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Review Article

Physiotherapy Intervention for Cornelia De Lange Syndrome - A Scoping Review

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Abstract

Aims & Objective: Introduction: Cornelia de Lange syndrome (CdLS) is a rare genetic disease. Children with CdLS typically require Physiotherapy, however evidence on the efficacy of Physiotherapy intervention in this population is limited. The aim of this review is to design Physiotherapy treatment protocol for the CdLS population. **Methodology:** We use six databases which includes, MEDLINE/PubMed, SCOPUS, PEDro, CINAHL, EBSCO and Cochrane were searched with predefined keywords specific to or related to Physiotherapy interventions from 2006 to February 2022 for the full-text English language articles. Articles published only in English between July 2006 and February 2022 were included which investigated the role of Physiotherapy to CDLS patients. **Results:** Total of 12 articles identified, 6 papers were involved in the review which was deemed as being of high quality. **Conclusion:** Physiotherapy treatments plays an important role in improving fine and gross motor function and participation during daily activities in a child with CdLS.

Key Words: Physiotherapy, Cornelia de Lange Syndrome, Genetic Disease.

Introduction

Cornelia de Lange syndrome (CdLS) is a rare genetic illness caused by abnormalities in seven genes that impair several organ systems during development. The majority of those impacted have mental disabilities and numerous deformities. In 1933, the first instance was discovered. Different names for this syndrome include Amsterdam dwarfism, Bushy syndrome, and Brachmann syndrome. The prevalence is believed to be 1/10000, however male to female ratios may be higher.[1] The symptoms that appear in the first few weeks after the child is born. Partial toe fusion curled fifth finger, short-hand, radial hypoplasia, missing arm, forearm, or fingers, radioulnar synostosis, and pectus excavatum have all been observed in patients with CdLS.[2] The history, physical examination, and facial traits can all be used to make a clinical diagnosis. Genetic testing can be used to confirm the diagnosis. Physical ability may be impacted by limb anomalies.[3] Facial dysmorphisms include a small head, arched eyebrows, long eyelashes, a short nose with a depressed bridge and anteverted nares, thin lips, and hypertrichosis. Scoliosis, joint contractures, and hip issues are all possible side effects.[4]

CdLS clinical characteristics are determined by the severity of the condition, as well as certain aspects that appear before birth and others that appear after delivery. The 4th month gestational Ultrasound Scan is a common aspect of pregnancy and is used to check for congenital malformations. This ultrasonologist expert

performs the 4th month scan, which they almost never miss diagnosing anomalies.[5] A prenatal ultrasound scan is a sort of testing that can be done during pregnancy and at different points during a pregnancy. On ultrasound, there have been several results that are suggestive of a CdLS diagnosis, such as limb differences depending on facial profiles and structural differences.[3]

In families where a causal mutation has not been identified, anxiety levels may be elevated throughout successive pregnancies. Intrauterine growth limitation and facial abnormalities may appear earlier than previously thought. Micrognathia and upper limb abnormalities are visible on the initial ultrasound, which might have led to an earlier diagnosis.[1] Early and frequent ultrasonographic anatomic assessment is recommended. Early ultrasounds should look for abnormalities in the upper limbs, whereas later ultrasounds should look at the facial profile. Three-dimensional sonography may become a useful diagnostic tool for early diagnosis of CdLS as ultrasound technology improves.[2]

The genetic test is used to confirm a child's diagnosis with CdLS. It is carried out to detect various mutations in various genes. In the mild, moderate, and severe categories, certain genes and mutation types appear many times. This test checks for genetic changes in Mom's blood, which also contains the blood of the baby, and it can help families better understand the recurrence risk for future pregnancies. This testing is not flawless, and it has some limits.[1] Certain things can be overlooked, and there may be more genes causing CdLS that have yet to be discovered. Testing also has other drawbacks, such as its high cost and the fact that it is rarely reimbursed by insurance. This type of testing can only be performed in a specialized lab and is not available in a regular lab. The test took longer than a standard test.[5]

Prenatal genetic testing can be done using DNA from placenta or amniotic fluid cells. Genetic testing can discover changes in any of the seven genes implicated to CdLS. The tests can help parents make decisions regarding additional testing, care, or treatment during pregnancy or after the baby is born.[6] The newest prenatal screening technique, non-invasive cell-free fetal DNA, can detect several genetic abnormalities in the growing baby in the mother's blood. This could be used to spot alterations in genes that could lead to CdLS. In families who have had a previous child with CdLS and a known mutation, this test may be helpful in determining which gene is impacted.[7] However, identifying the outcome with accuracy in families without a previous child with CdLS would be difficult or impossible, and substantial interpretation would be required. This method cannot be used to assess Mosaicism. As a result, this form of testing for CdLS might not be appropriate.[8] The most effective genetic test for detecting a change in a gene linked to CdLS is panel sequencing. Panel sequencing examines multiple genes at the same time. When testing for CdLS spectrum, the panel should include at least the seven identified CdLS genes. Additional genes that can generate a phenotype like CdLS will be included in most genetic testing facilities.[3]

In terms of cognitive and behavioral features, CdLS affects persons differently and can range from mild to severe. Cognitive functions include thinking, learning, remembering, paying attention, and reading. Individuals with CdLS are more likely than individuals without the syndrome to engage in certain activities known as phenotypic or behavioral characteristics.[2]

Adaptive behaviors are age-appropriate acts that people must engage in to function successfully in everyday life and live independently. Adaptive behaviors include things like dressing, grooming, food handling, safety, making friends, communication, cleaning, money management, and the ability to work.[1]

Individuals with CdLS struggle with adaptive behavior throughout their lives. As a result, many children, and people with CdLS will require assistance with daily tasks including washing and clothing. Many people with CdLS never learn how to communicate verbally.[5] Expressive communication abilities, the ability to express oneself are frequently weak in comparison to receptive language skills and ability to understand communication. Individuals with CdLS frequently employ nonverbal communication tactics such as social approach and pushing a person's hand away.[2]

CdLS has a wide range of communication abilities. Individuals with CdLS typically have significant communication challenges, and many do not acquire spoken communication.[5] Speech problems are common in CdLS patients due to altered muscular tone. Speech and communication problems can also be caused by visual impairment, hearing loss, and abnormalities in the oral anatomy or jawbone. Communication and comprehension difficulties can

also be caused by cognitive problems with memory, thinking and communication.[4]

The development of a child's bones and muscles, as well as the ability to move around and influence the environment, is referred to as motor development. Gross motor development using the larger muscles and fine motor development involving the smaller muscles are two types of motor development involving the small muscles of the body.[8]

Motor development is almost always delayed in CdLS, and developmental milestones should be regularly observed. Children with CdLS may accomplish milestones (such as sitting, walking, and speaking) at a younger age than children with CdLS caused by mutations in the NIPBL gene, according to some data. Most children with CdLS caused by a shift in NIPBL can sit, walk independently, and begin to speak by the age of five.[6]

When a family learns that their child has CdLS syndrome for the first time, whether during pregnancy or after birth, the truth may be more difficult and harsher, and the parents or one of them may have a negative attitude toward the child. A typical reaction to having everyone may expect all feelings, from wrath to anguish, remorse, shame, despair, and even refusal to accept the truth or kid. Many questions have arisen in the minds of parents, such as how we can help our child, is there a cure for it, and so on.[8] Parents, relatives, and neighbors play an essential part in the child-parent relationship; their daily and social lifestyles can have a bad or beneficial impact on this relationship. Parents should ignore what others say and tell friends that a child, like others, has his own abilities and that giving him the best care and attention possible will place him in a better position. The positive role of parents and their union, as well as the employment of psychologists and medical personnel, are all critical in reducing the severity of the trauma and making it acceptable to accept him as a family member.[6]

Physiotherapy is an important component of a child's or adult's overall health and well-being. It has the potential to improve their movement and wellness. Children with CdLS may experience a variety of orthopedic issues affecting their hands and upper body.[4] Physiotherapy can help to treat certain issues. Serial splinting, a Physiotherapy technique required for a club foot. This surgery is typically used on youngsters who have club feet. The examination of the affected child would assist the therapist in developing a treatment plan that is tailored to the needs of the individual. Sensory deprivation, motor training, and water therapy are some examples of this. Parents must participate in their child's therapy. The goal is to give the youngster the finest Physiotherapy experience possible. Parents can assist their children in developing the necessary skills and behaviors to improve their health.[7]

Methodology

Six databases which includes, MEDLINE/PubMed, CINAHL, EBSCO and Cochrane were searched with predefined keywords specific to or related to Physiotherapy interventions from 2006 to February 2022 for the full-text English language articles.

The scientific community is currently faced with the difficult issue of identifying reliable and practical CdLS therapy alternatives. We believe that physiotherapy, either alone or in combination with other medicines, would be more effective at preventing CdLS than currently available treatments. Physiotherapy has been suggested as a possible treatment for CDLS.

This scoping review aimed to establish physiotherapy treatment strategies for individuals with Cornelia de Lange Syndrome (CdLS). The review was structured in three phases, targeting key challenges such as growth and developmental delays, hearing impairment, and muscle weakness. Specifically, it focused on strengthening the trunk, back, and lower limb muscles, as well as muscles around the spine, which are particularly problematic in the CdLS population.

Table 1: Phase wise Physiotherapy Treatment Strategy in CdLS.

Phases	Abnormal development in patient with CdLS	Goals	Treatment
Phase 1 Age 0-2 years supervised	- The baby can't get attention easily. - The baby has delayed milestones. - The baby has problems with growth and development. - The child has absence or abnormal reflexes. - Gross head lag	- Gaining Attention of the child - To bring the child to normal developmental activities - Developmental growth - Developmental reflex - Head control	- Put a moving objects and make sounds in different directions - mat exercises are used to: mobilize and strengthen the trunk and limbs; and prepare for functional tasks - Carry the baby in a way which corrects abnormal positions and which brings both arms forward. - A more upright position helps the baby learn to hold his/her head up and look around
Phase 2 Age 2-4 years	- The child can't sit properly. - The child can't stand with support. - The child can't roll completely. - The child can't walk probably.	- Teach sitting with or without support. - Standing with support. - Rolling without support	- Improve rolling, sitting, crawling, during the ball, wedge, roll, and mat exercises. - Improve standing, walking with or without support and balance and coordination during parallel bar, balance board, standing frame, and tilting table.
Phase 3 Age 4-6 years	- Weak muscles - Weakness of upper limbs, lower limbs, abs back extensor	- Continuation of above phases addition to it. - Special school - Activity will be encouraged for example play with toys soft balls. - Encourage upper limb, lower limb, and back extensor activities.	- maintain stretches for upper and lower limbs during passive manual stretching. - Strengthening of upper and lower limbs and back extensor muscles during functional strengthening exercises - Balance exercises

Result

The first search approach for the scoping review resulted in the identification of 16 pertinent items. After careful examination, any duplicates were eliminated, leaving a total of 12 papers to be considered for inclusion. Out of these, a total of 9 articles were found to fulfill the initial qualifying criteria. After conducting a thorough examination, six publications (n = 6) were identified as meeting all the

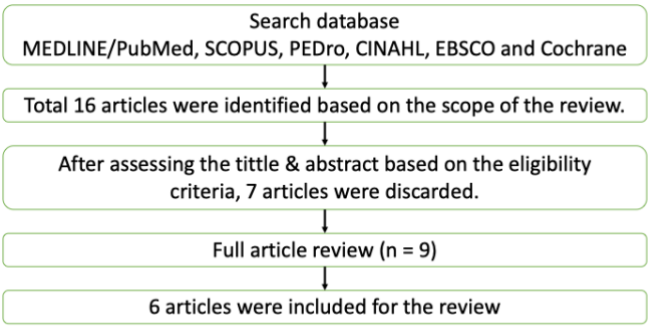

Fig. 1: Process of Literature search.

Table: Study Characteristics.

Study	Outcome
1 - CdLS Foundation Clinical Advisory Board Member, CdLS and Physiotherapy. CdLS Foundation.[9]	Physical therapy has the capacity to establish home-based programs to maximize the benefits for the child with CdLS.
2 - Cornelia de Lange Syndrome Synonyms.[4]	Physical therapy is suggested to improve mobility and lower the chance of developing orthopaedic problems later, such as contractures, scoliosis, and hip dislocation.
3 - Characterization of limb differences in children with Cornelia de Lange Syndrome.[13]	Physiotherapy is crucial for maintaining the strength and flexibility of muscles, particularly in children who have joint contractures and hypertonicity. Physical therapy (PT) can assist in improving walking abilities and developing gross motor skills required for activities such as kicking a ball or riding a bike.
4 - Intensive Neuromotor Therapy improves motor skills of children with Cornelia de Lange Syndrome: case report.[8]	A child's gross motor function and engagement in daily activities were both improved after receiving INMT for CDLS. To determine whether INMT is effective for children with CdLS, more research with bigger cohorts is required.
5 - Orthopaedic manifestations of Brachmann-de Lange syndrome: a report of 34 patients.[12]	BdLS is a disorder with unknown origins, identified by unique facial features and associated with growth and mental retardation, and limb anomalies, where patients frequently exhibit hand, elbow, and heel cord issues but seldom require surgical correction for these deformities.
6 - Interdisciplinary Therapy in Cornelia de Lange Syndrome.[1]	physical therapy: based on functional diagnosis – therapy of muscle tonus disorders, contractures, associated body deformities, scoliosis, and other secondary manifestations.

Discussion

The current study has tried to summarize the information regarding the use and awareness of Physiotherapy in CdLS population. It is a rare genetic syndrome where usually a mutation takes place during development, which affect growth and development with low birth weight, swallowing, GI reflux, hearing loss and with distinctive facial features.[9]

Treatment regimens include physiotherapy, occupational therapy, speech therapy, cochlear implant, and developmental pediatrician. A termed cohesinopathies in which intellectual and growth retardations are seen. Parental involvement and psychological counselling are the core support system of this syndrome.[10]

Time to time visit to the medical care provider is a routine involvement. Early intervention benefit from Physiotherapy, speech therapy or occupational therapy to promote development. Charting is important for recording growth and development. There is a risk for joint contractures, walking delay and scoliosis. They need special education because of cognitive limitations. The gather information revealed that the lack of specialized center for CdLs population make difficult to approach for the family to get Physiotherapy. Physiotherapy has also been proven to be effective and beneficial to this population.

Morphology scan/ Fetal anomaly scan: it is usually done 20/ 22 weeks anomaly scan which was done only to detect the Congenital anomalies. At this stage Ultrasound (US) scan was done for the body organ development, gestational age of the fetus and heart rate as well as sex determination. Diagnosis of CDLs starts from this stage of US, with a well-trained ultrasonologist can detect and diagnose the anomalies. Its far beyond the reach of gynecologist to diagnose the disease at this stage. The cause of this syndrome is gene mutation (NIPBL, RAD21, SMC3, HDAC8, and SMC1A).

The findings demonstrate that CdLs can benefit from physiotherapy in a variety of ways, stressing the importance of this treatment in the care and rehabilitation of these patients. Physiotherapy and rehabilitation can benefit and enhance motor function and mobility, hence ease their life day to day activities. Contractures of lower limb muscles can be benefit from sustain stretching.[11-13]

Conclusion

Physiotherapy techniques is a useful strategy for rehabilitation of individuals who suffered from CdLS and normalizing muscle tone, easing pain, promoting active movements, and improving the function of the activities of daily living, The goal of this review is to provide the CdLS child with the best possible Physiotherapy experience.

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