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INVESTIGATION OF THE EFFECT OF A PHYSIOTHERAPY AND REHABILITATION PROGRAM IN A CASE WITH CONGENITAL CENTRAL HYPOVENTILATION SYNDROME AND CEREBRAL PALSY: A CASE REPORT
KONJENİTAL SANTRAL HİPOVENTİLASYON SENDROMU VE SEREBRAL PALSİLİ OLGUDA FİZYOTERAPİ VE REHABİLİTASYON PROGRAMININ ETKİSİNİN İNCELENMESİ: BİR OLGU SUNUMU*

Mustafa BURAK[1], Sinem ERTURAN[2], Bulent ELBASAN[3]

[1]Firat University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Elazığ
[2]Ataturk University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Erzurum
[3]Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara

ABSTRACT
Congenital Central Hypoventilation Syndrome is a rare genetic disorder that presents from birth and prevents automatic control of respiration. Our aim in this study was to examine the effectiveness of a six-month physical therapy program applied to a patient with Congenital Central Hypoventilation Syndrome and cerebral palsy. A six-month-old patient who was diagnosed with Congenital Central Hypoventilation Syndrome and subsequently developed Cerebral Palsy due to asphyxia was included in the study. The case was enrolled in a physical therapy program for two days a week for six months in the home environment where they lived. The case was evaluated before and after treatment. In our case, the Modified Ashworth Scale, the Alberta Infant Motor Scale, the Hammersmith Infant Neurological Examination, Test of Sensory Functions in Infants, and the Face, Legs, Activity, Cry, Consol ability scale were used. In our case, pre-treatment and post-treatment scores were as follows, respectively: Alberta Infant Motor Scale score 3-8, Hammersmith Infant Neurological Examination score 6-17, Test of Sensory Functions in Infants score 2-9, and Face, Legs, Activity, Cry, Consol ability scale score 8-3. In our case, there was a significant improvement in Modified Ashworth Scale scores before and after treatment. Additionally, at the conclusion of the study, it was noted that the heightened pain and sensitivity resulting from the patient's extended stay in the intensive care unit reduced with the treatment. We believe that the administered physiotherapy and rehabilitation program offered support to the patient in achieving neuro-motor and sensory integration, underscoring the essential role of physiotherapy in rare diseases.

Keywords: Early intervention, congenital central hypoventilation syndrome, cerebral palsy.

ÖZ
Konjenital Santral Hipoventilasyon Sendromu, doğumdan itibaren ortaya çıkan ve solunumun otomatik kontrolünü engelleyen nadir bir genetik hastalıktır. Bu çalışmadaki amacımız Konjenital Santral Hipoventilasyon Sendromu ve serebral palsili bir hastaya uygulanan altı aylık fizik tedavi programının etkinliğini incelemekti. Çalışmaya Konjenital Santral Hipoventilasyon Sendromu tanısı alan ve sonrasında asfiksi nedeniyle serebral palsi gelişen altı aylık hasta dahil edildi. Olgu yaşadığı ev ortamında altı ay boyunca haftada iki gün fizik tedavi programına alındı. Olgu tedavi öncesi ve tedavi sonrası değerlendirildi. Olgumuzda Modifiye Ashworth Skalası, Alberta İnfant Motor Skalası, Hammersmith İnfant Nörolojik Muayenesi, Bebeklerde Duyusal Fonksiyon Testi ve Yüz, Bacaklar, Aktivite, Ağlama, Avutulabilme ölçeği kullanıldı. Olgumuzda tedavi öncesi ve tedavi sonrası skorlar sırasıyla Alberta İnfant Motor Skalası skoru 3-8, Hammersmith İnfant Nörolojik Muayenesi skoru 6-17, Bebeklerde Duyusal Fonksiyon Testi skoru 2-9 ve Yüz, Bacaklar, Aktivite, Ağlama, Avutulabilmeölçeği skoru 8-3 idi. Olgumuzda tedavi öncesi ve sonrası Modifiye Ashworth Skalası skorlarında önemli gelişme oldu. Ayrıca çalışma sonucunda hastanın yoğun bakımda uzun sure kalması sonucu artan ağrı ve hassasiyetin tedaviyle azaldığı kaydedildi. Uygulanan fizyoterapi ve rehabilitasyon programının hastaya nöromotor ve duyu entegrasyonunun sağlanmasında destek sağladığına ve nadir hastalıklarda fizyoterapinin önemli rolünün altını çizdiğine inanıyoruz.

Anahtar kelimeler: Erken müdahale, konjenital santral hipoventilasyon sendromu, serebral palsi.

Corresponding Author: PhD PT. Sinem ERTURAN snm.ertrn@gmail.com, 0000-0002-3135-5248, Atatürk University Faculty of Health Sciences, Erzurum.

Authors: PhD PT. Mustafa BURAK, ptmustafaburak@gmail.com, 0000-0002-2372-0102
Prof. Dr. Bülent ELBASAN, bulentelbasan@gazi.edu.tr, 0000-0001-8714-0214

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INTRODUCTION

Congenital central hypoventilation syndrome (CCHS) is a rare and lifelong condition characterized by abnormal respiratory control.[1] In 2003, it was discovered that mutations in the Paired-like homeobox 2b (PHOX2B) gene on chromosome 4p12 are responsible for this syndrome. The PHOX2B gene, located on chromosome 4p12, plays a key role in the development of autonomic nervous system reflex circuits in mice.[2] The main clinical manifestations of CCHS are adequate ventilation while awake, but alveolar hypoventilation during sleep. CCHS severely affects infants due to the lack of automatic control of breathing during sleep. This causes infants with CCHS to be exposed to progressive hypercapnia and hypoxia while asleep and also to continue to sleep without feeling dyspnea. This is because the respiratory neurons lack appropriate responses to hypercapnia and hypoxia, which leads to infants with CCHS being exposed to progressive hypercapnia and hypoxia while asleep.[3] Children with CCHS lack the perception of dyspnea and are unable to increase ventilation to meet the demands when faced with respiratory difficulties such as infection. Therefore, the goal of treatment is to provide adequate gas exchange using assisted ventilation during sleep. The American Thoracic Society recommends positive pressure ventilation via tracheostomy as a treatment option for patients with CCHS during their first few years of life. CCHS is a rare condition that may be under diagnosed. Since 1970, more than 1000 cases of CCHS have been reported globally.[4] The estimated incidence of CCHS is approximately one in 148,000 to 200,000 live births.[5]

Cerebral Palsy (CP), on the other hand, develops in the fetal or infant brain, causing movement and posture disorders as well as activity limitation. In children with CP, motor impairments are often accompanied by cognitive dysfunctions, sensory problems, communication and perception problems, and behavioral disorders or seizures or both.[6] The present case is a term male infant who was admitted to the hospital with respiratory distress, underwent multiple resuscitation due to respiratory arrest.

After being diagnosed with CCHS and the case was subsequently diagnosed with CP due to hypoxic ischemic encephalopathy. Treatment of the infant includes respiratory support via tracheostomy, medical treatment, and physiotherapy and rehabilitation. Rehabilitation applications are limited for CCHS because it is a rare disease and there is insufficient evidence to support the effectiveness of physiotherapy. This study, which was conducted to determine the framework of the physiotherapy and rehabilitation program to be applied to patients with CCHS and CP and to contribute to the intervention, reveals the results of a 6-month physiotherapy and rehabilitation program in a patient with CCHS and CP.

CASE REPORT

The male case was born with C/S from healthy pregnancy of a 30year-old mother as G1P1Y1, with a birth weight of 3750 g, a gestational age of 40 weeks+4 days, and an APGAR score of 8/9/10. There was no consanguinity between the parents. Due to respiratory distress and 90% oxygen, the patient was admitted to the neonatal intensive care unit and was followed up with nasal continuous positive airway pressure. Several attempts were made to wean it from mechanical ventilation (MV), but extubation was unsuccessful as the patient continued with episodes of desaturation during sleep and wakefulness. Brain Magnetic Resonance (MRI) and diffusion MRI were reported as normal according to the brain MRI results on day 18. Gene analysis sent on day 103 due to continued desaturations during sleep was defined as congenital central hypoventilation syndrome (PHOX2B+). Cardiopulmonary resuscitation was applied to the patient, who was connected to MV during sleep, due to sudden respiratory arrest on day 120.Hypoxic ischemic encephalopathy findings were observed in the patient who responded after the 5th adrenaline administration. In brain MRI results after respiratory arrest (on day 132), it was reported that cortical atrophy at the supratentorial level, thinning of the corpus callosum calibration, and signal enhancement areas (deep hypoxic ischemia) compatible with cytotoxic edema were observed at the corpus callosum genu splenium, at bilateral globuspallidus level. According to the control cranial and diffusion MRI results taken on day 147, the fourth ventricle was prominent in the midline and the subarachnoid spaces were increased in the posterior fossa. The third and lateral ventricles were slightly dilated. At the supratentorial level, diffuse cortical edema in both cerebral hemispheres and cortical signal enhancement areas consistent with cortical laminar necrosis were noted on T1W imaging. When compared with the cranial MRI examination on day 132, it was reported that there was atrophy and volume loss at the supratentorial level and there was no significant cytotoxic edema in this imaging.

This study is not within the scope of research that requires ethics committee approval. However, the family was informed about the study and all necessary permissions were obtained.

The case was evaluated with the following evaluation scales before starting the physiotherapy and rehabilitation program and after 6 months of treatment. Evaluation scales were administered by a specialist physiotherapist experienced in pediatric rehabilitation.

Behavioral status of the baby was taken into consideration during the evaluations. If our case was hungry, sleepless, or restless, the evaluations were interrupted. Two hours after feeding, evaluations were made with the family in a room where the light and temperature were comfortable. In cases where appropriate conditions could not be met, evaluations were terminated and they were conducted within the same week.

Modified Ashworth Scale (MAS): Used to assess muscle tone due to upper motor neuron damage, this scale has 5 levels. 0 indicates no tone increase, while 4 shows rigid tone in flexion and extension.[7] Assessment occurred supine, relaxed, with passive, rapid joint movements, scored accordingly.

Alberta Infant Motor Scale (AIMS): This reliable test measures motor performance delay (0-18 months) and progress before/after treatment. Child's movements scored: 1 for doable, 0 for not. 58 parameters assess weight transfer, posture, and movements against gravity in various positions. Compares baby's motor performance to peers using norm reference. An increasing

score indicates better motor development in the baby. Test lasts 20-30 mins.[8] Room conditions optimized (light, temperature, sound). Mother present during AIMS evaluation. Child's safety ensured. Spontaneous movements observed on treatment bed.

Hammersmith Infant Neurological Examination (HINE): This test assesses neurological disorder risk in preterm and term babies. It has 3 parts: motor neurologic exam, functional development, behavior evaluation. Predicts potential neurological issues, acting as a preventive battery. Applicable from birth to 24 weeks. Checks cranial nerves, posture, movement, tone, reflexes, abnormal signs, orientation, behavior. An increasing score indicates a decreased risk of CP. The maximum achievable score for HINE is 78. The optimal score for 9-12-month-old babies is 73, while for 6-month-old babies, it's 70. Scores below 57 for each month indicate a high-risk condition for CP diagnosis.[9] An experienced pediatric rehabilitation specialist conducted the HINE in suitable settings. Test items administered sequentially, supine and sitting positions.

Test of Sensory Functions in Infants (TSFI): This sensory function test assesses sensory defense behaviors in infants (4-18 months) through 5 subsections and 24 items. TSFI requires interaction with materials like plush toys, puppets, balls, tape, string, and A4 paper. Scores range 0-49, with norms for different age groups. The total score ranges from 0 to 49. An increase in the score indicates better sensory development in the baby. Scores between 44 and 49 indicate good sensory function in 10-12-month-old babies, scores between 41 and 43 indicate a risky condition, and scores between 0 and 40 indicate sensory processing problems.[10] Items applied and scored using standard materials. Test avoided when baby hungry or restless, considering emotional state.

Face, Legs, Activity, Cry, Consolability (FLACC): This scale assesses pain in non-communicative children aged 2 months to 7 years. Scores range from 0 (calm and relaxed) to 10 (Severe discomfort or pain). As the score increases, the sensation of pain and discomfort also increases. It has 5 criteria, scored 0, 1, or 2 each.[11] Baby's wakefulness noted during evaluation. Observed and scored over 1-5 minutes.

The case was enrolled in a 2-day-per-week, 30-45 minutes per session physical therapy program for 6 months in their home environment. The goal was to prevent postural issues, contractures, and promote normal motor development. The program included massage, intramuscular stretching, and functional activities in a supported sitting position, focusing on midline orientation, sitting, trunk control, and sensory development. Toys with different textures and swings for vestibular stimulation were used, along with ball activities. Neurodevelopmental treatment involved targeted activities for positioning, balance, motor development, transitions, and daily tasks.[12] The family was educated on the program's content, goals, and implementation.

Care was taken to ensure that the patient remained awake during the intervention. The session was interrupted, and the patient was connected to mechanical ventilation if there was a tendency to become drowsy. No additional respiratory support was required while the patient was awake and during the intervention, but vital signs were constantly monitored.

Difficulties were encountered during the interventions when working in the prone positions due to the patient's feeding through a Percutaneous Endoscopic Gastrostomy. Therefore, modified prone positions were used.

The parents' primary concern was that their baby was very sensitive to sensory stimuli and overreacted to position changes by crying. Therefore, the family visited the physiotherapy and rehabilitation program. The case, who spent the first 6 months of his life in the intensive care unit, had sensitivity to touch and position changes and did not experience sitting or prone positions during this period. In our case, there was no extremity movement, head-trunk control, or eye tracking. He was crying in response to the activity. During physical examination, severe stiffness was observed in the right arm and leg. The tone of the upper and lower extremity muscles, as assessed by the MAS, was increased. According to the MAS scores: elbow flexors right 3, left 2; hip flexors bilaterally 2; knee flexors right 4, left 3; and, plantar flexors 4 on the right and 2 on the left. The AIMS score used to assess motor skills was found to be 3, the HINE score used for neurological status assessment was 6, the FLACC score used for pain was 8, and the TSFI total score used to assess sensory functions was 2.After 6 months of physiotherapy and rehabilitation program, the following scores were obtained: elbow flexors right 2, left 1+; hip flexors right 1+, left 1+; knee flexors right 3, left 2; plantar flexors right 3, left 2; AIMS score 8; HINE 17; FLACC 3; and, TSFI score 9 (Table 1).

In the current developmental stage of our case, short-

Table 1. Pre-treatment and post-treatment results of our case

		Before Treatment		After Treatment	
		RIGHT	**LEFT**	**RIGHT**	**LEFT**
MAS	Elbow Flexors	3	2	2	1+
(min-max)	Hip Flexors	2	2	1+	1+
(1-5)	Knee Flexors	4	3	3	2
	Plantar Flexors	4	2	3	2
AIMS (min-max) (0-58)		3		8	
HINE (min-max) (0-78)		6		17	
FLACC (min-max) (0-10)		8		3	
TSFI (min-max) (0-49)		2		9	

Abbreviations:
MAS: Modified Ashworth Scale
AIMS: Alberta Infant Motor Scale
HINE: Hammersmith Infant Neurological Examination
FLACC: Face, Legs, Activity, Cry, Consolability
TSFI: Test of Sensory Functions in Infants

term head and neck control was achieved in the gross motor area. His ability to follow objects in the visual field for a short time improved, his negative reactions to activities and tactile stimuli decreased and no improvement was achieved in fine motor skills.

DISCUSSION

In our case, a physiotherapy and rehabilitation program was applied to facilitate motor development, prevent contractures and eliminate sensory problems and pain. The effectiveness of the 6-month physiotherapy and rehabilitation program was evaluated with appropriate test batteries before and after the treatments. At the end of the treatment, reductions in limb spasticity and pain and improvements in motor performance, neurological status, and sensory functions were observed in our case. Post-intervention scores were indicative of clinical improvement compared to the pre-intervention scores.

Ventilation is normally controlled automatically during sleep. When autonomic control is impaired, patients forget to breathe when they fall asleep. The pathophysiological mechanism of CCHS is unknown, but the mechanisms that integrate chemoreceptor inputs into respiratory centers are thought to be impaired.[13]Diagnosis and treatment of this disease is very difficult due to the rarity of the disease and limited diagnosis with specific genetic tests. Survival and quality of life can be improved with early tracheostomy and gastrostomy planning, efficient discharge process, access to home care programs, and even the possibility of diaphragmatic pacemaker implantation.[14]

As a result of a comprehensive literature search, we found that there was no other case of CCHS who developed CP due to asphyxia. However, there was one case of CCHS in which white matter damage was detected, although he did not experience asphyxia.[15]A lack of literature on the physiotherapy and rehabilitation program of individuals with CCHS was observed. The coexistence of CCHS and CP in our case further complicated the treatment of the case. Considering the clinical findings and the course of the disease, physiotherapy and rehabilitation intervention was planned to support motor development and solve sensory problems. According to our literature review, it is the first study to examine the effects of a physiotherapy program in a case with CCHS and CP.

Lee et al. evaluated the effect of physiotherapy and rehabilitation practices on spasticity in patients with CP. In the study, it was concluded that regular physical therapy reduces spasticity in children with CP.[16] The results obtained in our case show parallelism with the literature.

When the early-stage physiotherapy and rehabilitation practices are reviewed, it has been reported that high-risk infants with low birth weight or brain damage achieved more motor and behavioral progress in the treatment group, in which early-onset physiotherapy and rehabilitation applications and the control group who received only medical support were compared.[17] The results we obtained after the physiotherapy and rehabilitation program we applied in our case show parallelism with the results of these studies.

AIMS, which we used to evaluate motor performance in our study, is one of the frequently used early neurodevelopmental test batteries with proven validity and reliability that evaluates the quality of movement and changes in motor skill.[18] It has been reported in studies that it is useful in determining the neurological risk in the early period.[19,20]In our study, we evaluated the neurological status of our case with the HINE. When the studies are examined, we see that the HINE is mostly used to predict neurodevelopmental disorders such as CP in the early period. When the HINE is used together with General Movements and neuroimaging methods, it can be predicted whether neurodevelopmental disorders such as CP will develop. This test battery has optimal scores by months. At 9 or 12 months, scores equal to or higher than 73 are considered optimal, while at 3 and 6 months, 67 and 70 points and above, respectively, are considered normal values. Less than 57 points per month predicts CP by 90%.[9] For this reason, we used these test batteries with proven validity and reliability to evaluate our case in our study.[9,20] In our study, we found that the AIMS and HINE scores were very low, which showed us that the exposure was severe. The increase in HINE and AIMS scores after treatment was promising for treatment.

Our treatment approach incorporated sensory integration principles and utilized sensory strategies in enriched environmental settings. Studies have reported that sensory problems affect motor and cognitive development.[21,22] In our case, there were improvements in the results of the post-treatment TSFI evaluation in line with the literature.[23]

Since it was assumed in the past that babies do not feel pain, their pain status has generally not been questioned. The reason for this is thought to be the neurological development status of the babies and the lack of myelination of the central nervous systems. However, it has been reported that starting from the 26th week of pregnancy, babies begin to feel pain and, in some cases, experience even more intense pain for various reasons.[24] Babies who spend their initial days in neonatal intensive care units often undergo numerous painful invasive procedures. It has been reported that hospitalized infants experience an average of 14 painful procedures per day during the first 2 weeks of their lives.[25] All these processes improved pain sensitivity in our case. Our case, who responded by crying to touch and position changes, was able to tolerate position changes and exercises with decreased response after treatment.

The rehabilitation program we applied to our case included exercises such as weight bearing in different positions, massage for sensory and pain input, gradual weight bearing in sitting position, and spending time in prone position. The case was also encouraged to select and use visual, somatosensory, and vestibular inputs. Post-intervention scores were indicative of clinical improvement, compared with scores before the physiotherapy program. The lack of assessment of the patient's field of vision and communication skills is among the limitations of our study. Although HINE and AIMS scores do not constitute thresholds for clinically significant changes, the results of the study reveal improvements in HINE, AIMS, FLACC and TSFI scores after the rehabilitation program.

In conclusion, it was observed that our case with CCHS and CP showed a general improvement in motor skills,

sensory sensitivity, and pain after 6 months of physiotherapy and rehabilitation. Consequently, we hold the belief that physiotherapy and rehabilitation programs can be effective for patients with advanced levels of involvement, as seen in the present case.

Ethics Committe Approval: The Helsinki Declaration was adhered to in the study.
Informed Consent: Signed consent forms were obtained from the family.
Peer-review: Externally peer-reviewed.
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