Effect of Yoga as an Add-on Therapy in the Modulation of Heart Rate Variability in Children with Duchenne Muscular Dystrophy

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Abstract

Background: Duchene muscular dystrophy (DMD) is a progressive muscular disorder. Cardiac disorder is the second-most common cause of death in children with DMD, with 10%–20% of them dying of cardiac failure. Heart rate variability (HRV) is shown to be a predictor of cardio-autonomic function. Physiotherapy (PT) is advised for these children as a regular treatment for maintaining their functional status. The effect of yogic practices on the cardio-autonomic functions has been demonstrated in various neurological conditions and may prove beneficial in DMD. **Materials and Methods:** In this study, 124 patients with DMD were randomized to PT alone or PT with yoga intervention. Home-based PT and yoga were advised. Adherence was serially assessed at a follow-up interval of 3 months. Error-free, electrocardiogram was recorded in all patients at rest in the supine position. HRV parameters were computed in time and frequency domains. HRV was recorded at baseline and at an interval of 3 months up to 1 year. Repeated-measures ANOVA was used to analyze longitudinal follow-up and least significant difference for *post hoc* analysis and $P < 0.05$ was considered statistically significant. **Results:** In our study, with PT protocol, standard deviation of NN, root of square mean of successive NN, total power, low frequency, high-frequency normalized units (HFnu), and sympathovagal balance improved at varying time points and the improvement lasted up for 6–9 months, whereas PT and yoga protocol showed an improvement in HFnu during the last 3 months of the study period and all the other parameters were stable up to 1 year. Thus, it is evident that both the groups improved cardiac functions in DMD. However, no significant difference was noted in the changes observed between the groups. **Conclusion:** The intense PT and PT with yoga, particularly home-based program, is indeed beneficial as a therapeutic strategy in DMD children to maintain and/or to sustain HRV in DMD.

Keywords: *Duchene muscular dystrophy, heart rate variability, physiotherapy, yoga*

Introduction

Duchenne muscular dystrophy (DMD) is a steadily progressive primary muscle disease and is the most common form of neuromuscular disorder with an X-linked recessive pattern of inheritance that ultimately leads to loss of ambulation and death at a young age.[1,2] The incidence of DMD is approximately 15.9–19.5/100,000 live births.[3,4] In India, DMD has been found to account for 30% of all reported forms of muscular dystrophies.[5] Respiratory failure and cardiac involvement are the most common causes of death in children with DMD,[6] but with advancement in respiratory support techniques, cardiac disorders remain an important problem in the late stages of the disease. Research in this field reveals that there is an involvement of myocardium before the onset of clinically apparent cardiomyopathy in DMD.[7] However, it has been observed that, in a routine management of DMD children, assessment of cardiac function is not considered until the clinical manifestations are detected. Nonrecognition of cardiac impairment and treatment at the early stages can lead to poor outcomes. Hence, recognition and management of the cardiac autonomic dysfunction is an important strategy for prolonged life expectancy and better quality of life in children with DMD.

Heart rate variability (HRV) assessment is an economical, noninvasive, and sensitive procedure for investigating autonomic neurocardiac regulation.[8] HRV also provides a novel approach to the clinical diagnosis and prognostic measures. Several authors have used HRV to assess cardiac

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neural regulation.[9-11] Short-term HRV analysis is a good tool to investigate DMD children for evidence of cardiac autonomic dysfunction.[12] Our previous study demonstrated the need for routine assessment of cardiac functions using HRV measures, and short-term HRV analysis showed significant difference in the cardio-autonomic parameters among the DMD children than the healthy volunteers.[12]

Apart from medical management, physiotherapy (PT) in the form of physical exercise is considered as one of the vital rehabilitation strategies for the maintenance of physical function. The role of exercise has been studied in the modulation of cardiac functions and found that training induces a resting bradycardia accompanied by increased cardiac vagal modulation in healthy individuals.[13]

Yoga being the adjuvant therapy is considered as a simple practice that can be followed even at home with prior training. Practicing yoga has shown improvement in cardio-autonomic functions in normal individuals of different age groups.[14-16] Improvement in cardio-autonomic functions in healthy volunteers using different yoga modules and physical exercise has been documented.[17] However, the effect of yoga therapy to modulate HRV in DMD children has not been studied.

Materials and Methods

Subjects

This study was conducted at the National Institute of Mental Health and Neurosciences (NIMHANS). Approval for this study was obtained from the Institutional Ethics Committee. Two hundred children were screened, and 124 children with genetically confirmed DMD, in the age group of 5–10 years, who were self-ambulant or required minimal assistance for walking, were recruited after obtaining written assent and consent. Our cohort were drug naive at the time of evaluation and were recruited for the study after genetic testing which was available within 3–4 weeks after clinical examination. Children who had muscular dystrophy other than DMD, nonambulant children, and children/parents not willing to participate in the study were excluded from the study.

Study design

Age matched randomized controlled repeated measure design.

The patients were paired for age and randomly allocated to Group 1 (PT only) and Group 2 (yoga and PT [Y and PT]) using a computer-generated random table.

Assessment

HRV was used as the assessment tool in this study. Artifact-free, electrocardiograms were obtained for all patients in the supine position. Recordings were analyzed for time and frequency domain parameters according to the Taskforce report on HRV.[8] HRV parameters were computed in time and frequency domains. Time domain measures include the standard deviation of NN (SDNN) interval and root of square mean of successive NN (RMSSD) interval. Frequency domain consisted of total power (TP), low frequency (LF), and high frequency (HF) power values. The ratio of LF/HF power values was determined using the customized software. HRV assessments were done at the first presentation and sequentially at intervals of 3, 6, 9, and 12 months. All participants were given a compliance notebook to maintain exercise performance to make sure that children were practicing yoga and PT at home. Log books were reviewed on every visit.

Intervention

All children received the standard approved therapy of oral prednisolone at 0.75 mg/kg/day from the day of diagnosis and this was continued during the entire study period.

Physiotherapy

PT exercise was taught to children and parents in the Physiotherapy Department of NIMHANS. They were made to practice it under the supervision of physiotherapists initially for a period of 1 week. Once they learned the exercises, they were advised to carry it out at their homes. PT exercises were performed twice daily by the participants, morning and evening for 45 min per session, and were continued during the entire study period. Details of PT exercises are summarized in Table 1.

Yoga

Similarly, yoga practice was taught to the children and their parents by a trained, accredited yoga therapist. They were made to perform the yoga under the supervision of the yoga therapist for 1 week. Once they learned, they were advised to practice

Table 1: Physiotherapy exercises

Exercise	Duration (min)
Active and passive ROM exercises to all the joints	10
Active and active-assisted breathing exercises	5
Task-oriented exercises: Rolling, lying to sitting, sitting to standing, standing, walking, climbing one flight of stairs, throwing and kicking a ball, passing the ball from left to right and then from front to back and vice versa, hand activities	10
Activity-based breathing exercises: Blowing pieces of paper, blowing candle placed at varying distances, blowing balloons of different sizes, blowing a party whistle, blowing bubbles with a straw, picking up objects such as small pieces of paper or small thermocol balls, sucking through a straw and then keeping it at a particular orientation. (all activity-based breathing exercises started with a deep inspiration)	10
Stretching exercises: For trunk, chest wall, and commonly affected joints	10

ROM=Range of motion

yoga in their homes. Children in this group performed yoga in the morning and PT exercises in the evening, each session lasting for 45 min, and was continued during the entire study period. Detail of yoga practices is summarized in Table 2.

Data extraction

All the data were documented in a standardized pro forma and later decoded.

Data analysis

Basic demographic details were analyzed using descriptive statistics. Groups were compared using independent sample *t*-test for continuous variables. HRV data were square root transformed to produce normal distributions. Values are expressed in (mean [standard deviation]). Level of significance was kept at <0.05. RM ANOVA was used to analyze longitudinal follow-up and least significant difference for *post hoc* analysis.

Results

The age of the children participated in this study ranged from 5 to 10 years. The mean age at presentation was 7.9 ± 1.5 years. Mean height was 118.2 ± 8.4 cm (95–147 cm). Mean weight was 20.6 ± 4.3 kg (11–32 kg). Mean age at onset of DMD was 2.8 ± 0.6 years (1.5–4.0 years). Mean duration of illness was 5.1 ± 1.5 years (1–8 years). At the end of the study, 45 children completed the scheduled assessments in PT group and 43 children completed in Y and PT group. Details are explained in CONSORT diagram [Figure 1].

At baseline, DMD children showed significantly lower mean NN (PT: 606.1 ± 77.1 and Y and PT: 605.7 ± 78.5), higher average heart rate (PT: 100.4 ± 12.0 and Y and PT: 100.8 ± 13.0), and significantly reduced HF and HF normalized units (HFnu). The sympathovagal balance (SVB) was tilted toward sympathetic limb in DMD children. The time and frequency domain findings of HRV were similar in both the two study groups.

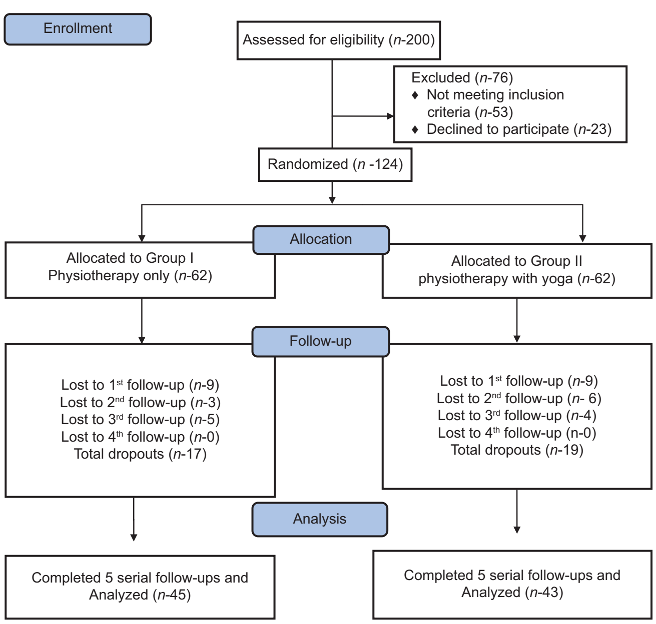

Figure 1: CONSORT flow diagram

After the PT protocol, SDNN, RMSSD, TP, LF, HFnu, and SVB improved at varying time points and the improvement lasted up for 6–9 months. Whereas the combined protocol of PT and yoga showed an improvement in HFnu during the last 3 months of the study period and all the other

Table 2: Yoga practices

Exercise	Duration (min)
Sukshma and Sthula Vyayama standing position	10
Manibandha sakti Vikasaka (wrist)	
Anguli shakti Vikasaka (finger)	
Kaponi shakti Vikasaka (elbows)	
Bhuja Bandha shakti Vikasaka (arms)	
Griva Shakti Vikasana I, II, III (neck)	
Purna Bhuja Shakti Vikasana (shoulders)	
Pada Mula Shakti Vikasaka	
Pada anguli shakti Vikasaka	
Rekha Gati shakti Vikasaka	
Pada sanchalana	
Heel walking	
Supine position	
Knee cap tightening	
Dorsal stretch	
Acute thigh flexion	
Breathing exercises	10
Hand stretch breathing	
Hands in and out breathing	
Tadasana breathing	
Tiger breathing and stretching	
Shalabhasana breathing	
Sethubandasana breathing	
Straight leg raising breathing	
Asanas	10
Standing: Tadasana and Vrikshasana	
Sitting: Vakrasana and Marjalasana	
Prone: Bhujangasana	
Supine: Pavanamukthasana, Markatasana and Sethubandasana	
Pranayama and kriya	7
Yogic breathing	
Kapalabhati	
Nadishuddi	
Bhastrika and Bhramari	
Meditation	8
Pranava japa: A, U, M, AUM.	
Mind Sound Resonance Technique (MSRT)	

parameters were stable up to 1 year. When compared age wise with baseline values up to 1 year, in PT group, there was no significant change in any of the HRV parameters, while, Y and PT group showed a significant improvement in HFnu in 5–6 years' group and mean NN and average HR in 7–8 years. However, no significant difference was observed between PT and Y and PT groups in other parameters. We observed that PT group demonstrated improvement in HRV parameters, but these effects were not long lasting, whereas Y and PT combination is more helpful in improving cardiac function between 5–8 years of age. Detailed data are provided in Tables 3 and 4.

Discussion

This study was conducted to know the added effect of yoga in the modulation of HRV among the children with DMD. The HRV measures were used to assess the sympathetic and parasympathetic nervous activities. In HRV measures, the HF component of the HRV indicates the vagal activity. In a given point of time, any rise in the HF power, especially HFnu, indicates a vagal dominance. Similarly, increased LF power indicates increased sympathetic activity. The LF-HF ratio indicates overall SVB. High LF-HF ratio denotes increased sympathetic activity and a low LF-HF ratio indicates increased parasympathetic activity.[18] In this study, the baseline HRV findings were showing predominant sympathetic overactivity (increased SVB and reduced HF; HFnu) along with decreased mean NN. Subsequently, the PT intervention showed noteworthy changes in HRV parameters. The parasympathetic domination was very obvious during the intervention and lasted up to 6–9 months. However, the added benefit of yoga showed further improvement in parasympathetic regulation (HFnu). The age-wise improvement toward vagal balance was significant in our study. There was an additional long-lasting improvement in autonomic modulation in 5–8 years of age of DMD children with Y and PT group. All these findings confirm that DMD children have autonomic dysfunction and these can be modulated by the interventions and stringent follow-ups. We also proved that yoga as an adjuvant therapy has an additional benefit in enhancing the neuro-cardiac autonomic controls.

Studies showed that skeletal muscle training can be beneficial in patients with DMD.[19-21] Despite the lack of studies addressing the use of yoga exercises as a complementary therapy for DMD patients, there have been several other clinical studies of yoga on healthy volunteers. A study on healthy adults aimed to find out the effect of yoga practice on HRV and showed increase in certain HRV parameters such as mean RR interval, SDNN, HF power, and HFnu.[22] There was also reduction in the resting heart rate, LF power, and LF/HF ratio. Several other studies on the effect of yoga on HRV exhibited an increase in the parasympathetic tone which is reflected through the HRV

Table 3: Comparison of serial evaluation of heart rate variability values in the two study groups

HRV values	Group	Baseline	3 months	6 months	9 months	12 months	Time effect	Interaction effect	Group effect	Pair-wise comparison
AVG	I	100.4±12.0	99.8±12.7	101.0±11.9	98.8±14.5	98.3±15.7	*F*=1.370	*F*=0.456	*F*=0.140	
HR	II	100.8±13.0	99.8±12.4	98.3±11.7	99.1±13.2	98.3±15.8	*P*=0.244	*P*=0.768	*P*=0.709	
Mean	I	606.1±77.1	611.2±83.6	602.7±77.9	621.2±97.6	600.7±126.2	*F*=0.533	*F*=1.210	*F*=0.387	
NN	II	605.7±78.5	608.7±75.3	618.5±73.3	616.4±85.8	637.3±92.3	*P*=0.711	*P*=0.307	*P*=0.536	
SDNN	I	54.5±27.1	52.3±26.7	45.4±22.8	57.3±32.3	55.1±32.0	*F*=1.721	*F*=0.978	*F*=0.061	¥
	II	52.7±27.4	52.1±23.3	52.4±26.8	52.4±27.1	61.3±49.9	*P*=0.161	*P*=0.407	*P*=0.806	
RMSSD	I	50.9±32.2	51.5±37.2	42.3±30.0	56.3±44.8	51.3±38.4	*F*=1.212	*F*=0.916	*F*=0.074	¥
	II	50.0±32.5	49.2±29.7	49.6±34.6	50.2±36.8	61.9±68.6	*P*=0.306	*P*=0.433	*P*=0.786	
TP	I	3440.1±3514.4	3357.9±3760.1	2639.8±2978.6	3978.9±4566.2	4166.5±5227.2	*F*=1.920	*F*=0.767	*F*=0.130	¥
	II	3217.5±3205.2	2957.7±2541.7	3374.9±3466.5	3305.3±3666.4	6256.3±1585.3	*P*=0.164	*P*=0.423	*P*=0.719	
LF	I	1043.1±997.6	784.7±790.4	680.4±711.6	1205.1±1435.1	1105.7±1346.6	*F*=2.418	*F*=1.473	*F*=0.082	$;¥;*
	II	824.3±768.3	765.7±761.3	913.9±960.2	816.9±792.1	1229.4±2128.4	*P*=0.082	*P*=0.230	*P*=0.775	
LFnu	I	40.7±15.5	37.5±16.5	41.4±18.3	42.1±19.7	47.9±42.9	*F*=1.015	*F*=0.954	*F*=0.958	
	II	38.9±16.8	38.3±17.0	39.55±15.3	40.0±16.1	46.1±40.5	*P*=0.308	*P*=0.333	*P*=0.331	
HF	I	1135.4±1718.9	1433.1±2485.6	1087.2±1849.2	1439.5±2549.0	1438.9±2212.1	*F*=1.497	*F*=1.097	*F*=0.162	
	II	1154.8±1478.5	1029.7±1188.9	1375.5±1972.5	1223.5±2052.6	2591.2±7043.6	*P*=0.229	*P*=0.327	*P*=0.688	
HFnu	I	36.3±12.3	39.8±15.6	38.6±17.9	34.9±16.4	40.4±16.0	*F*=2.640	*F*=0.642	*F*=0.658	*
	II	38.3±16.1	38.1±14.8	41.2±15.0	37.9±13.8	45.6±28.9	*P*=0.054	*P*=0.578	*P*=0.420	&
SVB	I	1.3±0.8	1.3±1.2	1.5±1.5	1.5±0.9	1.0±0.7	*F*=1.742	*F*=0.600	*F*=0.386	£;&
	II	1.3±1.1	1.2±1.1	1.2±0.9	1.2±0.8	1.1±0.8	*P*=0.141	*P*=0.663	*P*=0.537	

¥6 months–9 months, $Baseline–6 months, *3 months–9 months, &9 months–12 months, £6 months–12 months. (Special characters used for explaining pair-wise comparison.) RmANOVA was performed and the level of significance was kept at *P<0.05, **P<0.005, ***P<0.001. AVG HR=Average heart rate, Mean NN=Mean normal to normal interval, SDNN=Standard deviation of NN interval, RMSSD=Root mean square of successive difference, TP=Total power, LF=Low-frequency power, LFnu=Normalized power in LF band, HF=High-frequency power, HFnu=Normalized power in HF band, SVB=Sympathovagal balance

Table 4: Age-wise difference between baseline and 1 year for heart rate variability values in the two study groups

HRV value	Group	Age (years)	Difference (mean±SD)	*t*	*P*
Mean NN	I	5-6	14.37992±62.03602	0.836	0.420
		7-8	6.1764765±153.5266	0.166	0.870
		9-10	−18.3254±90.00215	0.734	0.477
	II	5-6	−25.4267273±107.5419	0.784	0.451
		7-8	−68.7821875±108.7914	2.529	0.023*
		9-10	10.6035833±94.09189	0.390	0.704
AVG HR	I	5-6	−3.14426±11.90255	0.952	0.360
		7-8	5.8659941±16.7861	1.441	0.169
		9-10	3.1109923±14.17627	0.791	0.444
	II	5-6	2.4112000±14.26399	0.561	0.587
		7-8	10.8590750±17.01534	2.553	0.022*
		9-10	−1.1215250±14.80025	0.351	0.798
RMMSD	I	5-6	4.572656±46.98794	0.351	0.732
		7-8	−9.18451±32.43975	1.167	0.260
		9-10	1.936506±33.71186	0.207	0.839
	II	5-6	−27.221390±121.8915	0.741	0.476
		7-8	−11.736875±42.02128	1.117	0.281
		9-10	6.5923250±23.37363	0.977	0.350
SDNN	I	5-6	2.7157231±31.78388	0.308	0.763
		7-8	−8.33492±27.51931	1.249	0.230
		9-10	2.9472308±32.33319	0.329	0.748
	II	5-6	−15.870209±82.12420	0.641	0.536
		7-8	−11.090112±32.31461	1.373	0.190
		9-10	2.7534000±14.61825	0.652	0.527
TP	I	5-6	−509.971±5384.759	0.341	0.739
		7-8	−2082.33±4551.915	1.830	0.087
		9-10	494.8591±5059.674	0.339	0.741
	II	5-6	−8212.712±29086.13	0.936	0.371
		7-8	−1417.6977±3404.623	1.613	0.123
		9-10	136.0203±1491.308	0.316	0.758
LF	I	5-6	186.2654±879.9361	0.763	0.460
		7-8	−532.716±1138.925	1.929	0.072
		9-10	92.68322±1097.833	0.304	0.766
	II	5-6	−1067.023±3805.714	0.930	0.374
		7-8	−237.8494±777.7343	1.223	0.240
		9-10	48.832416±529.4589	0.319	0.755
LFnu	I	5-6	−3.40772±18.73071	0.656	0.524
		7-8	3.014747±17.28707	0.719	0.482
		9-10	−201.813±734.5425	0.991	0.341
	II	5-6	7.2302545±17.75472	1.351	0.207
		7-8	−19.607537±61.68323	1.271	0.223
		9-10	−5.71610833±19.31088	1.025	0.327
HF	I	5-6	−61.9483±1302.8212	0.171	0.867
		7-8	−930.685±1998.178	1.920	0.073
		9-10	69.43690±2565.328	0.098	0.924
	II	5-6	−4262.2603±12773.71	1.107	0.294
		7-8	−396.5508±45.84320	0.689	0.501
		9-10	87.056333±814.9730	0.370	0.718
HFnu	I	5-6	1.502715±11.82704	0.458	0.655
		7-8	−7.33064±14.89069	2.030	0.059
		9-10	−5.01836±21.07287	0.859	0.407
	II	5-6	−7.946718±7.758805	3.397	0.007*

Contd...

Table 4: Contd...

HRV value	Group	Age (years)	Difference (mean±SD)	*t*	*P*
		7-8	−10.41004±45.84320	0.908	0.378
		9-10	1.4620250±11.60500	0.436	0.671
LF/HF	I	5-6	−0.2074018±1.300502	0.575	0.576
		7-8	0.3304157±0.821599	1.658	0.117
		9-10	0.1817788±1.105768	0.569	0.580
	II	5-6	0.50744072±1.086184	1.549	0.152
		7-8	0.28493473±1.659231	0.665	0.517
		9-10	−0.27319881±1.308870	0.723	0.485

AVG HR=Average heart rate, Mean NN=Mean normal to normal interval, SDNN=Standard deviation of NN interval, RMSSD=Root mean square of successive difference, TP=Total Power, LF=Low frequency, LFnu=Normalized power in LF band, HF=High frequency, HFnu=Normalized power in HF band, LF/HF=Ratio between LF power and HF power

measures.[14,23] To our knowledge, the present study is the first to address and confirm the safety and efficacy of yogic exercises along with PT in children with DMD. The yogic exercises used in the present study are distinctive and were aimed at improving the muscular strength. Each school of yoga has various physical postures (asanas), breathing practices (pranayama), and meditation as their components. In our study, we used Sakthivikasaka (a practice aimed to improve the overall muscular function), selected asanas, pranayama, and meditation (guided meditation). Although the effect of Sakthivikas has not been studied, it can be considered as a practice equivalent to performing moderate-intensity exercise. Since yoga comprises both physical activity in the form of sakhivikasakas and asanas and pranayama, it has advantage in the modulation of HRV through mechanisms similar to practicing physical exercises in addition to practicing pranayama and meditation.

The possible beneficiary effect of interventions on DMD may be due to several mechanisms. It includes a reduction in the catecholamine, angiotensin II, and an increased bioavailability of nitric oxide.[24] Complex neurophysiological mechanism, mediated through limbic, hypothalamic medullary axis and the medullary cardiovascular center, is thought to be the reason for improvements in the HRV after the practice of slow pranayamas.[18] On the other hand, HF yoga breathing practices such as Kapalabhathi are found to enhance sympathetic activity by reducing the vagal tone.[25] Overall relaxation and calming the mind through physical and breathing practices is the primary goal of yogic practices. Finally, we could see that yoga does have a positive effect on skeleton muscle as well as neuro-cardiac beneficiary with probable above-discussed mechanisms.

Strengths and limitations of our study

Strengths

To our knowledge, this is the first study involving DMD children, with follow-up for 1 year, with large samples, to study the effect of yoga. It was a longitudinal, prospective, age-matched, two-group randomized study, with controlled RM design. The DMD being a progressive disease, performing exercise and yoga might have reduced the deleterious effects on such patients. The primary objective of the study was to show that yoga and exercises can be performed by patients with DMD. Although there was 30.6% and 27.4% dropout in yoga and exercise groups, this study showed that yoga exercises are feasible, harmless, and can actually improve HRV in DMD children.

Limitation

This study was not blinded for assessments and interventions.

Conclusion

Since modulation of HRV is an indicator of stable cardiac function and assessment of cardiac function using HRV measure and therapeutic measures, we advised that combined PT and yoga can be initiated as one of the rehabilitation strategies in children with DMD. This can also be a home-based PT, and yoga programs appear to be beneficial and cost-effective in the management of patients with DMD if started early.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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