Assessment of respiratory function and sleep disorders in children with myopathy

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Sri Lanka Journal of Child Health, 2021; **50**(2): 215-221

Abstract

Background: Impaired activity of respiratory muscles and poor lung mechanisms predispose to sleep disordered breathing in neuromuscular disorders. Although it may lead to major morbidity, its relation to respiratory function is poorly defined.

Objectives: To evaluate respiratory muscle function and sleep disorders in children with myopathy and their relationship to daytime and nocturnal symptoms and oxygen saturation.

Method: A cross-sectional study was carried out on 30 children, 20 males and 10 females, diagnosed with myopathy at Abou El Reesh Paediatric Hospital, Cairo University. Arterial blood gases, creatine kinase (CK), aspartate transaminase (AST) and alanine transaminase (ALT) levels were measured. All subjects underwent respiratory function tests using spirometry, overnight polysomnography and diaphragmatic ultrasound.

Results: Patients were assigned into 2 groups based on respiratory function tests assessed by spirometry. Group A included 14 patients with normal respiratory function tests and Group B included 16 patients with abnormal respiratory function tests. A significant difference was noted as regards symptoms suggestive of poor sleep quality, including somnolence, waking unrested and frequent awakening (p=0.005). Apnoea hypopnoea index (AHI) was significantly higher in group B patients (p=0.04). AHI was abnormal in 43% of patients in group A and 69% of patients in group B. Obstructive apnoeic and hypopnoeic events were detected in all patients with abnormal AHI. No significant difference was noted regarding sleep staging, sleep efficiency or total sleep test (TST). There was no significant difference between both groups as regards arterial blood gases, CK, ALT, AST or diaphragmatic ultrasound.

Conclusions: Myopathic children with abnormal respiratory function had a significant increase in symptoms related to sleep deprivation as well as abnormal AHI. In the diagnosis of sleep disordered breathing in myopathic children polysomnography was useful but daytime blood gas analysis was not useful. Children with muscle disorders should be assessed by respiratory function tests and polysomnography, even if they do not have symptoms suggestive of respiratory muscle involvement.

DOI: http://dx.doi.org/10.4038/sljch.v50i2.9558

(Key words: Myopathy, respiratory symptoms, arterial blood gases, respiratory function, polysomnography, diaphragmatic ultrasound)

Introduction

In children with neuromuscular disease (NMD), respiratory muscle weakness is frequently not obvious and is difficult to estimate[1]. Muscle weakness predisposes to repetitive pneumonia and atelectasis, leading ultimately to respiratory failure[1,2]. Clinical assessment of respiratory function in myopathic patients is a poor predictor of sleep-disordered breathing (SDB) and objective respiratory diagnostic tests are essential[2,3]. SDB includes hypoventilation, central apnoea and obstructive sleep apnoea (OSA) leading to critical cardiovascular morbidities and neurological deficits[4]. Polysomnography (PSG) reveals SDB in such patients and helps quantify and show the beneficial impacts of non-invasive positive ventilation[5].

Objectives

To evaluate respiratory muscle function and sleep disorders in children with myopathy and their relationship to daytime and nocturnal symptoms and oxygen saturation.

Method

Thirty children of both genders with myopathy were involved in this cross sectional study. They were recruited from the Neuromuscular Disorders Clinic, Abou El Reesh Paediatric Hospital, Cairo

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(Received on 29 April 2020: Accepted after revision on 19 June 2020)

The authors declare that there are no conflicts of interest

Personal funding was used for the project.

University between January 2017 and August 2017. Their ages ranged from 6-16 years, excluding patients with pulmonary causes of hypoventilation, patients on corticosteroid treatment, those unable to perform the required pulmonary function manoeuvres and patients with severe NMD requiring oxygen therapy.

Baseline data in the form of age, gender, consanguinity, family history, motor and developmental milestones, symptoms of muscle weakness and symptoms of SDB were collected. Blood samples were taken for measuring arterial blood gases (ABG), creatine kinase (CK), alanine transaminase (ALT) and aspartate transaminase (AST). All patients underwent pulmonary function test (spirometry), polysomnography (PSG) and diaphragmatic ultrasound. Jaeger Master Screen Spirometry was done using the closed-circuit technique. This system was adjusted to calibrate body temperature and pressure of saturated gas and volumes (Jaeger Co). Height was measured using a stadiometer. The patient breathed normally (tidal breathing) with the mouth piece in place and nose clips closing the nose; then the patient inhaled deeply through the mouth piece and exhaled as forcefully and rapidly as possible for 6 seconds or until the end of the test. This closed technique creates a flow-volume loop with tracings both above (exhalation) and below (inhalation) the X axis. The following are printed by the spirometer: the flow volume curve, volume time curve and the actual and predicted values.

Parameters measured by spirometry include forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio. Values that fell below 80% of the lower limit of the predicted values were classified as abnormal[6,7].

- Obstructive pattern with a normal FVC (decreased FEV1/FVC ratio, normal FVC).
- Obstructive pattern with reduced FVC (decreased FEV1/FVC ratio, decreased FVC).
- Restrictive pattern (decreased FVC, normal or above normal FEV1/FVC).

Patients were divided according to spirometry results into 2 groups:

Group A: with normal respiratory function.
Group B: with abnormal respiratory function.

PSG was carried out for 6 to 8 hours using a digital package 'Somnologica' on a personal computer using Microsoft Windows 10 ® platform. PSG was attended by a professional technician and a nurse and assessed by 2 expert polysomnographers. PSG was performed utilizing on average 18 channels. Two electro-oculography (EOG) were put off the horizontal line to score horizontal and vertical movements. Six electroencephalography (EEG) channels central, frontal, and occipital were applied by 10-20 system of EEG electrode arrangement with an average referential montage (F3-A2, F4-A1, C3-A2, C4-A1, O1-A2, O2-A1). Two electromyography (EMG) channels were used for submentalis and tibialis anterior muscles.

Air flow was monitored using nasal pressure and oronasal airflow (thermistor). Chest and abdominal belts were applied to monitor respiratory effort. Electrocardiography (ECG) electrodes were applied. Sound was detected via a microphone. According to the American Academy of Sleep Medicine Manual (AASM) for the Scoring of Sleep version 2.5, 2018 the record was scored[8].

The following sleep parameters were recorded: total sleep time (TST), sleep efficiency, sleep staging, apnoea/hypopnoea index (AHI), and periodic limb movement index (PLMI). Attacks of central apnoea were scored when cessation or decrease of ventilatory effort during sleep occurred for 20 seconds or lasted for at least 2 missed breaths associated with absent inspiratory effort all through the entire duration of the event associated with oxygen desaturation (≥3%)[9]. Attacks of obstructive apnoea were scored when there was complete cessation of airflow for at least 2 missed breaths, associated with >90% decrease in signal amplitude for ≥90% of the entire respiratory event, compared to the pre-event baseline amplitude, associated with continuous inspiratory effort all through the entire period of diminished flow[9].

Hypopnoeas were scored when there was ≥50% decline in amplitude of nasal pressure for at least 2 breaths, associated with oxygen desaturation (≥3%)[9]. AHI was known as combined average number of apnoeas and hypopneas that happen per hour of sleep**.** AHI ≤1/hour is considered normal, 1-5 mild, 5-10 moderate and >10/hour severe. PLMI was known as total number of periodic limb movements per hour of sleep and PLM index >5/hour was classified as abnormal[10,11].

Diaphragmatic ultrasound was done using an ultrasound scanner equipped with a multi-frequency linear transducer using a Toshiba apparatus (Nemio XG). Patients were examined in the supine position during spontaneous respiration. The probe was positioned on the lateral thoracic cage in the right 7th or 9th intercostal space between the midclavicular and antero-axillary lines. High resolution B-mode allowed a view of the diaphragm, recognized as the region between two bright hyper-echogenic parallel lines (the pleural and peritoneal membranes). To record

diaphragmatic excursion during respiration, M mode is performed[12].

Diaphragm thickness was evaluated at the zone of apposition during inspiration and expiration, utilizing a linear higher frequency transducer[13]. The zone of apposition is the area of the chest wall where the lower rib cage reaches the abdominal contents. The probe is placed between the antero-axillary and mid-axillary lines, perpendicular to the chest wall. Diaphragmatic thickening is evaluated by the thickening fraction (thickness at end inspiration – thickness at end expiration) / thickness at end expiration. Increment in diaphragmatic thickness during inspiration is considered as an indirect measurement of muscle fibre contraction. A chronically paralysed diaphragm is atrophic, thin and does not increase in thickness during inspiration[14].

Ethical Issues: Written informed consent was given by the patient's parents for their children to enlist in the study. Approval for this study was obtained from the Institutional Ethical Committee of Abou El Reesh Paediatric Hospital, Cairo University (ethical committee number: I-111014).

Statistical analysis: Data were analysed using SPSS© Statistics version 24 (SPSS© Corp., Armonk, NY, USA). Continuous numerical variables were introduced as mean and standard deviation (SD) and were compared utilizing the unpaired t-test. Categorical variables were introduced as number and percentage. Discrete numerical differences were compared utilizing the Mann-Whitney U test. Correlations were tested using the Spearman rank correlation. $p < 0.05$ was viewed as statistically significant.

Results

Thirty myopathic patients (20 males and 10 females) were included in present study. Of the 30 patients 15 (50%) had Duchenne muscular dystrophy (DMD), 8 (27%) had congenital myopathies, 5 (17%) had myotonic dystrophy and 2 (6%) had limb girdle dystrophy. Patients were assigned into 2 groups based on respiratory function tests assessed by spirometry; group A (14 patients) with normal respiratory function and group B (16 patients) with abnormal respiratory function. The demographic data of groups A and B are shown in Table 1.

Table 1: ***The demographic data of groups A and B***

Variable	Group A *(n=14)*	Group B *(n=16)*	*p*
Age - Mean (SD)	09.2 (2.6)	10.56 (3.3)	0.23
Male - n (%)	09 (64.3)	11 (68.8)	0.796
Positive consanguinity - n (%)	10 (71.4)	07 (56.3)	0.389
Positive family history - n (%)	05 (35.7)	08 (50.0)	0.431
Delayed motor development - n (%)	04 (28.6)	08 (50.0)	0.232
Delayed mental development - n (%)	03 (21.4)	02 (12.5)	0.513
Difficult walking - n (%)	14 (100)	16 (100)	
Difficult climbing stairs - n (%)	13 (92.9)	15 (93.8)	0.92
Day time sleepiness - n (%)	0 (0)	07 (43.8)	*0.005**
Waking up tired - n (%)	0 (0)	07 (43.8)	*0.005**
Frequent awakening - n (%)	0 (0)	07 (43.8)	*0.005**

Age, gender, consanguinity, family history, motor and mental development and symptoms of muscle weakness were not significantly different in the 2 groups. However, symptoms suggestive of poor sleep quality including somnolence, waking unrested and frequent awakening were significantly different in the 2 groups (Table 1). The laboratory tests and blood gases of groups A and B are shown in Table 2.

Table 2: ***The laboratory tests and blood gases in groups A and B***

Variable	Group A (n=14)	Group B (n=16)	p
	Mean (SD)	Mean (SD)	
Creatine kinase (CK)	8401.75 (11666.75)	12994.62 (30292.35)	0.63
Aspartate transaminase (AST)	265.5 (116.67)	156.2 (196.91)	0.51
Alanine transaminase (ALT)	245.33 (226.56)	173 (293.7)	0.73
PaO_2	93.85 (3.02)	92.56 (2.34)	0.21
$PaCO_2$	39.03 (8.22)	38.85 (6.47)	0.95
HCO_3	25.49 (4.65)	24.04 (4.47)	0.39
pH	7.38 (0.06)	7.38 (0.05)	0.78

CK, AST, ALT, PaO_2, $PaCO_2$, HCO_3 and pH were not significantly different in groups A and B (Table 2). Spirometry parameters in groups A and B are shown in Table 3. Group A revealed normal respiratory function while group B revealed abnormal restrictive pattern (FVC 71.7±16.62, FEV1% 77.22±16.09).

Table 3: ***Spirometry parameters in groups A and B***

Variable	Group A *(n=14)*	Group B *(n=16)*	p
	Mean (SD)	Mean (SD)	
Forced vital capacity (FVC)	82.93 (9.43)	71.7 (16.62)	*0.047**
Forced expiratory volume in one second (FEV1)	95.37 (12.82)	77.22 (16.09)	*0.006**
FEV1/FVC (%)	104.15 (11.6)	106.29 (10.61)	0.61

Polysomnography parameters in groups A and B are shown in Table 4 and the apnoea/hypopnoea index (AHI) in groups A and B are shown in Table 5. A significantly higher AHI was detected in group B patients, classified as obstructive sleep apnoea (OSA). Obstructive apnoeic and hypopnoeic events were detected in all the patients with abnormal AHI. No significant differences were noted between groups A and B as regards sleep staging, sleep efficiency or TST (Tables 4 and 5).

Table 4: ***Polysomnography parameters in groups A and B***

Variable	Group A (n=14)	Group B (n=16)	p
	Mean (SD)	Mean (SD)	
Total sleep time (TST) (min)	352.97 (28.9)	353.29 (19.33)	0.97
Sleep efficiency (%)	98.57 (1.27)	97.41 (03.16)	0.21
Apnoea/hypopnoea index (AHI)	0.85 (0.97)	02.68 (03.24)	*0.04**
N1 (%)	02.87 (02.9)	10.63 (21.49)	0.19
N2 (%)	48.96 (17.19)	42.28 (18.68)	0.32
N3 (%)	42.55 (14.19)	44.95 (17.16)	0.68
Rapid eye movement (REM)	05.6 (06.9)	02.25 (03.55)	0.11
Periodic limb movement index (PLMI)	0.09 (0.35)	0 (0)	0.29

Table 5: ***Apnoea/hypopnoea index (AHI) in groups A and B***

	Group A *(n=14)*	Group B *(n=16)*	p
Normal AHI - n (%)	8 (57)	5 (31)	0.15
Abnormal AHI - n (%)	6 (43)	11 (69)	

Diaphragmatic ultrasound findings in groups A and B are shown in Table 6. Diaphragmatic thickness during inspiration or expiration and diaphragmatic thickness fraction were not significantly different in groups A and B.

Table 6: ***Diaphragmatic ultrasound in both study groups***

	Group A (n=14)	Group B (n=16)	p
	Mean (SD)	Mean (SD)	
Diaphragmatic thickness during inspiration	5.85 (4.14)	7.84 (3.59)	0.17
Diaphragmatic thickness during expiration	6.61 (1.73)	6.86 (1.33)	0.26
Diaphragmatic thickness fraction (%)	45.5 (18.18)	46.5 (18.40)	0.88

Discussion

SDB are frequently underestimated in NMD, including myopathy, till respiratory manifestations during day time appear[14]. SDB may present prior to manifestations of respiratory failure[4]. Thirty myopathic patients were included in study, ages ranging from 6 to 16 years. Majority **(**66.7%**)** of subjects recruited were males as 50% of patients included in study were DMD. Woodcock *et al*[16] (2016) conducted a research including patients with NMD less than 16 years living in Yorkshire health authority and recognized that 69% of patients were males. Parents reported positive consanguinity in 63.3% of studied patients**,** in agreement with Woodcock *et al* who showed that consanguinity was related to the higher rate of NMD[16].

Patients were assigned according to spirometry

results into 2 groups, Group A having normal findings and group B having an abnormal restrictive pattern, probably caused by weak muscles and skeletal abnormalities such as kyphoscoliosis which can restrict lung capacity[17]. There was significant reduction in mean FEV1 and FVC in group B compared to group A in agreement with Sawnani *et al* (2015) who reported reduced mean FVC (79.5%±29.1) and Suresh *et al* who investigated respiratory function in DMD; however FVC was lower (54%) than that in the present study, probably due to wider age range (2–16), and different sample (DMD only)[18,19]. Clinical manifestations denoting poor sleep quality as reported by the parents were significantly higher in group B patients. These manifestations included daytime sleepiness, frequent awakening and waking unrested.

ABG were within the normal range in both study groups, in contradiction to the study by Ragette R, *et al*[20] which revealed a severe increment of PCO_2 with decreased pulmonary and respiratory muscle function, indicating progressive respiratory muscle exhaustion due to the broad gap between sleep imposed demands and respiratory muscle capacity. Hoque R[15] stated that overnight pulse oximetry cannot substitute for PSG as it can miss SDB events that are not associated with oxygen desaturation or hypercapnia, and recommended repeated PSG if patients develop symptoms of SDB or respiratory deterioration as measured by spirometry.

No significant difference was noted between both groups as regards sleep staging, sleep efficiency or TST. A significantly higher AHI was detected in group B patients, classified as OSA. PSG was abnormal in 21.4% and 56.3% in groups A and B respectively. These findings are in agreement with Suresh S, *et al*[19] who reported abnormal PSG in 31% of patients; however, they considered AHI criteria of ≥ 5, classified as OSA as well. Polat M, *et al*[21] reported OSA in 17% of DMD using PSG without capnography, nor spirometry, while Sawnani H, *et al*[18] found that 63.6% of subjects had OSA, 33.6%, had central sleep apnoea and 17% had hypoventilation.

A limitation in the present study is that capnography was not feasible so that hypoventilation was not assessed. Respiratory distress was detected by researchers during REM sleep; NMD patients are more liable to SDB due to decrease respiratory drive during sleep causing diminished alveolar ventilation and decreased respiratory muscle activity especially during REM stage[22]. However, in the present study, REM Stage was low in both groups and most of the SDB events were noted in the non REM sleep. SDB is precipitated by impaired muscle activity during sleep, as negative inspiratory intrathoracic pressure created by the intact diaphragm in presence of weak pharyngeal muscles leads to narrowing and increased resistance of the upper airway, manifesting as OSA. Later in the course of the disease, the diaphragm is involved, so that the negative intrathoracic pressure created will be diminished, manifesting as obstructive hypopneas[4]**.** SDB is particularly evident in REM stage, due to exaggeration of the upper air way muscles by hypotonia[17]**.**

All patients have normal movement and apposition of the diaphragm. This is in line with a study carried out by Stubgen JP *et al*[23], which noted that the diaphragm was not disproportionately affected in a study done on twenty adult patients with limb girdle muscular dystrophy. Quijano-Roy S, *et al*[24] revealed elective diaphragmatic involvement during a maximal voluntary inspiratory manoeuvre in studied patients with Collagen VI myopathies independent of their clinical severity. Wehbi S, *et al*[25] noted a significant diaphragmatic dysfunction due to a constant decrease in FVC in patients with a wide range of age and clinical severity.

This study draws attention to possible involvement of respiratory muscles in myopathic children, with normal daytime ABG, diaphragmatic ultrasound and spirometry. It is critical that clinicians recognize the subclinical cases and take appropriate action to prevent and manage respiratory involvement as early as possible. PSG and spirometry can detect respiratory involvement that can be missed by daytime ABG. PSG (ideally with capnography), scored with AASM age appropriate criteria, is the gold standard in assessment of SDB and hypoventilation in children with myopathy. The authors recommend the use of paediatric criteria for scoring SDB to avoid its underestimation.

Conclusions

Myopathic children with abnormal respiratory function had a significant increase in symptoms related to sleep deprivation as well as abnormal AHI. In the diagnosis of sleep disordered breathing in myopathic children polysomnography was useful but daytime blood gas analysis was not useful. Children with muscle disorders should be assessed by respiratory function tests and polysomnography even if they do not have symptoms suggestive of respiratory muscle involvement.

References

1. Voulgaris A, Antoniadou M, Agrafiotis M, Steiropoulos P. Respiratory involvement in patients with

neuromuscular diseases: A narrative review. *Pulmonary Medicine* 2019; 2019. https://doi.org/10.1155/2019/2734054 PMid: 31949952 PMCid: PMC6944960

2. Chiang J, Mehta K, Amin R. Respiratory diagnostic tools in neuromuscular disease. *Children* 2018; **5**(6):78. https://doi.org/10.3390/children5060078 PMid: 29914128 PMCid: PMC6025604

3. Panitch HB. Respiratory implications of paediatric neuromuscular disease. *Respiratory Care* 2017; **62**(6): 826-48. https://doi.org/10.4187/respcare.05250 PMid: 28546380

4. Arens R, Muzumdar H. Sleep, sleep disordered breathing, and nocturnal hypoventilation in children with neuromuscular diseases. *Paediatric Respiratory Reviews* 2010; **11**(1): 24-30. https://doi.org/10.1016/j.prrv.2009.10.003 PMid: 20113988 PMCid: PMC2818522

5. Fermin AM, Afzal U, Culebras A. Sleep in neuromuscular diseases. *Sleep Medicine Clinics* 2016; **11**(1):53-64. https://doi.org/10.1016/j.jsmc.2015.10.005 PMid: 26972033

6. Alfrayh A, Khoja T, Alhusain K, Alshehri S, Gad A, Madani M. FEV1 and FVC pulmonary function reference values among 6-18-year-old children: a multi-centre study in Saudi Arabia. *East Mediterranean Health Journal* 2014; **20**(7):424-30. https://doi.org/10.1016/j.jsmc.2015.10.005 PMid: 26972033

7. Culver BH. Pulmonary function testing in clinical respiratory medicine. 4th ed. Saunders; 2012. p. 133-42. https://doi.org/10.1016/B978-1-4557-0792-8.00009-X

8. Malhotra RK, Kirsch DB, Kristo DA, Olson EJ, Aurora RN, Carden KA, *et al*. Polysomnography for obstructive sleep apnoea should include arousal-based scoring: an American Academy of Sleep Medicine position statement. *Journal of Clinical Sleep Medicine* 2018; **14**(7):1245-7. https://doi.org/10.5664/jcsm.7234 PMid: 29991439 PMCid: PMC6040795

9. Berry RB, Brooks R, Gamaldo CE, Harding SM, Marcus C, Vaughn BV, *et al*. for the American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.5. Darien, IL: *American Academy of Sleep Medicine*; 2018. http://www.aasmnet.org/

10. Cataletto ME, Lipton AJ, Murphy TD. Childhood Sleep Apnoea Workup. 2019.

11. Dehlink E, Tan H. Update on paediatric obstructive sleep apnoea *Journal of Thoracic Disease* 2016; **8**(2): 224–35. https://doi.org/10.1055/s-0034-1375578 PMCid: PMC4739955 PMid: 26904263.

12. Sarwal A, Walker FO, Cartwright MS. Neuromuscular ultrasound for evaluation of the diaphragm. *Muscle and Nerve* 2013; **47**(3):319-29. https://doi.org/10.1002/mus.23671 PMid: 23382111 PMCid: PMC3581727

13. Chavhan GB, Babyn PS, Cohen RA, Langer JC. Multimodality imaging of the paediatric diaphragm: Anatomy and pathologic conditions. *Radiographics* 2010; **30**(7):1797- 817. https://doi.org/10.1148/rg.307105046 PMid: 21057121

14. Fayssoil A, Behin A, Ogna A, Mompoint D, Amthor H, Clair B, et al. Diaphragm: pathophysiology and ultrasound imaging in neuromuscular disorders. *Journal of Neuromuscular Diseases* 2018; **5**(1):1-0. https://doi.org/10.3233/JND-170276 PMid: 29278898 PMCid: PMC5836400

15. Hoque R. Sleep-disordered breathing in Duchenne muscular dystrophy: an assessment of the literature. *Journal of Clinical Sleep Medicine* 2016; **12**(06):905-11. https://doi.org/10.5664/jcsm.5898 PMid: 27070248 PMCid: PMC4877324

16. Woodcock IR, Fraser L, Norman P, Pysden K, Manning S, Childs AM. The prevalence of neuromuscular disease in the paediatric population in Yorkshire, UK; variation by ethnicity and deprivation status. *Developmental Medicine and Child Neurology* 2016; **58**(8):877-83. https://doi.org/10.1111/dmcn.13096 PMid: 26968877

17. Katz SL. Assessment of sleep-disordered breathing in paediatric neuromuscular diseases. *Pediatrics* 2009; **123**(Suppl. 4): S222-5. https://doi.org/10.1542/peds.2008-2952E PMid: 19420148

18. Sawnani H, Thampratankul L, Szczesniak RD, Fenchel MC, Simakajornboon N. Sleep disordered breathing in young boys with Duchenne muscular dystrophy. *Journal of Pediatrics* 2015; **166**(3):640-5. https://doi.org/10.1016/j.jpeds.2014.12.006 PMid: 25722267

19. Suresh S, Wales P, Dakin C, Harris MA, Cooper DG. Sleep-related breathing disorder in Duchenne muscular dystrophy: disease spectrum in the paediatric population. *Journal of Paediatrics and Child Health* 2005; **41**(9-10):500-3. https://doi.org/10.1111/j.14401754.2005.00691.x PMid: 16150067

20. Ragette R, Mellies U, Schwake C. Patterns and predictors of sleep disordered breathing in primary myopathy. *Thorax* 2002; **57** (8):724-8. https://doi.org/10.1136/thorax.57.8.724 PMid: 12149535 PMCid: PMC1746391

21. Polat M, Sakinci O, Ersoy B, Sezer RG, Yilmaz H. Assessment of sleep-related breathing disorders in patients with Duchenne muscular dystrophy. *Journal of Clinical Medicine Research* 2012; **4**(5):332. https://doi.org/10.4021/jocmr1075w PMid: 23024736 PMCid: PMC3449431

22. Irfan M, Selim B, Rabinstein AA, Louis EK. Neuromuscular disorders and sleep in critically ill patients. *Critical Care Clinics* 2015; **31**(3): 533-50. https://doi.org/10.1016/j.ccc.2015.03.007 PMid: 26118919 PMCid: PMC5034932

23. Stübgen JP, Ras GJ, Schultz CM, Crowther G. Lung and respiratory muscle function in limb girdle muscular dystrophy. *Thorax* 1994; **49**(1):61-5. https://doi.org/10.1136/thx.49.1.61 PMid: 8153942 PMCid: PMC474090

24. Quijano-Roy S, Khirani S, Colella M, Ramirez A, Aloui S, Wehbi S, *et al* Diaphragmatic dysfunction in collagen VI myopathies. *Neuromuscular Disorders* 2014; **24**(2):125-33. https://doi.org/10.1016/j.nmd.2013.11.002 PMid: 24314752

25. Wehbi S, Essid N, Briñas L, Leclair-Richard D, Viollet L, Romero NB, *et al* Searching for pulmonary outcome measures in early onset COL6 related myopathy. *Neuromuscular Disorders* 2011; **21**(9):661-2. https://doi.org/10.1016/j.nmd.2011.06.827