



Physiotherapy and functionality in MECP2 duplication syndrome: A case study

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ABSTRACT

Background: MECP2 duplication syndrome is a rare disease usually caused by DNA duplication in the Xq28 region. This condition causes delayed motor development and/or intellectual disability and spasticity in patients. The Bobath concept applied to pathologies with similar manifestations showed good results in the rehabilitation process despite the complications of the syndrome. However, there is still a lack of studies that prove the benefits of Bobath, specifically in the MECP2 duplication syndrome. **Objective:** Quantify motor changes in a child with MECP2 duplication syndrome after physiotherapy treatment based on the Bobath concept. **Methods:** This is a case study carried out with a six-year-old male child with a confirmed medical diagnosis of MECP2 duplication syndrome. Initially, the child was subjected to four assessments: anamnesis, neurofunctional assessment, application of the gross motor function classification system (GMFCS) and gross motor function measure (GMFM-88) scales. Subsequently, the child participated in 12 weeks of treatment through techniques using the Bobath concept, being reassessed at the end of the protocol using the GMFCS and GMFM-88 scales to quantify possible motor changes. **Results:** An improvement in dimensions A (lying and rolling), B (sitting), C (crawling and kneeling), and D (standing) on the GMFM-88 scale was observed after 12 weeks of treatment. On the other hand, the result remained unchanged on the GMFCS scale. **Conclusion:** The intervention based on the Bobath concept could improve the functions lying, rolling, crawling, kneeling, and standing on a patient with MECP2 duplication syndrome.

Keywords: MECP2 duplication syndrome; Motor development; Bobath.

BACKGROUND

The MECP2 gene is important in the proper functioning of nerve cells and can duplicate, causing a serious neurological disorder called MECP2 duplication syndrome⁽¹⁾. The cause is usually pointed out by DNA duplication in the Xq28 region, with the syndrome inherited from the X chromosome, that is, the individual inherits it from the mother, who is, however, asymptomatic⁽²⁾.

According to ESCH (2008),² the main clinical characteristics of the disease include early childhood hypotonia, delayed motor development and/or intellectual disability, which is found in almost all patients, spasticity, recurrent infections, and seizures, the latter an important factor in the clinical worsening of the patient, such as loss of speech and ambulation^(2,3). The characteristics of the MECP2 duplication syndrome are similar to those found in Rett syndrome. The disease is also characterized by a neurodevelopmental disorder caused by mutations in the MECP2 gene. Besides the most common cause being intellectual disability, other clinical characteristics are impairment of cognition and communication, respiratory disorders, and gait changes, that is, diseases that can significantly affect the child's motor development^(4,5).

Motor development is the process of changes in human movement, which undergoes constant changes throughout life as a result of factors of restrictions of the individual, environment, and tasks that stimulate these changes⁽⁶⁾. As already

mentioned, patients diagnosed with MECP2 duplication syndrome can present motor disorders. However, the Bobath concept, also known as a neurodevelopmental treatment, is one of the most used in the rehabilitation of motor development disorders and has as principles the inhibition of abnormal reflex activity and the facilitation of normal movement^(7,8). Some of the benefits of applying these principles are improved muscle tone and optimized postural alignment⁽⁹⁾. The Bobath concept has revolutionized neurorehabilitation, but studies that prove its effectiveness in the treatment of motor changes in patients with MECP2 duplication syndrome, as well as other physiotherapeutic techniques, are still scarce.

The Bobath application showed good results in other pathologies with similar motor disorders. The Bobath effectiveness in the study carried out by Firmino et al. (2015)⁽¹⁰⁾ was shown through surface electromyography (EMG) in a seven-year-old child with spastic quadriplegic cerebral palsy (CP), being possible to observe a higher activation of the paravertebral and internal oblique/transverse abdominal muscles in a single session, which provided an improvement in postural alignment at the end of treatment⁽⁸⁾. Another study, also carried out with children diagnosed with spastic CP, showed significant results in improving spasticity and gross motor learning after three months of rehabilitation with techniques based on the Bobath concept⁽¹¹⁾.

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Although there is a lack of studies in the literature that shows the effectiveness of motor rehabilitation techniques in patients with MECP2 duplication syndrome, this study hypothesized that the principles of the Bobath concept applied to the motor changes caused by this disease may lead to positive results of improvement in motor dysfunctions. This study aimed to quantify motor changes in a child with MECP2 duplication syndrome after physiotherapy treatment based on the Bobath concept.

METHODS

This is a case study approved by the Ethics and Research Committee of the Anhanguera University of São Paulo – UNIAN (protocol number 3.782.074).

Sample

The sample consisted of a six-year-old male child, white, gestational age of 36 weeks, APGAR of nine and ten at birth, and a clinical diagnosis of MECP2 duplication syndrome. The disease was confirmed by a medical report, which presented other associated comorbidities, such as seizures and gastroesophageal reflux, in addition to a history of recurrent pneumonia and the presence of hypersecretion.

Procedures

The child was subjected to four assessments before the treatment protocol: anamnesis, neurofunctional assessment, gross motor function classification system (GMFCS), and gross motor function measure (GMFM-88). GMFCS and GMFM-88 were applied again after the intervention. Anamnesis consisted of a questionnaire applied to the parents to characterize the patient.

The neurofunctional examination consisted of the assessment of the muscle tone according to the modified Ashworth scale, postural patterns, balance reactions (prone, supine, seating, four supports, kneeling, and standing), and motor performance. The functionality levels were assessed the next day according to the GMFCS and GMFM-88 scales. GMFCS is a validated and reliable scale widely used in clinical practice and research with children who have motor disorders, especially with a CP diagnosis.

It is a scale that verifies the severity of motor impairment, with an emphasis on sitting and walking, being classified into five levels of independence and functionality of the child. The GMFCS is classified into Level I – children move without restrictions, Level II – children have limited gait in an external environment,

Level III – children need support for locomotion, Level IV – children need technology-assisted mobility equipment, and Level V – children have severe movement restriction even with advanced technologies^(12,13).

The GMFM-88 scale was applied to verify the evolution of the treatment. This scale consists of 88 items, and each observed item receives a rating on a 4-point ordinal scale, where 0 = does not initiate, 1 = initiates 10% of the activity, 2 = partly completes 10% to <100% of the activity, 3 = completes the activity, and NT = not tested.

The scale consists of 5 dimensions, namely: A: lying and rolling, B: sitting, C: crawling and kneeling, D: standing, and E: walking. The sum of what the child was able to achieve in each item is performed for each dimension and the total sum of all dimensions must be divided by five at the end⁽¹⁴⁾.

Treatment protocol

All follow-ups were performed at a physiotherapy school clinic in the city of Rio Claro, São Paulo, Brazil. A clinical evaluation was carried out before all sessions to check the feasibility to initiate the care, consisting of analysis of the peripheral oxygen saturation (SpO₂), pulmonary auscultation, heart rate (HR), respiratory frequency (RF), and presence or absence of cyanosis. The following equipment was used for the treatment: Foam Mat, stretcher, triangular foam wedge, therapy ball, backrest, toys, and an auxiliary device (knee stabilizer). The sessions were held twice a week for 12 weeks and lasted 40 minutes.

The child was submitted to physiotherapy sessions based on the Bobath neuroevolutionary concept (Figure 1). The treatment protocol was carried out based on the study by Brianeze et al. (2009)⁽¹⁵⁾, considering the Bobath techniques in children with CP, but adapted by the conditions of the child in the present study. Given the limitation in finding scientific articles that demonstrate the effects of physiotherapy in children with the MECP2 duplication syndrome, Bobath was chosen among several existing approaches due to the positive results in other pathologies that culminate in motor disorders. The treatment consisted of 30 minutes of motor stimulation and 10 minutes for respiratory physiotherapy, as the child in the study had hypersecretion verified through pulmonary auscultation.



Motor stimulation (30 minutes)	Abdominal strengthening, pelvic joint mobilization, and strengthening of obliques by handling with the therapy ball, stimulation on two feet with and without knee stabilizer, passive stretching in lower limbs and sensory integration (IS) for dorsiflexion.
Respiratory physiotherapy (10 minutes)	Bronchial hygiene maneuvers and nasal clearance.

Figure 1. Treatment protocol used in the study.

RESULTS

A total of 24 sessions of 40 minutes each, with a frequency of two weekly sessions, were carried out. The patient showed signs of clinical stability in all sessions, considered by a SpO₂ higher than or equal to 90%, HR from 70 to 100 bpm, RF from 12 to 25 bpm, and absence of cyanosis. The neurofunctional assessment data are shown in Table 1.

Table 1. Data from the neurofunctional assessment before and after 12 weeks of care.

Variable	Pre	Post
Postural Balance	Unable	Unable
Orthostatism	Unable	Unable
Fine motor skills	Unable	Unable
Bedside sedestation	Unable	Unable
Modified Ashworth scale	1 for LL and 0 for UL	1 for LL and 0 for UL
Clonus	Present	Present

*Note: Pre: assessment measures before the application of the protocol; Post: assessment measures after 24 sessions of application of the protocol; LL (lower limbs); UL (upper limbs).

The patient did not present static balance before the sessions, in addition to the presence of clonus, inability to orthostatism for at least five seconds supported on the backrest, inability to balance on the ball when facing swings, inability to stand up and remain in bedside sedestation alone, and difficulties to develop tasks that required gross and fine movement in the upper and lower limbs.

After a few sessions, the patient showed improvement in balance reactions and postural straightening on the ball, ability to orthostatism on the backrest for more than five seconds, improvement in the movement of standing and bedside sedestation, and fine movements, such as grabbing toys with both hands, were improved. Table 2 shows the scores for the initial and final assessment of GMFM-88. The total score increased by 1.60% after the physiotherapeutic treatment was applied.

Table 2. Results of the GMFM-88 scale before and after physical therapy treatment.

Dimension	GMFM	GMFM	Final
	Initial	Final	result
A – Lying and rolling	25%	29%	4%
B – Sitting	15%	41%	26%
C – Crawling and kneeling	21%	26%	5%
D – Standing	0%	5%	5%
E – Walking, Running, and jumping	0%	0%	0%
Final score (%)	2.44%	4.04%	1.60%

*Note: GMFM: Gross Motor Function Measure

The results showed an improvement in the item “supine, lifts head 45°” of dimension A, in which the patient only initiated the movement, but started to complete the task independently. In the activity “prone on forearms, lifts head upright, elbows extended, chest raised/weight on right and left arm, fully extends opposite arm forward”, the patient did not initiate the movement and started to initiate the movement.





In dimension B, the child showed an evolution in the items "supine, hands grasped by examiner, pulls self to sitting with head control" and "sit on mat, maintains, arms free, 3 seconds" because he only initiated the movement and started to complete partially the tasks. The activities "supine, rolls to right/left side, attains sitting" and "sit on mat, touches toy placed 45° behind child's left side, returns to start" were not completed before but started to be partially completed. The following activities also started to be partially completed: "sit on mat, supported at chest by therapist, lifts head upright/midline, maintains 3/10 seconds", "right/left side sit, maintains, arms free, 5 seconds", "sit on mat, lowers to prone with control", and "sit on mat with feet in front, attains 4 point over right/left side". The activity "sit on mat, arms propping, maintains, 5 seconds" was only partially completed, but started to be completed in its entirety independently.

In dimension C, the patient presented evolution in the items "prone, creeps forward 1.8 m" and "sit on mat, attains high kneeling using arms, maintains, arms free, 10 seconds", in which he started the task and started to partially complete the movement. In dimension D, the child evolved in the item "standing, maintains, arms free, 3 seconds", starting to partially start with the aid of a knee stabilizer. The patient was unable to perform this activity previously. Regarding GMFCS, the patient previously had level V, which remained unchanged after the protocol.

DISCUSSION

The present case report aimed to describe the rehabilitation process of a six-year-old boy with MECP2 duplication syndrome. The application of the treatment protocol generated an increase in the score of the GMFM-88 scale, showing an improvement in dimensions A (lying and rolling), B (sitting), C (crawling and kneeling), and D (standing). The application of a short-term protocol could not generate improvement in dimension E of GMFM-88. According to a systematic review carried out by Fonzo, Sirico, and Corrado (2020)⁽¹⁶⁾, 2 out of the 22 studies that present alternatives for rehabilitation of patients with Rett syndrome (RS), whose disease also shows alterations in the MECP2 gene, had protocols with less than three months of treatment. The patients in both case reports^(17,18) showed better motor performance than our patient and already performed the gait. A review carried out by Lim et al. (2020)⁽¹⁹⁾ presented 11 studies directed at gross motor function,

affecting 35 different individuals with RS. All studies achieved partial gains in function, gait, or transient movements, but only the study by Lotan et al. (2012)⁽²⁰⁾ showed cases with the same age group as our patient, and the improvement in gait occurred after 18 months of follow-up.

The average duration of the intervention for patients with Rett syndrome is 50 minutes per session, three sessions a day, and four days a week for 61.6 weeks,¹⁹ suggesting that the clinically significant change may require high-intensity interventions. Although there are two reviews in the literature related to the rehabilitation of patients with Rett syndrome, we are unaware of the existence of research that used the Bobath method as a form of treatment. This method is widely applied in other pathologies that affect the locomotor system, as shown by Tekin et al. (2018)⁽²¹⁾. The sample was composed of 15 children with clinical types of diparesis (8) and hemiparesis (7) aged between five and 15 years. The gross motor function skills of patients were assessed using the GMFCS and GMFM-88 scales. A significant improvement in gross motor skills was observed after eight weeks of treatment.

Knox and Evans (2002)⁹ also applied the Bobath technique to 15 children with CP, aged between two and 12 years. The GMFM-88 and GMFM-66 scales were assessed before the treatment was initiated and after six weeks of rehabilitation. The sessions lasted 75 minutes, three times a week. The motor function result after the intervention obtained a significant improvement in the total GMFM scores ($p=0.009$).

Yalcinkaya et al. (2014)⁽²²⁾, found a similar result when assessing 28 children with CP admitted to an outpatient clinic. Patients aged between two and 12 years were assessed using the GMFM and GMFCS scales and the Bobath concept was applied during the hospital stay (50.9 ± 18.45 days). An improvement was observed only in the general GMFM score at discharge. We could not observe changes in the GMFCS scale, possibly due to the patient's cognitive deficit, as suggested by Drobnyk et al. (2019)⁽²³⁾. Individuals with characteristics of this syndrome take more time to process the information, which possibly will increase the time of rehabilitation compared to those who do not present this alteration.

CONCLUSION

This study presented a case study of a six-year-old child with MECP2 duplication syndrome who improved the score of the GMFM-88 scale in dimensions A (lying and rolling), B (sitting), C (crawling and kneeling), and D (standing) after 12 weeks of treatment. Thus, this



case study showed that the physiotherapy intervention with the Bobath concept generated improvement in some of the disabling characteristics of the MECP2 duplication syndrome.

Authors' contributions: CRSP: Responsible for the structure of the article, data collection, article writing and final review. GDE: data collection and article writing; RSS: data collection and article writing. RSZ: data collection and article writing. KCSO: data analysis, statistics and article writing. All authors approved the final manuscript and there was no conflict of interest.

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