Original Article

Electrophysiological Study in the Right Upper and Lower Limbs in Infants with Lumbosacral Meningomyelocele and in Normal Infants: A Case–control Study

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Abstract

Objective: The study aimed to assess the electrophysiological parameters (Hofmann reflex [H-reflex] and motor nerve conduction velocity [MNCV]) on children's upper and lower limbs with lumbosacral meningomyelocele (MMC) and age-matched control to see the effect of the MMC on the cervical segment of the spinal cord. **Materials and Methods:** The present study was performed on infants with lumbosacral MMC. Twenty-five infants were examined with a mean age of 50 days of either sex. Out of them, 13 infants were in control and the remaining 12 were diagnosed with MMC. The H-reflex parameter and MNCV were recorded in these children's right upper and lower limbs. **Results:** H-reflex was elicited in all the control group babies. In MMC, the H-reflex was elicited in the upper limbs. However, H-reflex was not elicited in the lower limbs of a few MMC babies. The upper limb's H-reflex parameters and conduction velocity were significantly higher than those corresponding lower limbs in control babies. In MMC, where the H-reflex was elicited, such differences in the lower and upper limbs were not observed. However, the values of MNCV in the upper limb (right median nerve) were significantly less, and the values of Hmax in the lower limb (soleus muscle) were significantly more in MMC babies than in the control group. **Conclusions:** The values of electrophysiological parameters were higher in the upper limbs as compared to the corresponding lower limbs in control. These values were not altered in the upper limbs than those corresponding lower limbs of MMC, suggesting that motor function development was impaired/delayed in the spinal segment cranial to MMC lesion, and motor impairment in MMC children is mostly a result of upper motor neuron dysfunction.

Keywords: *Hofmann reflex, motor nerve conduction velocity, spina bifida*

Introduction

A congenital neural tube defect condition, also known as meningomyelocele (MMC), is caused when the neural tube fails to close at roughly 3–4 weeks of gestation.[1] In addition, brain dysmorphologies, hydrocephalus, and Chiari type II malformation may often associate with it. Although the natural history of MMC has altered throughout the years, studies of neuronal impairment are often done in infancy or childhood.[2] More people with MMC are living to maturity due to improvements in neurosurgical therapies for the shunt management of the related hydrocephalus and primary spinal lesion. Their physical or neurological development and changes with age were little known. MMC patients also have urine, bowel problems, and sensory-motor deficiencies in their lower limbs, making it difficult for them to stand and move about, leading to dependence on wheelchairs.[3] Several deficits in perception and cognitive growth were also reported.[4,5]

Most children with MMC also have impaired upper limb function. Many clinical investigations on older children and a few research on young adults provided the framework for understanding upper limb motor function in people with MMC.[3-5] Bimanual coordination, finger-and-hand dexterity, planning, speed, and motor weakness are among the upper limb motor impairments in MMC.[2-9] Upper limb dysfunction in MMC leads to more physical dependency in these children. The reason for the upper limb motor dysfunction (cranial to MMC segment) was not clear.

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No literature was available on quantitative investigations of upper limb motor function in MMC adults or children. Thus, we plan the study to compare the electrophysiological parameters, i.e., Hofmann reflex (H-reflex) and conduction velocity, on children's upper and lower limbs with MMC and age-matched control to see the effect of the MMC on the cervical segment of the spinal cord.

Materials and Methods

The present case–control study was performed between MMC and control children. The Institute of Medical Sciences (IMS), Banaras Hindu University's Ethical Committee, duly approved the study protocol with IRB number Dean/2014-15/EC/513, ECR/526/Inst/UP/2014/RR20. The study included 25 children with a mean age of 50 days of either sex admitted to the Pediatric Surgery Department of SS Hospital at Banaras Hindu University, Varanasi, Uttar Pradesh, India. Twelve had MMC in the lumbosacral region, with an average MMC sac size of 5 cm × 5 cm. The remaining 13 were age-matched controls. These babies were born at full term with birth weights above the 10th percentile of the local Indian standard.[10] Children with hemodynamic instability, septicemia, hypoglycemia, meningitis, major head trauma, other neurological disorders, hydrocephalus, or other genetic defects were excluded from the study.

At the Department of Physiology, IMS, Banaras Hindu University Varanasi, Uttar Pradesh, India, electrophysiological examinations were carried out. After receiving parental consent in writing, electrophysiological examinations were performed. The GRASS stimulator (GRASS Technologies, 600 East Greenwich Avenue, West Warwick, RI02893, USA) and data acquisition system (Biopac Student Lab Advance System) were used to record the electrophysiological parameters. The method of recording parameters was already standardized in the Neurophysiology Research Unit, Department of Physiology, IMS.[11-13] Before electrophysiological examinations, history of diseases and anthropometric and clinical examinations were done. Then, electrophysiological parameters were examined in the children's right upper and lower limbs. For electrophysiological examination in the right upper limb, the babies were placed comfortably in a supine position on the mother's lap, and the forearm was kept extended firmly. After proper skin cleaning with spirit, surface-active recording electrodes (Ag-AgCl) were firmly put over the skin with the help of adhesive tape after applying conducting jelly over the abductor pollicis brevis muscle in the thenar compartment of the hand. Both H-reflex and motor nerve conduction velocity (MNCV) parameters were recorded at the same recording electrodes. The median nerve was stimulated in the cubital fossa to elicit, H-reflex parameters. However, for MNCV to stimulate the right median nerve at two distinct locations along its course, stimulating electrodes were placed at the cubital fossa first and then at the wrist lateral to the palmaris longus tendon.

They were comfortably positioned on the mother's lap for an electrophysiological assessment of the right lower limb. The right lower limb was held extended by putting a small cushion below it. For noninvasive H-reflex, the active recording electrode was placed on the belly of the soleus muscle midline at the junction of the upper 2/3 and lower 1/3 of the calf area. The posterior tibial nerve was stimulated at the popliteal fossa. At the same time, the active recording electrode was positioned across the belly of the abductor digiti minimi muscle directly below the fifth metatarsal bone on the lateral part of the sole to record MNCV. The right posterior tibial nerve was first stimulated at the popliteal fossa and then behind the medial malleolus to drive the MNCV. We used the submaximal strength stimulus for eliciting H-reflex and the supramaximal stimulus strength for M-response. The single stimulus (with 0.1–0.2 ms duration) was delivered percutaneously on the posterior tibial/median nerve. A minimum interval of >3 s is required to fully recover from the initial stimulus. The data acquisition system monitor recorded the elicited compound muscle action potential (CMAP).

The shortest latencies of CMAPs were measured with the help of a marker and scalp provided within the software. At this time, the H-reflex latency (HRL) and maximum amplitude of H-reflex (Hmax) were noted.

Surface Electromyography (EMG) was also recorded from the same recording sites during the baby's resting position and when he was made active by tapping on the sole in the case of the lower limb and pinching the fingers in the case of the upper limb. Each baby completed the examinations in one sitting.

The graphical and statistical analyses were conducted using the SPSS 16.0 (SPSS Inc. SPSS for Windows, Version 16.0. Chicago, SPSS Inc), MS Excel (Microsoft Corporation. Microsoft Excel [Internet] 2013), SigmaPlot 10 (Systat Software Inc., SigmaPlot 10.0, Point Richmond, CA, USA). Standard deviation and arithmetic mean were computed for quantitative variables. There were few instances in each category, and the data were not normally distributed. Therefore, the differences in electrophysiological parameters between the groups were evaluated for statistical significance using the nonparametric Mann–Whitney *U*-test. $P = 0.05$ or below was deemed significant.

Results

In the present study, anthropometric parameters (weight, age, head circumference, and crown heel length [CHL]) of control and MMC are given in Table 1. CHL in the MMC group was significantly lower ($P < 0.05$) than in the control group. Other anthropometric parameters were comparable in both the control and MMC groups.

All healthy infants exhibited the H-reflex. The values of H-reflex parameters and MNCV in normal children were within the normal limit of their respective age groups.

In the right upper limb of the MMC group, the H-reflex was elicited in all babies. The values of HRL (12.15 ± 1.79 ms), Hmax (1.66 ± 1.04 mv), maximum amplitude of the M-wave (Mmax) (3.00 ± 1.11 mv), and H/M% (54.63% ± 27.69%) were similar to the control group. The value of H-reflex conduction velocity (HRCV) (36.65 ± 10.56 m/s) was similar to the control group. However, the values of MNCV (52.25 ± 2.46 m/s) were significantly lesser than the control group. Surface EMG at rest values (0.04 ± 0.03 mv) and action (0.25 ± 0.21 mv) was similar to the control group [Table 2].

In the right lower limb of the MMC group, the H-reflex was not elicited in all MMC groups. Out of 12 MMC babies, H-reflex was absent in three babies. The values of Hmax (1.70 ± 0.87 mv) were significantly higher than the control group. The values of HRL (12.11 ± 0.81 ms), Mmax (3.41 ± 1.55 mv), and H/M% (39.30% ± 18.64%) were similar to the control group. HRCV (36.30 ± 4.99 m/s), MNCV (45.90 ± 11.61 m/s), and other electrophysiological parameters were similar to the control group. The values of surface EMG at rest (0.03 ± 0.02 mv) and action (0.55 ± 0.47 mv) were similar to the control group [Table 3].

Hmax, H/M%, and MNCV in the upper limb were considerably greater than the corresponding lower limb in the control group. However, the difference in the values of H-reflex parameters and conduction velocities in the lower and upper limbs in the MMC group was not observed [Figures 1-3].

Table 1: Anthropometric measurements (mean±standard deviation) of control and meningomyelocele babies

Parameters	Group I normal infants (*n*=13)	Group II MMC (*n*=12)	I versus II
Age (days)	50.37±26.89	33.15±28.32	NS
Weight (kg)	3.66±0.87	3.73±0.94	NS
CHL (cm)	52.93±3.85	49.66±2.00	*P*<0.05
HC (cm)	36.03±2.28	35.69±2.78	NS
MAC (cm)	10.20±0.35	10.38±0.34	NS
MCC (cm)	10.86±0.35	11.27±0.35	NS

MMC: Meningomyelocele; CHL: Crown heel length; HC: Head circumference; MAC: Mid-arm circumference; MCC: Mid calf circumference; NS: Not significant

Table 2: Electrophysiological parameters (mean±standard deviation) in right upper limb of control and meningomyelocele babies

Parameter	Group I normal (*n*=13)	Group II MMC (*n*=12)	I versus II
HRL (ms)	12.93±2.48	12.15±1.79	NS
Hmax (mv)	1.80±0.97	1.66±1.04	NS
MRL (ms)	0.85±0.20	0.95±0.21	NS
Mmax (mv)	2.94±1.21	3.00±1.11	NS
H/M%	58.66±20.85	54.63±27.69	NS
HRCV (m/s)	36.56±9.97	36.65±10.56	NS
MNCV (m/s)	56.80±2.32	52.25±2.46	*P*<0.05
EMG at rest (mv)	0.03±0.01	0.04±0.03	NS
EMG at act (mv)	0.20±0.11	0.25±0.21	NS

HRL: H-reflex latency; MNCV: Motor nerve conduction velocity; EMG: Electromyography; HRCV: H-reflex conduction velocity; MMC: Meningomyelocele; NS: Not significant; Hmax: Maximum amplitude of H-reflex; Mmax: Maximum amplitude of the M-wave; MRL: M response latency

Discussion

In the present study, H-reflex was elicited in the right lower and upper limbs in all normal infants. H-reflex was also induced in the right upper limb of MMC infants. However, it was absent in the lower limbs of a few babies suffering from MMC. The absence of the H-reflex in the right lower limb suggests that certain elements of the spinal reflex arc may be impaired in these individuals, as the H-reflex is an electrically induced monosynaptic reflex (MSR).[14] The spinal cord injury may disrupt the monosynaptic pathway, leading to the loss of the spinal H-reflex in most of the MMC infants. In MMC, the spinal cord, its roots, and ganglia are unprotected by the vertebral column and exposed to the body's surface. There is always a risk of injury with the slightest pressure on the exposed sac. Further ischemia is prevalent as the neural structures are not well connected with the vasculature, leading to spinal cord injury to that segment.[15,16] Our previous study also observed the absence of H-reflex in the lower limb in MMC infants.[11]

The electrophysiological examinations of the right upper limb were done to see the effect of the MMC (lumbosacral region) on the cervical segment of the spinal cord (cranial to MMC lesion). The H-reflex parameters were present in all the MMC babies at the right upper limb (median nerve-abductor pollicis brevis). These parameters were almost comparable with a control group. However, MNCV in

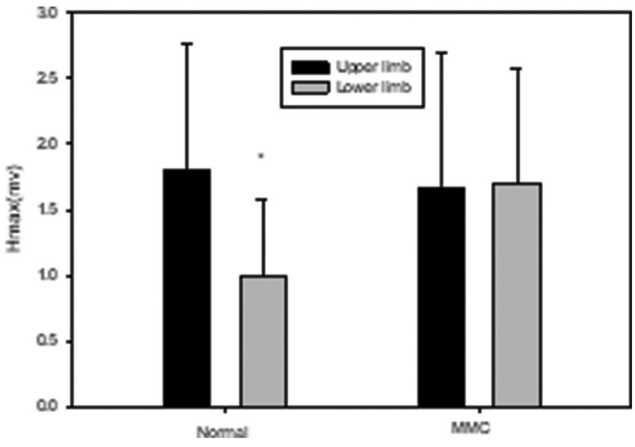

Figure 1: Each bar depicts the mean ± SD values of Hmax (mv) of the control and MMC groups' right upper limb and lower limbs. The asterisk (*) indicates a significant difference between the upper limb and the corresponding lower limb within group. MMC: Meningomyelocele; SD: Standard deviation; Hmax: Maximum amplitude of H-reflex

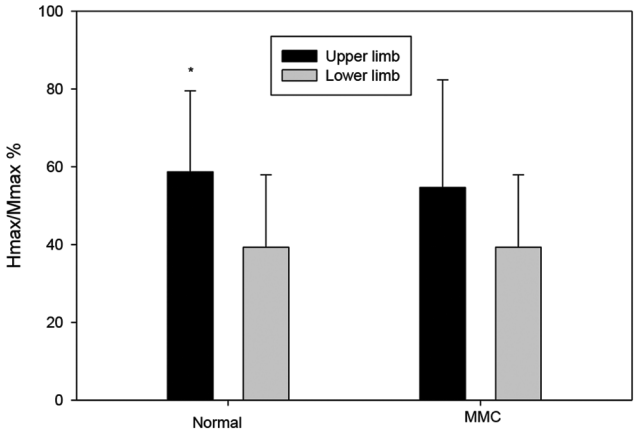

Figure 2: Each bar depicts the mean ± SD values of Hmax/Mmax ratio of the control and MMC groups' right upper limb and lower limbs. The asterisk (*) indicates a significant difference between the upper limb and the corresponding lower limb within group. MMC: Meningomyelocele; Hmax: Maximum amplitude of H-reflex; Mmax: Maximum amplitude of the M-wave; SD: Standard deviation

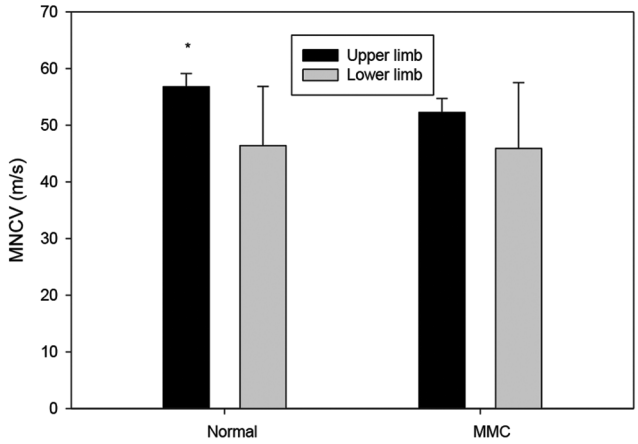

Figure 3: Each bar depicts the mean ± SD values of MNCV (m/s) of the control and MMC groups' right upper limb and lower limbs. The asterisk (*) indicates a significant difference between the upper limb and the corresponding lower limb within group. MNCV: Motor nerve conduction velocity, MMC: Meningomyelocele; SD: Standard deviation

Table 3: Electrophysiological parameters (mean±standard deviation) in right lower limb of control and meningomyelocele babies

Parameters	Group I normal infants (*n*=13)	Group II MMC (*n*=12)	I versus II
HRL (ms)	13.14±1.73	12.11±0.81 (9)	NS
Hmax (mv)	1.00±0.58	1.70±0.87 (9)	*P*<0.05
MRL (ms)	0.63±0.14	0.39±0.04	NS
Mmax (mv)	3.15±1.30	3.41±1.55	NS
H/M%	35.27±17.88	39.30±18.64 (9)	NS
HRCV (m/s)	34.65±4.99	36.20±4.99 (9)	NS
MNCV (m/s)	46.40±10.46	45.90±11.61	NS
EMG at rest (mv)	0.03±0.02	0.03±0.02	NS
EMG at act (mv)	0.44±0.36	0.55±0.47	NS

HRL: H-reflex latency; MNCV: Motor nerve conduction velocity; EMG: Electromyography; HRCV: H-reflex conduction velocity; MMC: Meningomyelocele; NS: Not significant; Hmax: Maximum amplitude of H-reflex; Mmax: Maximum amplitude of the M-wave; MRL: M response latency

MMC babies' upper limbs (median nerve) was significantly lesser than in the control group. MNCV depends on nerve fiber diameter, myelination of nerve fibers, and internodal distance. The myelination/maturation of the central nervous system develops during the 1st year of life. Conduction time shortens and nerve conduction velocities rise quickly at this time. These maturational mechanisms take place before skeletal muscle development.[17] At the same time, other investigators reported slow MNCV in nerves of the lower limb (peroneal and tibial nerves) in MMC.[18] Furthermore, postulate the hypothesis that this is due to the retarded myelination of nerves.[18] High-field proton magnetic spectroscopy and studies using diffusion tensor tractography on MMC children and adults revealed abnormal association pathway development as well as defective neuronal myelination.[1,19] The reasons for the reduced myelin thickness in neurons are probably multifactorial. Spinal cord defects, poorly developed pathways, and unknown genetic anomalies that coexist with this state may consistently fail to myelinate adequately, indicating the decreased efficiency of myelin repair processes and potential degradation of axonal microstructure.[1,20-23]

H-reflex elicitation in the right lower limb was seen in MMC infants; the values of Hmax were significantly higher compared with normal babies. The value of Hmax represents the maximum amplitude of reflexly excitable motoneurons, and H/M% indicates the ratio of the reflexly excitable motor neuronal pool.[14] In MMC after spinal cord injury, a simultaneous cascade of occurrences at the systemic, molecular, and cellular levels was onset by nerve damage, which altered the excitability of the neuronal motor pool.[24] Havton and Kellerth showed in an adult cat that unilateral ventral root transaction induced an ipsilateral increase in MSR strength of adjacent intact spinal segment motoneurons by almost two times even after 6–12 weeks of injury.[25] These cellular and molecular changes may increase excitability in viable motor neurons, leading to increased Hmax and H/M% in our study of MMC. However, the values of other H-reflex parameters and nerve conduction velocity were comparable to the control group. Other investigators reported slow conduction velocity in lower limbs' tibial and peroneal nerves in MMC.[18] Lesser HRCV and Mmax were also reported in infants with MMC.[11]

When comparing electrophysiological parameters of the same side of the upper limb with the corresponding lower limb, in the control group, the values of Hmax, H/M%, and MNCV were considerably higher in the upper limb. The values of electrophysiological parameters in the lower and upper limbs in MMC did not demonstrate such differences as observed in the control group. Although the parameters

in the upper limb were almost comparable with the control group except for MNCV, which was significantly lesser. It indicates a developmental delay in motor function or weakness in the upper limb in children with MMC. Upper limb motor dysfunction was reported along with sensory and motor deficits of the lower limb in older children and adults with spina bifida.[2-4,6,7] The effects of MMC and spinal cord lesion levels on motor function are somewhat unclear. Sival *et al*. studied spina bifida and reported that the lower motor neuron damage was restricted toward the caudal direction and left behind the upper spinal segment. The newborns with MMC saw reduced anterior horn cells and abnormal vascularization in the spinal section caudal to the MMC. The spinal section anterior to the MMC did not show any of these anomalies.[16,26-28] Grimm claimed that impaired hand function was linked to larger lesion levels, whereas Dennis *et al*. reported no association between MMC lesion level and hand function.[3,6] Children with MMC are often associated with brain dysmorphology, and the clinical neurologic examination has shown a more significant connection between upper motor neuron dysfunction and motor disability.[29] The present study indicates motor dysfunction in spinal segment cranial to MMC lesion and subclinical motor dysfunction in upper limbs is present early in these lumbosacral MMC children.

The present study had a limited sample size and was preliminary in nature. We did not observe the electrophysiological parameter in the left limbs nor follow-up on age changes in these MMC patients as the study was fully dependent on the outpatient department follow-up and cooperation of parents. We also did not observe the electrophysiological parameter in another form of MMC, i.e., cervical MMC and thoracic MMC children.

Conclusions

In the present study, the electrophysiological parameters, i.e., H-reflex, were not intact in the MMC children's lower limbs. Where H-reflex was intact, the values of Hmax were higher, suggesting excitable motor neurons due to a simultaneous cascade of events induced by the spinal cord injury in MMC children. H-reflex parameters and conduction velocity in upper limbs were not different from the corresponding lower limbs in children with MMC, suggesting that motor function development was impaired/delayed in spinal segment cranial to MMC lesion and motor impairment in MMC children is mostly a result of upper motor neuron dysfunction. Hence, early start of physiotherapy/treatment modality for upper limbs in these babies may be minimized or prevent upper limbs disability.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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