Functional Effects of Common Cerebral Palsy Treatment Methods

Ph.D. Thesis Booklet

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1. Introduction

5.1.1. What is the topic?

This work aimed to evaluate the effects, particularly functional effects, and the magnitude of changes of two commonly performed procedures in children with cerebral palsy: upper-limb botulinum toxin injections (BoNT-A), and femoral deroation osteotomy (FDRO) surgeries.

5.1.2. What is the problem to solve?

Although there is no definitive cure for cerebral palsy (CP), several orthopedic interventions are used to limit the secondary musculoskeletal consequences. Safety, short-term, and direct effects of the common interventions are usually well-documented; however, effects on function, pain levels, participation, life quality, and patient satisfaction are lacking.

CP is a very diverse condition; even similarly categorized patients may present remarkable individual differences. Optimal care, therefore, should always be tailored to the individual. However, deciding on the best management

option can be challenging, even in the case of frequent problems, like spasticity and gait difficulties.

Among the many available interventions, we investigated two commonly performed procedures to aid personal decisions about them: upper-limb BoNT-A injections and FDRO surgeries.

5.1.3. What is the importance of the topic?

Cerebral palsy is the leading cause of physical disability in childhood. The prevalence has remained unchanged for decades; approximately 1 in every 500 children is affected by CP. Except for the very severe cases, life expectancy with CP remains similar to that of typically developing children. Therefore, reaching the best possible quality of life and function is of special importance.

5.1.4. What would be the impact of our research results?

A better understanding of what to expect from upper-limb BoNT-A injections and orthopedic surgeries containing FDROs will help patients and caregivers to decide whether to undergo these invasive interventions. We hope

the results will help professionals from different fields of CP care (surgeons, physiotherapists, neurologists, rehabilitation specialists, etc.) develop similar expectations and facilitate understanding and shared decision-making about BoNT-A and FDRO, and their optimal timing. Furthermore, the identified lack of knowledge in the literature can direct future CP research.

2. Objectives

2.1. Study I. – No Evidence of Functional Benefit after Upper Limb Botulinum Toxin Treatment in Children with Cerebral Palsy

This study aimed to assess what upper limb BoNT-A treatment can add to the non-invasive physical therapies in children with spastic cerebral palsy. The primary outcome of interest was upper-limb function; secondary outcomes were muscle tone, activity, participation, health-related quality of life, and client satisfaction. Our overall goal with this study was to provide clarification

and a critical appraisal equally to treating physicians and policymakers.

2.2. Study II. – Impact of Femoral Derotation Osteotomy on Gait in Ambulatory Children with Cerebral Palsy

The main goal of this study was to systematically review, synthesize, and contextualize the results of orthopedic surgeries with FRDOs in ambulatory children with CP with centralized hips, where the surgery aimed to improve gait function. The goals of this study were to aid orthopaedics in setting up correct indications for this major surgery and to aid clients in reaching informed decisions. Furthermore, to facilitate understanding among professionals involved in CP care, to ‘maximize potential outcomes and minimize risk.’

3. Methods

The studies were performed in accordance with the Cochrane Handbook, and the PRISMA 2020 guidelines were followed. The protocols of the studies were preregistered on PROSPERO, under No. CRD42021283865 and No. CRD42022312486.

3.1. Search A comprehensive literature search was performed in six major databases: CINAHL, Cochrane CENTRAL, Embase, PubMed, Scopus, and Web of Science. The search for the BoT-A study was conducted in October 2022 with the search key cerebral palsy AND (botox OR botulinum OR botulotoxin OR BoNT OR BoNT-A or btx), and for the FDRO study in May 2023 with the search key "Cerebral Palsy" AND osteotomy. No filters or restrictions were applied except for the FRDO study, where Scopus search was limited to titles, abstracts, and keywords.

3.2. Eligibility Criteria

BoNT-A study: randomized controlled trials comparing upper-limb BoNT-A-treated and no-BoNT-A groups of

children with spastic cerebral palsy. Outcome measures: upper limb function, body function, health-related life quality, muscle tone, spasticity, individual goals, pain, adverse events, and client satisfaction.

Criteria for the FDRO study: studies comparing the gait analysis results of patients with cerebral palsy before and after an FDRO surgery. Patients had to be under 18 years at the time of the operation. Outcomes measures: gait scores, temporospatial gait parameters, pelvic, hip, knee, and ankle kinetics and kinematics, foot progression angle, pain, quality of life, patient or family satisfaction, adverse events.

3.3 Selection and data collection processes

Study selection was performed independently by two reviewers according to the predefined criteria. Agreement between reviewers was quantified using Cohen's kappa coefficient, which exceeded 0.8 in every study, confirming the high reliability of the selection process. One author performed the data extraction, which was then verified by a second reviewer to ensure accuracy and completeness.

3.4 Quality assessment

The quality of evidence was assessed using validated tools. As the BoNT-A study had solely randomized controlled trials, the Cochrane RoB 2 tool was applied, and the GRADE framework was used to evaluate the overall strength of the evidence. For the FDRO study, the MINORS tool was used to assess the quality of non-randomized studies. Where sufficient data were available, potential publication bias was evaluated using funnel plots and Egger's test.

3.5. Statistical analysis

A meta-analysis was conducted for every distinct outcome with at least three independent data. Given the anticipated heterogeneity between studies, random-effects models were used. Mean differences (MD) or standardized mean differences (SMD) with 95% confidence intervals (CI) were calculated for continuous outcomes. Odds ratios (OR) were used for dichotomous variables. Heterogeneity was quantified using the I^2 statistic, with thresholds of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. Subgroup analyses were

conducted where possible, such as comparing proximal versus distal FDRO localization. All statistical analyses were performed using the R software environment with the meta and dmetar packages.

4. Results

4.1. BoNT-A study

4862 publications were screened, and 20 records of 14 independent studies were eligible. Altogether, 621 patients were enrolled: 83% had unilateral, 17% bilateral involvement. Mean patient age ranged from 3.5 years to 9.5 years.

The included studies used numerous different measurement methods. Regarding the primary outcome, upper-limb function, data from two functional tests could be meta-analyzed: Melbourne Assessment MD 3.13 (95% CI -3.13 to 9.3) and Assisting Hand Assessment MD 3.84 (95% CI -1.86 to 9.54). No significant functional gain was established.

A significant decrease was noted during the toxin effect in muscle tone and spasticity. Ashworth scale wrist MD -0.85 (CI -1.42 to -0.27), Ashworth scale elbow MD -0.53 (CI -1.06 to 0), Tardieu scale elbow MD -51.07 degrees (CI -91.7 to -10.4) BoNT-A groups had better goal achievement: GAS T scores MD 9.55 (CI 6.05 to 13.04); and better client satisfaction: improvement had an odds ratio of 8.44 (CI 1.34 to 53.08).

4.2. FDRO study

1,427 publications were screened. 46 articles of 26 independent studies or databases qualified for final inclusion. Altogether, 1,144 patients were reviewed, the vast majority belonging to the GMFCS II-III category. The mean patient age at surgery ranged from 8 to 12,5 years.

The primary outcome, gait function, was measured by three different gait scores among the eligible studies. A significant improvement was revealed: SMD 0.99 (CI 95% 0.52 to 1.47)

Significant improvements were found in rotations: pelvic rotation MD 6.6° (CI 2.2 to 11), hip rotation MD -14.4° (CI -16.7 to -12.1), foot progression angle MD -16.1° (CI -18.3 to -14).

No deterioration was noted in any examined parameter. In-toeing gait was corrected in 74% one year postoperatively and 69% five years after the operation. The recurrence rate was 13%.

5. Conclusions

5.1. BoNT-A study

The decrease in spasticity and muscle tone caused by the upper-limb botulinum toxin injections in children with spastic cerebral palsy was not associated with functional improvement measured by the Melbourne Assessment, nor by the Assisting Hand Assessment.

Although no functional benefit could be established, better goal attainment was noted in the BoNT-A groups compared to the no-BoNT-A groups.

Caregivers in the BoNT-A groups were more satisfied with treatment results compared to the no-BoNT-A groups.

Discrepancy between objective and subjective parameters requires further investigation.

5.2. FDRO study

Gait-improving orthopedic surgeries with FDROs demonstrate statistically and clinically meaningful improvements in gait quality, hip rotation, and foot progression angle in ambulatory children with cerebral palsy presenting with in-toeing gait. The average gait score improvement equals 10 GDI.

In-toeing gait was corrected in 74% one year postoperatively and 69% five years after the operation. The recurrence rate was 13%.

Long-term results are less robust, presumably because of the natural course of CP-related gait deterioration.

Kinetics, walking energy, pain, quality of life, and subjective patient-reported outcomes are missing.

6. Bibliography

Publications related to the thesis:

Gresits O, Vezér M, Engh M A, Szabó L, Molnár Zs, Hegyi P, Terebessy T (2025).
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