Physiotherapy for Children with CLN2 Disease

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Abstract

CLN2 disease (neuronal ceroid lipofuscinosis type 2) is a rare, genetic, paediatric-onset, neurodegenerative lysosomal storage disorder characterised by seizures, ataxia, rapid loss of motor function and language ability, dementia, visual loss and early death. Physiotherapy plays an important role in the management of CLN2 disease, aiming to maintain the best possible functioning and autonomy of the child, support the child's participation in everyday life, limit secondary complications and maintain or improve quality of life.

This article discusses the physiotherapeutic treatment of children diagnosed with CLN2 disease. Based on the author's clinical experience, frequent muscular impairments associated with CLN2 disease, their impact on affected children's sensorimotor abilities and autonomy, and physiotherapy interventions are described. Common muscular deficits included abnormal muscle tone leading to poor trunk control, difficulty standing upright, often accompanied by equinus contractures and movement disorders such as myoclonus. The use of orthotic and adaptive medical devices that support an erect posture in locomotion and positioning appear to be particularly beneficial for prolonging sensorimotor control, communication and food intake.

In conclusion, early initiation of physiotherapy is recommended and should include the provision of adaptive walking, standing, sitting and positioning aids.

Keywords

CLN2 disease, neuronal ceroid lipofuscinosis type 2, physiotherapy, medical aids, sensorimotor symptoms.

Introduction

CLN2 disease (neuronal ceroid lipofuscinosis type 2, OMIM #204500) is a rare, autosomal-recessive, neurodegenerative lysosomal storage disorder. This genetic disorder results from mutations in tripeptidyl peptidase 1 (TPP1), a soluble lysosomal enzyme involved in protein degradation [1,2]. Deficiency in TPP1 enzyme activity results in intracellular accumulation of a protein-rich material called ceroid lipofuscin, which is associated with glial activation and neuronal loss [3].

CLN2 disease is a rapidly progressive disorder characterised by language delay, motor and visual deterioration, refractory seizures, and dementia [1,4,5]. Generally, the disease initially manifests between the ages of 2 and 4 years, most commonly as seizures and/or ataxia, and a history of language delay [1,4,5]. As the disease progresses, affected children lose voluntary movement, develop movement disorders (e.g. ataxia, myoclonus and spasticity), lose their ability to eat and drink (dysphagia) [6], become blind and bedridden, and die prematurely [1,4,5].

Physiotherapy and the use of medical aids plays an important role in the management of CLN2 disease and can help to maintain function and independence for as long as possible and thereby optimise the quality of life of patients and their caregivers [5]. Williams et al. recommend two to three physiotherapy sessions per week [5]. In the absence of disease-specific studies for this extremely rare disorder, physiotherapeutic approaches developed and tested in patients with similar muscular deficits (e.g. in children with cerebral palsy) can be applied to CLN2 disease (e.g. the Bobath [neurodevelopmental treatment] concept [7,8] and the

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Castillo Morales® concept [9,10]). This article discusses frequently occurring motor impairments (and associated swallowing difficulties) and the use of physiotherapy and adaptive standing and seating equipment in children diagnosed with CLN2 disease. To the best of our knowledge, it is the first paper focusing on the physiotherapeutic management of CLN2 disease.

Methods

This is a descriptive review of muscular impairments associated with CLN2 disease, their impact on affected children's sensorimotor abilities and autonomy, and physiotherapy interventions from a single centre. Sixteen patients aged between four and eleven years who were diagnosed with CLN2 disease were managed at the Paediatric Physiotherapy Practice in Hamburg, Germany between February 2014 and July 2018. Individually tailored physiotherapy was performed 2 or 3 times a week for 30-40 minutes according to the Bobath and the Castillo-Morales concepts [9,10], in collaboration with therapists in the individual children's school, kindergarten or hospice.

Results

Physiotherapeutic Goals

The objectives of physiotherapeutic treatment for children with CLN2 are to support children's ability to participate in everyday life activities, by promoting their ability to walk, stand and sit, as well as to communicate and eat and drink with minimal external intervention for as long as possible. This includes early intervention such as the implementation of augmentative and alternative communication methods in anticipation of language loss to help the children express their thoughts/wishes (e.g. through the use of voice-output communication aids) and continued support over the course of the disease. Importantly, even with the most severe symptoms, regular standing or sitting (e.g. at the table with the family) can be achieved with standing devices or therapy chairs.

The physiotherapeutic interventions seek to: maximise functional independence/participation in daily activities, with early use of medical aids (e.g. standing devices); improve food intake/safe swallowing by educating parents on the most appropriate supportive body positioning; reduce the risk of patients developing secondary complications (e.g. respiratory infections following aspiration of food into the lungs or joint contractures resulting from spasticity/immobility); enable children to maintain upright positions in order to support the above goals; and set functional goals with the patients' families and counsel them on treatment and care options throughout the course of the disease.

Prevalent Sensorimotor Symptoms

The 16 children with CLN2 disease demonstrated recurrent muscular dysfunctions and compensation patterns. In terms of functional limitations, conspicuous features of CLN2 disease were the rapid loss of the ability to walk, difficulty concentrating and the effects of muscle dysfunction on orofacial function impacting the ability to eat. Common neuromuscular disorders included abnormal muscle tone and movement disorders (e.g. hypo/hypertonia, spasticity, myoclonus and dystonia); these are listed in Table 1. The muscular deficits described in Table 1 influence each other. For example, hypertonia in the back of the legs results in a forward displacement of the torso (see Figure 1),

Table 1. Prevalent sensorimotor symptoms associated with CLN2 disease and their effect on patients observed at the Paediatric Physiotherapy Practice in Hamburg, Germany.

Muscular impairment	Impact on posture and movement	Functional limitations	Adaptive equipment
Hypotonia (reduced muscle tone)	Patients have difficulty pulling themselves upright and sustaining postural control against gravity Forward displacement of the upper body that positions the body's center of gravity outside its base of support	Reduced trunk control Increasingly unable to stand, walk and sit upright without trunk support	Walkers, standing devices, therapy chairs and other aids that provide postural support for the upper body and thereby offer mobility or allow the child to play, eat, etc.
Hypertonia (increased muscle tone) in the posterior leg, particularly in the calf muscle and supinators of the feet	Tendency to equinus deformity, internal rotation/supination of the feet Compensatory changes for more stability in stance: knee hyperextension, backward pelvis tilt, exaggerated hip flexion, forward displacement of the upper torso (also see Figure 1)	Inability to stand and walk upright without assistance	Orthoses correct the misalignment, provide stability in the legs and enable weight bearing; if required, orthoses can be combined with walking and standing devices to provide trunk stability
	Worsening equinus deformity (lower-limb extensor hypertonia) requires increasing weight shifting to allow the patient to balance, which leads to further postural control deficits and functional impairments		

Table 1. Cont.

Muscular impairment	Impact on posture and movement	Functional limitations	Adaptive equipment
	Backward displacement of the pelvis, which is often accompanied by a ventral pelvic tilt, leads to an overextension of the large gluteal muscles, making them difficult to activate; inactivity causes weakening	Inability to stand and walk without assistance Independent transitional movements only possible in positions close to the ground	Orthoses together with walking or standing devices allow the child to adopt an erect posture and enable activation of the gluteal musculature
	The backward displacement of the pelvis and slightly bent hip leads to a forward displacement of the upper trunk that prevents activation of the abdominal and anterior stabilising muscles; inactivity leads to muscle weakening	Reduced trunk control Reduced head and neck control	Corrected positioning (e.g. in a standing device) enables the use of the muscle groups and facilitates posture control
	The rounded shoulders render arm activities to the front and above shoulder height difficult and exhausting; declining use of arms causes further decline in muscle endurance	Difficulty lifting arms and reaching	A well-adapted therapy chair provides optimal positioning for independent head and neck control and for the child to play games with the hands/arms
	The forward curvature of the upper trunk causes a head-forward position; eye contact requires hyperextension of the neck; this strains the neck and jaw muscles; the mouth is frequently pulled open	Impaired mouth closure, which impedes orofacial functions such as swallowing and speaking Difficulty directing eyes/gaze towards a visual target	Therapy chairs or standing devices that allow the child to hold his/her head upright above the shoulder girdle; use of support points (e.g. the tray of a therapy chair or standing device) can help the child hold up his/her head
Dystonia, truncal incoordination	Additional instability of the trunk intensifies the issues described above (e.g. goal-directed motion, gaze focus in space, walking and standing)	Inability to walk, stand and sit independently	Sitting, standing and walking is possible with much assistance; requires stability generating pressure points and support possibilities on the aids (e.g. a belt at the height of the sternum or lateral pieces in the rehabilitation buggy)
Myoclonus	Myoclonic twitches and jerks primarily impede (a) directed motions (e.g. of the arms) and (b) calming of the child in the advanced stages of the disease; the sudden involuntary movements frequently appear to exhaust and frighten the children	Inability to sit independently	Assistive devices such as adaptive standing devices, rehabilitation buggies or materials for optimal positioning in bed that provide spatial delimitations can give the child an idea of his/her spatial position and thus a feeling of security. To prevent injury, it is essential to adjust the assistive aids appropriately
Opisthotonus (whole-body hyperextension with head, neck and spine arched backwards) with existing myoclonus	Extreme muscle spasms can occur in the late stages of the disease. As a result, the child cannot independently find rest in any position; sleep is severely disturbed; saliva swallowing is impeded, which can frequently result in choking, which further distresses the child		Assistive equipment (e.g. aids for optimal positioning in bed) must be chosen/adapted on a case-by-case basis to help reduce myoclonic activities. For discrete activities, the child can be placed in an upright position either supported by the parents or by a standing device

which existing hypotonia in the torso is increasingly unable to overcome. Muscle reactions such as hypotonia, myoclonus and dystonia also occur in the orofacial area; this results in an inability to close the jaw. The tongue may also exhibit myoclonic muscle jerks or twitches, such as lateral and rotating motions, or dystonic activities, exerting intermittent pressure on the palate.

Significance of an Upright Posture for Sensorimotor Abilities and Communication

Optimising the childrens' ability to move and/or adopt age-appropriate positions (e.g. standing upright) strengthened their mental alertness and motivation to utilise motor abilities. Even

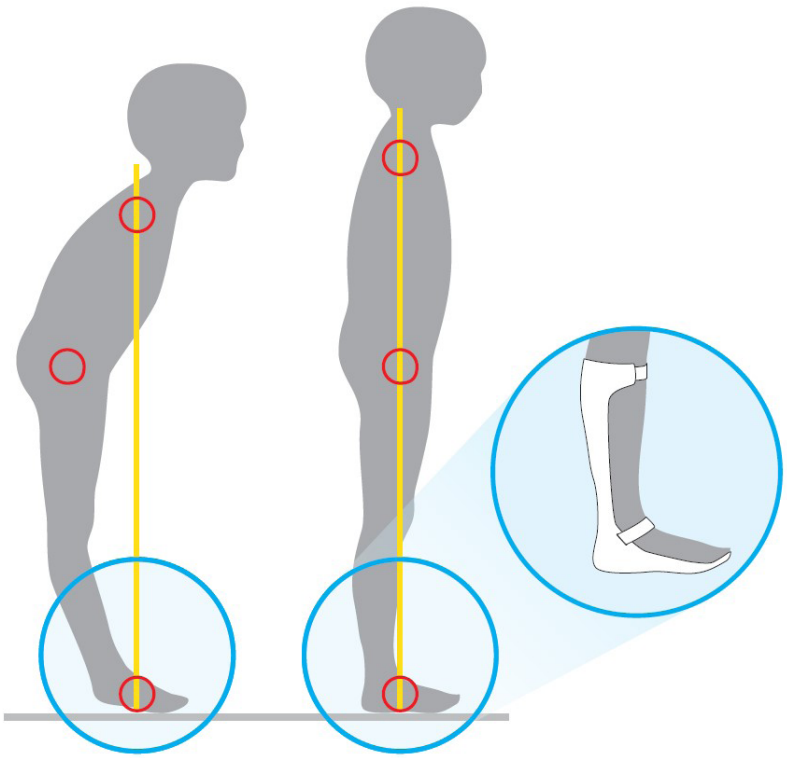

Figure 1. Children with CLN2 disease who developed equinus contractures, typically compensated for this foot deformity by hyperextension of the knees, backward displacement of the pelvis, forward displacement of the trunk and hyperextension of the neck. As a result, their ability to stand and walk became severely restricted and independent standing and walking rapidly became impossible. The equinus position can be corrected with the help of orthoses. As a result, the child can assume a more favourable upright position, which greatly supports standing and walking. Positive effects may also be observed on communication, independence and contracture prophylaxis.

if part of the musculature could no longer sustain an upright posture (e.g. increased trunk instability), the child could still walk alone with an adaptive walking device (e.g. with torso support). The ability of a child to independently control his/her legs and determine the direction to walk represents an expansion in independence. In light of the early loss of a child's ability to walk as CLN2 disease progresses, it is necessary to support and maintain the ability to stand and sit upright for as long as possible. In this way children with CLN2 disease can obtain postural control with relatively little effort and motivation, adapting an optimal position from which to engage in functional activities such as communicating, eating and playing (Table 1). Being at the same eye level as other children or parents when communicating and eating promoted these functions and thereby could greatly improve their quality of life.

Management of Muscular Limitations

To delay development or reduce the severity of movement disorders associated with CLN2 disease, early initiation of physical therapy and the use of medical aids are recommended. Therapeutic and medical aids, such as sensorimotor inserts, rotation bandages, orthoses and adaptive standing devices, and a description of their function are listed in Table 2.

Physiotherapeutic techniques, such as muscle stretching and stabilising pressure toward the joint can temporarily help regulate hypertonia, such as spasticity. Position correction and medical aids can also reduce muscular hypertonia when in use. When extensor hypertonia causes equinus deformity, orthoses can be used to hold the foot in a normal, plantigrade position and enable weight bearing; this allows temporary normalisation of muscle tone (Figure 1). The children with CLN2 disease generally appeared to tolerate orthoses well during physical activity such as standing and walking without any apparent discomfort or pain. Orthoses must not be applied if they cause pain. For existing myoclonus, appropriate positioning of the child (e.g. on the more severely impaired side of the child's body) allows the body weight to exert a regulating effect on muscle tone, which reduces myoclonic muscle activity (Table 2). These therapeutic interventions allow the child to be supported in his/her proprioception, enabling adoption of physiologic postures and enhancing the implementation of physiologic movement patterns. However, because CLN2 disease is progressive, eventually appropriate positioning will not be able to overcome the deficits caused by the disease.

As part of the treatment of orofacial dysfunction according to the Castillo-Morales concept, parents are instructed to support their child's independent food intake for as long as possible. To

Table 2. Description of the main tools used, effects observed, and challenges encountered at the Paediatric Physiotherapy Practice in Hamburg, Germany.

Medical aid	Description of function
Orthopaedic shoes with sensomotoric insoles	Support the position of the feet and stability of the ankles and thereby upright posture and head position Facilitate walking and standing
Ankle orthoses	Provide medial and lateral stability for the ankle Hold the feet in plantargrade position and correct axis deviations Facilitate walking and standing
Lower-leg orthoses	Allow the child to stand/walk on the whole foot, which otherwise remains in the equinus (pointed) foot position; adjustable to adapt to hypertonia in calf muscles The pressure from the child's weight helps regulate muscle tone and provides prophylaxis against contracture Increased independence, as longer phases of standing/walking are possible
Therapy chair	Ensures a stable, upright, age-appropriate seating position; this is important for food intake and play, as the child is stabilised from the trunk to the pelvis The stable trunk position facilitates head control, orofacial activities and arm and hand movements. Chairs should be adapted to the child and his/her abilities (e.g. supportive pads, protective straps, footboards, custom height-adjustable tables)
Wheelchair/ rehabilitation buggy	Mainly used for safe, stable and upright transportation Allows children to participate in everyday life and move independently (wheelchair) Reclining wheelchairs/buggies may be useful in the event of epileptic seizures
Walker	In combination with orthoses, a more normal (up to near-normal) gait can be achieved Enables upright, age-appropriate positions, in which the child can walk safely, despite balance problems/dystonia Attainment of age-appropriate, upright positions motivates participation in everyday life Can be individually adapted to the child's needs
Upright standing device	Allows stable standing postures, in which children can put their weight on both feet, stabilising the head (even when they are usually unable to do so) Strongly assisted stable posture control supports orofacial functions (e.g. mouth closure, swallowing) Communicative skills such as eye contact are facilitated Digestion and respiration are supported
Bed support	Non-slip, supportive, fixed bed upholstery, which supports the position of the child in bed Individualised, stable bed positioning enables improved recovery in lying position, improving the quality of sleep

achieve this goal, caregivers are educated about how their child can achieve optimal swallowing through postural management (with positioning aids that support trunk stability and head position) and the use of utensils (e.g. adapted cups).

The most physiologic position with a straight neck that is achievable offers a good basis for the functions of swallowing and speaking. Depending on the severity of the limitations, postural support is provided by the parents/caregivers or by adaptive equipment.

Passive standing devices and frames can provide long-term benefits even in the later stages of the disease, when the child can no longer sit or stand on his/her own. Starting in a lying position and being supported based on his/her abilities (if necessary, complete leg, hip, trunk and head support), the child can be tilted into an erect posture permitting him/her to feel and bear his/her own body weight. Standing normalises the tone of and stretches the muscles, which may prevent contractures, and positively affects respiratory and gastrointestinal functions.

Special Considerations in the Physiotherapeutic Treatment of the Child with CLN2 Disease

Factors complicating the treatment of a child with CLN2 disease are the complexity of the symptoms, which include cognitive, sensorimotor and communication deficits and rapid disease progression. Physiotherapy must be tailored to the individual needs of the child and the disease stage. Thus, the degenerative nature of CLN2 disease dictates that the therapeutic goal evolves from maintaining function in early-stage disease to maintaining quality of life in spite of loss of function in later stages [5]. In addition to the progressive worsening of sensorimotor functions due to neurodegeneration, physical impairments can be temporarily exacerbated by emotional

situations or fatigue (e.g. side effects of medications for seizure control).

These fluctuations in the physical and emotional health of the child require constant observation and therapeutic adjustments. It may also be necessary to change the location where therapy is provided and treat the child at his/her home. This reduces the burden on the child and family and allows for implementation of a practical therapy plan that is relevant to the patient's everyday life. To ensure the best possible management of the child, a properly functioning interdisciplinary team of doctors, therapists, psychologists, orthopaedic technicians, dieticians, health insurers, etc. is necessary, so that in conjunction with the family, changes can be made quickly to respond to the child's needs.

Discussion

Physical therapy has a beneficial effect on children diagnosed with CLN2 disease. The early initiation of therapy tailored to individual children's needs and the early use of medical aids are recommended [5]. The use of medical aids allows the child to be as self-sufficient as possible as the disease progresses. Adjustable standing devices and postural aids can be used long term across the different disease stages. In comparison, mobility aids (e.g. walkers) can be used for shorter periods of time. It is also important to educate, enable and support the patient's parents. Effective management of children with CLN2 disease requires good communication and close interdisciplinary collaboration among the medical, social, psychological and therapeutic team and the patient's family/caregivers. All parties need to work together to effectively address the multifaceted and complex problems occurring in children with CLN2 disease. This interdisciplinary and long-term care can be coordinated for example through a socio-educational centre.

The perceived effectiveness of supported standing in children with CLN2 disease is consistent with the findings of a systematic review on paediatric supported standing programs examining 30 high-quality research studies in children with atypical development, with or without a neuromuscular diagnosis, including cerebral palsy [11]. This review found moderate to strong evidence for a beneficial effect of supported standing on lower-extremity range of motion, lower-leg spasticity or tone, muscle power, interaction with peers and the environment, functional activities (e.g. walking, activities of daily living, transfers) and, in high-dose programs of supported standing, on bone mineral density [11]. Furthermore, case report and survey evidence supports a possible positive impact on bowel function and reflux, hip stability, alertness and well-being [11]. A survey of 319 paediatric and adult patients with various congenital or acquired disabilities (e.g. cerebral palsy, syndromes, multi-disabilities, spina bifida, multiple sclerosis, amyotrophic lateral sclerosis, traumatic brain injury, stroke, virus, tumours) who used standing devices confirmed that the users (or their caregivers) perceived a positive impact on well-being and quality of life [12]. Similarly, the recommendation to use adaptive seating equipment in children with CLN2 disease is supported by findings from a systematic review that concluded that special-purpose adaptive seating systems may be able to improve self-care and play behaviour at home among children with severe cerebral palsy [13].

Conclusions

While physiotherapy is a valuable factor in the palliative management of patients with CLN2 disease, it is not possible to draw firm conclusions from case analyses. However, the use of physiotherapy and assistive equipment described appears to contribute to the maximisation of positioning and functioning, ability to undertake daily activities, social interaction and well-being in children with CLN2 disease. Further research is needed to measure and compare the effect of the current and alternative physiotherapeutic concepts and assistive technology devices on functioning, activities of daily living, social participation, quality of life and ease of care in children with CLN2 disease. Such studies will need to overcome challenges relating to the heterogeneous and complex clinical presentation of CLN2 disease, the application of many interventions at the same time, the highly individualised physiotherapy approach and the degenerative nature of the disease (goal to slow worsening rather than improve outcomes). In addition, studies need to account for the impact of the motivation and skill level of caregivers as well as the impact of enhanced therapeutic environments on children with CLN2 disease.

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Declaration of Conflicting Interests

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