	Severe sensory polyneuropathy, Axonal type.
Genetic Analysis	Many variant of uncertain significance	Presence of two expanded alleles in the GAA	Not done

	(VUS) genes were shown in Whole exome sequencing(WES)	sequence of FXN (Frataxin) gene.	
ECHO	Left ventricular hypertrophy Normal Left ventricular function		
Pulmonary Function Test	Normal	Not able to do pulmonary function test	He could not do forceful and prolonged exhalation.
Intra operative Neuro monitoring	Pre-operatively, SSEP did not show any reliable potential on either upper or lower limbs bilaterally. Transcranial motor evoked potentials showed very minimal morphology on extremely high intensity and parameters with minimal signal recording from extensor halluces brevis ONLY.	No replicable monitorable base line was recorded in all modalities – SSEP, Transcranial motor evoked potential inspite of supramaximal electrical stimulation.	No recordable, monitorable base line values in all modalities - SSEP, Transcranial motor evoked potential inspite of supramaximal electrical stimulation.
Surgical Procedure	Bilateral Thoracic 3, 4 and Lumbar 2, 3 pedicles were instrumented and held with cobalt chromium rod. Post op Cobb – 6.6 degrees	Pedicle screw instrumentation from Thoracic 3 vertebra to Sacral 1 Vertebra and fusion was done. Post op Cobb angle – 11.3 degrees. (Figure 3)	Pedicle screw instrumentation from Thoracic 3 vertebra to Sacral 1 Vertebra and fusion was done. Post op Cobb angle – 18.4 degrees
Post op Intensive Care	Uneventful.	Uneventful	Uneventful
Post op Neurological Status	Same as pre-operative status	Same as pre-operative status	Grade 1 reduction in neurology in the lower limbs when compared to the pre-operative status

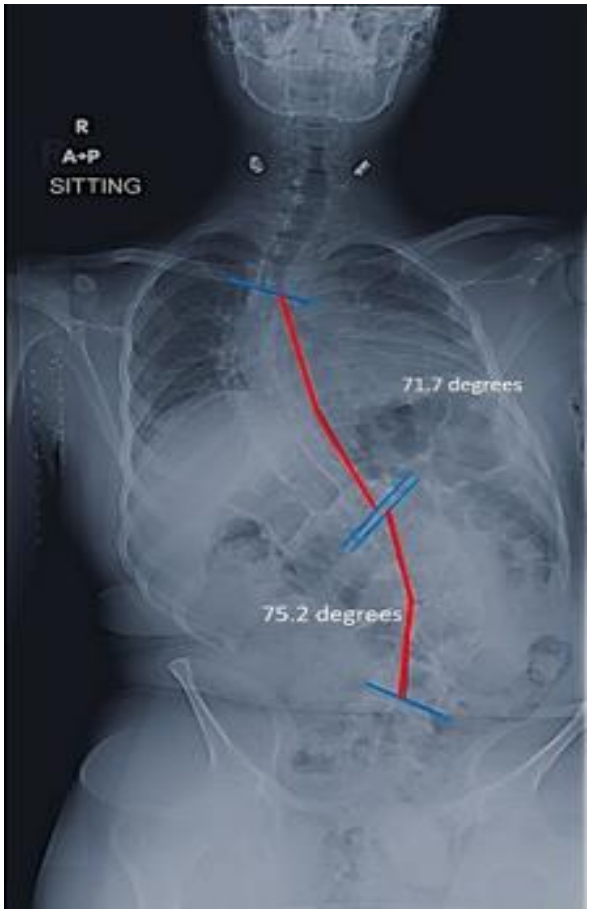

Fig 1: Plain radiograph (sitting) antero-posterior view of whole spine of a boy with Friedreich's ataxia showing double major curve - right thoracic scoliosis with 71.7 degrees and left lumbar curve with 75.2 degrees (Figure 2) and right costo pelvic impingement

Fig 2: Post-operative plain radiograph (standing) antero-posterior view of whole spine showing Pedicle screw instrumentation from Thoracic 3 vertebra to Sacral 1 Vertebra with Post op Cobb angle – 11.3 degrees

Results

There was minimal response in Motor evoked potential in the child who was walking. Transcranial motor evoked potentials showed very minimal morphology on extremely high intensity and parameters with minimal signal recording from extensor halluces brevis ONLY.

No reproducible or replicable baseline response was present in all the modalities of IONM in spite of supramaximal stimulation in the other two patients. Post operatively, one patient developed grade 1 reduction in neurology compared to the pre-operative status. All three of them had good correction and good sitting balance after surgical correction (6-18 degrees).

Discussion

FRDA is an autosomal recessive, progressive movement disorder that causes neuro degeneration of the spinal cord and cerebellum. The pathology initially affects the dorsal nerve root ganglion which in turn affects the spino-cerebellar tracts and finally causes ataxia, dysarthria, and loss of co-ordination.

Typical presentation of the disease occurs in 75-80% of the affected individuals. The natural course of the disease starts with children developing symptoms between the age of 10 – 16 years [5, 6, 7] with frequent falls, inco-ordination of gait and difficulty in balance. Gradually weakness and incoordination increases to ataxic gait, dependency on mobility aids and finally they become wheel chair bound within 10 years of onset of the disease. Typical signs include presence of cerebellar signs, absent tendon reflexes, loss of vibration and proprioception, weakness of the distal muscles, ataxic gait, and progressive scoliosis. All our patients had similar clinical presentation and two among them were wheel chair bound. The atypical presentations include LOFA (late onset Friedreich's ataxia), VLOFA (very late onset Friedreich's ataxia) [2, 8, 9] and FARR (Friedreich's ataxia with retained reflexes) [2, 10]. The presentations of LOFA and VLOFA are seen in 15% of the population where symptoms manifest at the age of 26-39yrs for LOFA and > 40 years for VLOFA. The progression of the disease is very slow when compared to the typical presentation. FARR affects approximately 12% of the individuals.

Multi-disciplinary team approach is warranted in the management of Friedreich's ataxia. Scoliosis in these individuals is gradually progressive and the indications for surgery includes progressive scoliosis > 50 degrees, loss of sitting balance and poor neck control [11, 12]. The role of brace in the treatment of scoliosis is doubtful and their only indication being delay in scoliosis surgery [13].

Multi modal Intraoperative Neuro-monitoring plays a vital role in corrective surgery for scoliosis. Prior to the introduction of IONM, Stagnara wake up test was the only reliable test available to assess global motor control [14]. However, it had its own negative role in relation to patients with Neuromuscular Scoliosis with associated intellectual disabilities and motor weakness[14]. Multiple studies have proven that both MEP and SSEP monitoring are essential for optimal outcome [15, 16, 17]. Owen *et al*. had reported 96% reliable responses in patients with Neuromuscular Scoliosis [18]. Multiple reports were published on the role of IONM in patients with Friedreich's ataxia (Table 3) [11, 19, 20, 21]. However only few modalities of IONM were attempted on them. Our study reports the role of Multimodality neuromonitoring in patients with Friedreich's ataxia. Only the patient who had ataxic gait (Table 1), had a minimal response in Motor evoked potential in her extensor halluces brevis. No reproducible or replicable baseline response was present in all the modalities of IONM in spite of supramaximal stimulation.

Intra-operative neuromonitoring in patients with Friedreich's ataxia remains a challenge. It is advisable to utilize O-arm for safe insertion of pedicle screws in patients with Friedreich's ataxia. 'Stagnara wake-up' test can be used to assess integrity of the spinal cord in these patients. The advantage is that patients with FRDA do not have intellectual difficulties when compared to other patients with neuromuscular scoliosis.

Table 3: Comparision of studies related to IONM in Friedrich's ataxia.

Author	Number of patients	Modality of Neuromonitoring used	IONM response
Milbrandt *et al* [11]	11	SSEP	Was effective in 1 patient only
Lawrence *et al* [19]	1	MEP, SEP	No response with SEP, Some response with MEP.
D K Sengupta *et al* [20]	2	MEP, SEP	No response
Bayoumi AB *et al* [21]	1	MEP	No response
Current Study	3	SSEP, MEP, EMG,	Response was seen only in 1 patient in Extensor hallucis brevis muscle only.

Conclusion

Intra-operative neuromonitoring in patients with Friedreich's ataxia do not show reliable or reproducible data. The good old 'Stagnara wake-up' test will always be a useful option to assess integrity of the spinal cord in these patients. Correlation of IONM is limited probably related to the ambulatory status of the patient. Awareness to Spine surgeons regarding the presentation of this rare disease, the limited role of IONM and the need for alternative measures like O-arm is needed for these subset of patients.

References

1. Friedreich N. Ueber Degenerative Atrophie der Spinalen Hinterstränge. Arch Pathol Anat Phys Klin Med. 1863; 26:391-419.
2. https://rarediseases.org/rare-diseases/friedreichs-ataxia/-, 2018.
3. Pandolfo M. Treatment of Friedreich's ataxia. Expert Opin Orphan D. 2013; 1:221-234.
4. Pandolfo M, Manto M. Cerebellar and afferent ataxias. *Continuum (Minneap Minn*). Movement Disorders. 2013; 19(5):1312-1343.
5. Harding AE. Friedreich's ataxia: a clinical and genetic study of 90 families with an analysis of early diagnostic criteria and intrafamilial clustering of clinical features. Brain 1981; 104:589-620.
6. Dürr A, Cossee M, Agid Y, Campuzano V, Mignard C, Penet C, *et al*. Clinical and genetic abnormalities in patients with Friedreich's ataxia. N Engl J Med. 1996; 335:1169-1175.
7. Delatycki MB, Paris DB, Gardner RJ, G A Nicholson, N Nassif, E Storey, *et al*. Clinical and genetic study of Friedreich ataxia in an Australian population. Am J Med Genet. 1999; 87:168-174.

8. Parkinson MH, Boesch S, Nachbauer W, Caterina Mariotti, Paola Giunti. Clinical features of Friedreich's ataxia: classical and atypical phenotypes. *J Neurochem.* 2013; 126:103-117.
9. Lecocq C, Charles P, Azulay JP, Wassilios Meissner, Myriam Rai, Karine N 'Guyen, *et al*. Delayed-onset Friedreich's ataxia revisited. *Mov Disord.* 2016; 31:62-69.
10. Martinez AR, Moro A, Abrahao A, Ingrid Faber, Conrado R Borges, Thiago JR Rezende, *et al.* Non neurological Involvement in Late-Onset Friedreich Ataxia (LOFA): exploring the phenotypes. *Cerebellum.* 2017; 16:253-256.
11. Milbrandt TA, Kunes JR, Karol LA. Friedreich's ataxia and scoliosis: the experience at two institutions. J Pediatr Orthop. 2008; 28:234-238.
12. Piazzolla A, Solarino G, De Giorgi S, Moretti L, De Giorgi G. Cotrel Dubousset instrumentation in neuromuscular scoliosis. *Eur Spine J* 2011; 20:S75-84.
13. Tsirikos AI, Smith G. Scoliosis in patients with Friedreich's ataxia. J Bone Joint Surg Br. 2012; 94:684-689.
14. Vauzelle C, Stagnara P, Jouvinroux P. Functional monitoring of spinal cord activity during spinal surgery. Clin Orthop Relat Res. 1973; (93):173-178.
15. Hyun SJ, Rhim SC. Combined motor and somatosensory evoked potential monitoring for intramedullary spinal cord tumor surgery: correlation of clinical and neurophysiological data in 17 consecutive procedures. Br J Neurosurg. 2009; 23:393-400.
16. Hyun SJ, Rhim SC, Kang JK, Hong SH, Park BR. Combined motor and somatosensory-evoked potential monitoring for spine and spinal cord surgery: correlation of clinical and neurophysiological data in 85 consecutive procedures. Spinal Cord. 2009; 47:616-622.
17. Pelosi L, Lamb J, Grevitt M, Mehdian SM, Webb JK, Blumhardt LD, *et al*. Combined monitoring of motor and somatosensory evoked potentials in orthopaedic spinal surgery. Clin Neurophysiol. 2002; 113:1082-1091.
18. Owen JH, Sponseller PD, Szymanski E, Hurdle M. Efficacy of multimodality spinal cord monitoring during surgery for neuromuscular scoliosis. *Spine.* 1995; 20:1480-1488.
19. Lawrence H. Phillips II MD, John S. Blanco MD, Michael D. Sussman MD. Direct spinal stimulation for intraoperative monitoring during scoliosis surgery. *Muscle & Nerve* Volume18, Issue3 March, 1995, 319-325
20. Sengupta DK, Grevitt MP, Freeman BJ, Mehdian SH, Webb JK, Lamb J, *et al*. Combined Somato-sensory (SEPS) and Motor evoked potential (MEPS) monitoring in Orthopaedic spinal surgery. Orthopaedic Proceedings. *BritSpine,* 2002, 84(3).
21. Ahmed B Bayoumi, Zafer Orkun Toktas, Baran Yılmaz, Orkun Koban, Murat Sakir Eksi, Hulya Aydin Gungor, *et al*. "Paradoxical Abnormalities of Intra and Postoperative Neuroelectrical Recording of a Scoliotic Child with Friedreich's Ataxia". EC Neurology 3.2, 2016, 350-353.