Micturition reeducation in children with cerebral palsy

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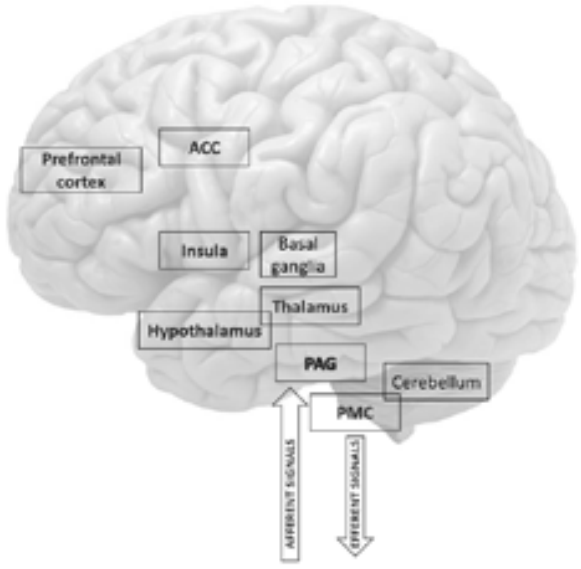
Introduction

Cerebral palsy (CP) is one of the most prevailing syndromes affecting children, with a prevalence of 2.11 per 1000 live-births. CP describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain (1). The definition of CP was reviewed, as more attention should be given to activity restriction and non-motor problems often accompanying CP (1). Nevertheless, no mention of lower urinary tract dysfunction (LUTD) or incontinence particularly is made in the new CP definition. Although lower urinary tract symptoms (LUTS) are associated with poor quality of life and health status, urinary incontinence in children with CP is often considered a normal, unavoidable or minor problem (2, 3).

The International Children's Continence Society (ICCS) subdivides LUTS in children into four groups, i.e. storage symptoms (increased/decreased frequency, incontinence, urgency and nocturia), voiding symptoms (hesitancy, straining, weak stream, intermittency and dysuria), pain-related symptoms and other symptoms (4). LUTS are relevant when present after acquiring bladder control or the age of five years old (4-6).

To assure efficient voiding the bladder and pelvic floor muscles need to act in a coordinated way. During the bladder filling phase the bladder or detrusor has to relax and the pelvic floor muscles have to contract to prevent urine loss. Whereas the pelvic floor muscles have to relax and the bladder contracts during the voiding phase. Underlying conditions for daytime incontinence in typically developing children are often related to dysfunction between bladder and pelvic floor during bladder filling phase or voiding phase. This coordinated activity is directed through the nervous system, with the impact of higher brain centers making voluntary control of voiding possible (fig 1).

Figure 1: *Anatomical representation of higher brain centers related to bladder control*



Legend: ACC Anterior cingulate cortex; PAG Periaqueductal gray; PMC Pontine micturition center

Lesions of the nervous system can result in LUTD, depending on the level of the lesion (7). Lesions above the pons, as expected in children with CP, remove inhibition of bladder contraction during the bladder filling phase.

It is generally accepted that incontinence must be treated. Treatment should be individualized to the child and specific underlying condition (8). Often a combination of treatment modalities is necessary. The ICCS provided an algorithm for the management of children with non-neurogenic daytime incontinence. If no comorbidities are present, all children should start with standard urotherapy.

The ICCS also provided recommendations for therapeutic intervention in the presence of a neurogenic bladder (9). Unfortunately, little attention is given to the use of urotherapy. Standard urotherapy specifically is not mentioned at all.

This PhD project includes several studies conducted with the primary aim to highlight and understand the incidence of LUTS and urinary incontinence in children with CP and contribute to the possible conservative treatment strategies for urinary incontinence in children with CP.

Incidence

Cerebral palsy is a condition beginning in early childhood and persisting through the lifespan (10). As result suffering and costs associated with LUTD can be significant (11). Understanding the incidence of LUTS and incontinence specifically, will indicate the need for evaluation and treatment.

By means of a systematic review the existing scientific literature on the presence of LUTS and pathological urodynamic findings in subjects with CP was investigated. Literature concerning children and adults with cerebral palsy was evaluated.

Twenty-seven studies fulfilled inclusion criteria**.** Studies report that 55.5 % of the children and adults with CP experience one or more lower urinary tract symptom. Excluding hesitancy, no clear differences in LUTS and urodynamic findings were found between children and adults. Urinary incontinence is the most frequently observed symptom in children with CP, with a prevalence rate ranging from 20 to 94 % (12, 13).

Storage symptoms are more common than voiding symptoms due to the high prevalence of neurogenic detrusor overactivity. Patients with voiding symptoms and pelvic floor overactivity are less present but seem to be more prone to progress to upper urinary tract dysfunction in adult life. It is suggested that subjects with storage symptoms more often stay stable and respond to medication, while subjects with voiding symptoms can progress to retention in adult life (14). Recent literature also states that neurogenic detrusor overactivity with reduced bladder capacity in childhood can evolve to neurogenic detrusor underactivity and distention of the bladder with age (15, 16).

Of the children who are dry at adult age, most achieve continence by the age of five years (17, 18). Therefore Reid and Borzyskowski (1993) suggest children with CP can merit early urological evaluation (19). ICCS guidelines recommending urologic evaluation when LUTS are present after the age of five years should also be used in children with CP (4). After the age of five years spontaneous achievement of continence drastically decreases and

parents and physicians should not assume lower urinary tract dysfunction as a normal feature in these children.

Urinary incontinence may be reinforced by the presence of negative prognostic factors. When risk factors for incontinence can be identified in children with CP, attention to these factors may be enhanced and emphasis and direction of treatment can be individualized to the child.

Therefore, a second study identified risk factors for the presence of urinary incontinence in children with CP. A cross-sectional case-control study was conducted including children with CP with or without incontinence. Risk factors were subdivided in three clusters, namely demographic and general medical data, CP classification and bladder and bowel dysfunction. Univariate and multivariate analysis was performed for variables and clusters respectively. A final associative logistic model including all clusters was developed.

Concerning demographic and general medical data, incontinence was associated with intellectual disability (Odds Ratio (OR) 7.69), swallowing problems (OR 15.11), the use of mobility and positioning aids (OR 27.50) and the use of laxatives (OR 13.31).

Within the cluster of CP classification, incontinence was positively associated with dyskinesia (OR 5.67) or combined spasticity and dystonia (OR 4.78), bilateral involvement (OR 4.25), functional impairment with GMFCS (gross motor function classification system) level IV (OR 10.63) and V (OR 34.00) and severe impairment in manual (OR 24.27) or communication skills (OR 14.38). Children with hemiplegia were less likely to be incontinent. Plasticity of the nervous system can enable the unaffected side to assume more control over the bladder during development(15).

Concerning bladder and bowel dysfunction, lower maximum voided volume (OR 0.97) and oral fluid intake (OR 0.96) influenced urinary incontinence negatively. Pathological uroflow curves were not significantly associated with incontinence.

The final associative model defined functional impairment, intellectual disability and oral fluid intake as predictive factors for incontinence. Although children with and without incontinence did not drink enough, oral fluid intake seemed to be an important predictive factor for incontinence. Multivariate analysis demonstrated that an increase of oral fluid intake equal to one percent of recommended fluid intake could have considerable effect on the odds of incontinence.

Diagnosis

The use of non-invasive evaluation of lower urinary tract function by means of uroflow measurement combined with electromyography testing of the pelvic floor (uroflow/EMG) could be informative and explanatory in children with CP to underline influence of pelvic floor hypertonia on micturition.

Current literature demonstrates that many factors, such as age, gender, toilet posture and environmental factors, influence the results of uroflowmetry (20-26). Before the implementation of uroflow/EMG is possible in a population of children with CP, there is the critical raising question of the potential effect of the electrodes on the natural voiding pattern of the subject. Therefore, we investigated if the standard protocol for uroflowmetry, recommended by the ICCS, remains accurate when integrating EMG measurement by means of superficial electrodes (27). This in a population of typically developing children without urinary incontinence.

Based on demonstrated results and time- and cost-efficiency, recommendations are to initiate the procedure with a single uroflowmetry measurement followed by one measurement of uroflow with EMG testing. Literature states that flow rates can be affected by comfort, privacy and anxiety of the patient (28). The possibility to use a uroflow measurement without EMG testing before actual testing could provide a comfortable and private environment for introduction of uroflow measurement to the child. This may lower the sense of anxiety within the child during further testing. The presence of both uroflow measurement and EMG testing during the first void could make habituation more difficult and minimize comfort during the second void, resulting in less evolution to the natural voiding pattern of the child.

Additionally, ICCS guidelines mention voided volumes less than 50 % of expected bladder capacity for age (EBC) are not reliable to interpret. The systematic review in this PhD project reported 73.5 % of the subjects with CP exhibit a reduced bladder capacity compared to EBC. Mean bladder capacity in the review was 58.5 % of the EBC, with a lowest average capacity rate of 47 % of EBC reported by Fernandes Silva et al. (2014) (29). Reduced bladder capacity could therefore influence accurate interpretation of uroflowmetry in children with CP.

Therapy

Despite the high prevalence of urinary incontinence in children with CP, treatment strategies in this population are poorly investigated. The ICCS suggests therapy for urinary incontinence should start with urotherapy (8). Yet no indication of this is made in guidelines for neuropathic bladder dysfunction (9). Some previous studies have tried to implement parts of urotherapy, but none have administered urotherapy as instructed by the ICCS for typically developing children(4, 8, 15, 30, 31)). Treatment generally contains pharmacotherapy or invasive treatment strategies (14, 15, 19, 30). In addition, effectiveness of the chosen treatment is seldom the primary objective of the study.

We applied standard urotherapy as primary starting point in training and investigated if urotherapy could be the basis of an evidence based, effective rehabilitation treatment for incontinence in children with CP. For this purpose a study population of children with cerebral palsy and urinary incontinence and typically developing children with urinary incontinence received treatment for one year. When necessary, standard urotherapy could be strengthened with specific urotherapy interventions or pharmacotherapy. Standard urotherapy, specific urotherapy interventions and pharmacotherapy were individualized to the child based on probable underlying conditions.

Within the group of children with CP, significant overall time-effects were found for daytime incontinence ($p < 0.001$), frequency of daytime incontinence ($p = 0.002$), frequency of enuresis ($p = 0.048$), storage symptoms ($p = 0.011$), good toilet posture ($p = 0.034$) and fecal incontinence ($p = 0.026$).

Results suggested urotherapy can be the basis of an effective long-term treatment for urinary incontinence in children with CP, but effectivity rate of urotherapy is lower and changes occur slower in time in children with CP compared to typically developing children. Increasing fluid intake and bladder capacity and managing constipation were important factors influencing achievement of continence.

Our research, in agreement with previous literature, found that a great amount of subjects with CP had never been put on a toilet before testing as part of the study (32). In accordance with the age where most children with CP experience spontaneous continence achievement and ICCS guidelines, treatment is recommended as early as possible when incontinence past the expected age of bladder control occurs.

Nonetheless, some children with CP can still achieve continence in older age, which indicates the need for continued evaluation and treatment effort throughout the childhood and adolescence of the child (33).

Conclusion

Urinary incontinence in children with cerebral palsy is a frequently present and important problem as a result of neurogenic bladder dysfunction, cerebral palsy characteristics and modifiable environmental factors. Being more or completely dry can positively influence quality of life and health status of the child. This will improve future functioning and adaptation in society and increase the independence level of the child. Despite the obtained information in this doctoral thesis, many factors with possible influence to the presence of incontinence and treatment effectiveness are yet to be investigated.

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