Running title: Effect of infant sign training on speech-language development

A protocol for a randomized-controlled trial to investigate the effect of infant sign training on the speech-language development in young children born with cleft palate

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Abstract

Background. Children born with a cleft palate with or without cleft lip (CP±L) are known to be at risk for speech-language disorders that impact educational and social-emotional growth. It is hypothesized that speech-language intervention delivered before the age of three years could decrease the impact of CP±L on speech-language development.

Aim. Infant sign training in combination with verbal input expands the natural communication of young children including multimodal speech-language input (i.e., verbal and manual input) via caregivers who act as co-therapists. This project aims to determine the effectiveness of infant sign training in one year-old children with CP±L by comparing different interventions.

Methods & procedures. This is a two-center, randomized, parallel-group, longitudinal, controlled trial. Children are randomized to either an infant sign training group (IST group), a verbal training group (VT group), or no intervention control group (C group). Caregivers of children who are assigned to the IST group or VT group will participate in three caregiver training meetings to practice knowledge and skills to stimulate speech-language development. Outcome measures include a combination of questionnaires, language tests and observational analyses of communicative acts.

Expected outcomes & results. It is hypothesized that speech-language development of children with CP±L will benefit more from IST compared to VT and no intervention. Additionally, the number and quality of communicative acts of both children and caregivers are expected to be higher after IST. This project will contribute to the development of evidence-based clinical practice guidelines regarding early speech-language intervention in children with CP±L under the age of three years.

Introduction

With an incidence of approximately 1/700 in live births, orofacial clefts are the most common congenital malformation[1]. In approximately 80%, a cleft of the palate with or without a cleft of the lip and/or alveolus (CP±L) is present[1]. Several early speech and language milestones have been identified to be delayed or distorted in young children with CP±L, including consonant inventory size, complexity and onset of babbling, onset of first words, and early vocabulary acquisition[2-4]. These early delays place children with CP±L at higher risk for persistent speech-language delays and challenges in school[5]. In addition, a CP±L can also impact hearing, feeding and physical appearance resulting in a decreased quality of life.

Due to the cleft in the palate, the mouth and nose of children born with CP±L are coupled. This results in the inability to build up enough intra-oral air pressure during the production of high-pressure consonants[6]. Although improvements are made following surgical repair of the palate (usually performed around 12 months of age[7]), some of these difficulties continue to be present in the speech of children with CP±L. Specifically, they exhibit smaller consonant inventories and produce fewer oral stops in their meaningful and non-meaningful utterances compared to children without CP±L[4]. Hearing loss has recently been highlighted as a possible predictor of poor speech in individuals with CP±L[8]. Lohmander, et al. [8] found mild hearing loss to impact presence of canonical babbling at 10 months of age, the number of different consonants produced at 12 months of age and to be related to consonant proficiency at 36 months in children with CP±L. Moreover, repeated middle-ear infections resulting in fluctuating hearing sensations during the development of the central auditory system may result in atypical auditory processing[9,10]. Impaired auditory skills, such as auditory attention, processing words in a noisy background and temporal processing, have been related to problems with speech-language development[10,11].

Early delays in speech-language development may have an impact on caregiver-child interactions. Caregivers provide less complex semantic input in response to children with CP±L who produce less canonical babbling utterances[12] or who produce less intelligible speech with lower word rates[13]. Hence, caregivers' responsive and language-facilitating behavior is determined by infant input. Moreover, young children with CP±L do not use their vocabulary as frequently during communicative interaction compared to children without CP±L[14]. When children make fewer communicative attempts using verbal utterances, they have fewer opportunities to practice sound production and to receive feedback from their communicative partners[13]. This could imply that these at-risk children do not receive the optimal support and stimulation in natural everyday communication and have fewer opportunities to learn new language and practice speech sounds compared to children without CP±L.

It has been suggested that early naturalistic interventions (i.e., delivered under the age of three years old) can lessen the impact of CP±L on speech-language development[15]. These interventions aim

to stimulate verbal vocabulary growth by embedding targeted speech goals within language and conversation activities. Hence, they aim to improve the child's speech-language development. Caregivers or speech-language pathologists (SLPs) are the facilitators that model correct speech and language[15]. A systematic review by Lane, et al. [15] concluded that early naturalistic interventions, such as enhanced milieu teaching (EMT) and focused stimulation, have the potential to increase the phonemic inventories and use of oral consonants in children with CP±L. In particular, an adaptation of EMT, Enhanced Milieu Teaching with Phonological Emphasis (EMT + PE), has provided evidence-based data to support vocabulary use and expand sound inventories and accuracy for young children with non-syndromic CP±L[16-20]. However, studies in this population merely focus on vocal productions in early speech-language development without examining the complete communicative act that includes gestural and eye-gaze components in addition to vocalizations and words[14].

We could question if exploiting an additional input modality, such as training symbolic gesture use, may support speech input and enhance language development in this population. Gesture, speech, and language are "tightly coupled" neurologically and developmentally[21]. Bates, et al. [21] reviewed the evidence demonstrating common underlying neural correlates for gesture use and language development. Moreover, they highlighted the co-emergence of gesture use and language milestones in early development. *Deictic gestures* (e.g., giving, showing, pointing) are among the first gestures produced by typically developing children between 8 to 10 months[22] and are correlated with word comprehension[21]. Around 12 months, word production (naming) starts together with the reproduction of brief actions associated with specific objects (i.e., *recognitory gestures,* e.g. pretending to drink from an empty cup). Before the onset of the 25-word milestone, symbolic gestures emerge. *Symbolic gestures* carry meaning in their form to symbolize a referent, and that form does not change with context. No object is present when performing these gestures (e.g., flapping arms to represent a bird). They can also be observed used in combination with spoken words to form short utterances[23]. When caregivers deliberately and specifically provide enhanced gesture training to infants to promote early communication development, symbolic gestures are also referred to as 'baby signs' or 'infant signs'. These infant signs differ from official sign languages in that they are not intended to be used as a complete language or as a replacement for oral vocabulary but as a symbolic support to spoken language in early childhood[24]. Depending on the training program used, these infant signs are adopted from official sign languages or newly developed signs[25].

A growing scientific interest has been seen in the use of infant signs to support speech-language development and caregiver-child interaction in typically developing children and children with developmental delays[24]. A review by Fitzpatrick, et al. [24] revealed that the effectiveness of infant sign training to enhance early communication development or to foster caregiver-child interaction and caregiver responsiveness in typically developing children remains unclear due to a small number of

published studies and their mixed findings. However, no evidence was identified to suggest that training infant signs interferes with typical child development. Based on a randomized-controlled trial, Kirk, et al. [25] found parents in the infant sign training group to be more responsive to their child's non-verbal cues and encouraged more independent action by their infant than those in the (verbal training only) control group. More recent studies also concluded that children's use of infant signs influences qualities of adult-child interaction, eliciting greater responsiveness and richer communication[26-30]. Vallotton, et al. [29] found that the adults' sensitivity to children's attention, interests and needs when using infant signs is crucial to promote children's communicative behaviors.

Early infant sign intervention may also have clinical potential where there is risk of language delay or impairment[25]. Kirk, et al. [25] investigated the impact of infant signing on receptive and expressive language development during longitudinal follow-up of children from 8 to 20 months old. No significant group differences were found between children in the infant sign training group, the verbal training only control group and the no intervention control group. However, boys who had low baseline expressive communication scores and were enrolled in the infant sign training group showed a significant increase of expressive communication compared to boys who were not exposed to infant sign training. The authors concluded that where verbal abilities are weak or impaired, infant sign training may help compensate for language difficulties.

When signs are used to promote or support verbal language in clinical populations, it is also referred to as 'Key Word Signing' (KWS). KWS is an alternative and augmentative communication method that consists of simultaneously supporting speech with manual signs. Such as in using infant signs, only key content words in a sentence are supported by a sign without integrating the grammatical features. Several reviews conclude that the use of multimodal cues (i.e., manual sign and spoken word) facilitate language learning in children with autism spectrum disorder, Down syndrome, developmental delays or physical disabilities[31-33]. However, most included studies had a limited number of participants and yielded primarily single-subject within-group designs.

Children with CP±L rely on non-verbal communicative acts when verbal development is delayed[14]. In the absence of sufficient vocal complexity, children with CP±L may rely more on gestures to communicate until their intelligibility improves. Scherer, et al. [14] suggested to focus early intervention on mapping words to existing non-verbal communicative acts in order to maximize opportunities for practice. Improving children's intelligibility may increase the opportunities for these children to engage in early, frequent and high-quality interactions with their caregivers[13]. Infant signing increases caregiver responsiveness[28] and studies suggest that infant sign use and caregivers' subsequent responsiveness lead to joint-attention opportunities[34]. Hence, training caregivers in their responsiveness to non-verbal communicative acts and increasing their use of expansions and

semantically related contingent utterances could hypothetically benefit speech- language development in children with CP±L.

Given the reciprocity between the child's productions and caregiver responsiveness in speech-language learning, early intervention needs to address both actors in this process. Training infant signing in children with CP±L involving their caregivers meets this requirement. However, no specific research has been done on this topic in children with CP±L. It is hypothesized that infant signs may support the intelligibility of verbal utterances produced by children with CP±L. Improving children's intelligibility may increase the opportunities for these children to engage in early, frequent and high-quality communicative interactions with their caregivers[13] resulting in a richer social and linguistic environment. By supporting the child's strengths (i.e., the use of gestures), more meaningful utterances and successful experiences will be created. Second, caregivers who are trained as co-therapist in infant signing, are more responsive to their child's non-verbal cues[25]. This responsiveness may increase the opportunities to provide more frequent and more complex speech input to their child with CP±L. Moreover, the support of their verbal utterances by infant signs creates a bimodal communication that enriches the communicative input. A study by Adamson, et al. [35] revealed that joint attention between an adult and young child can be more easily established by using multimodal input (i.e., verbal stimulus + gaze and pointing) than by using auditory input (i.e. verbal stimulus) alone. This bimodal communication input may be especially important for those children with CP±L with hearing loss and/or impaired auditory skills. In children with CP±L who are at risk for delayed speech-language development, it is hypothesized that infant sign training increases the speech-language development as a result of the improved caregiver-child interaction.

The primary objective of the current study is to explore if children with CP±L who are enrolled in infant sign training at the age of 12 months have increased receptive and expressive language skills compared to children with CP±L who are enrolled in verbal training or not involved in any intervention at all. The secondary objectives are: (1) To explore if children with CP±L who are enrolled in infant sign training at the age of 12 months have (a) improved speech skills and (b) demonstrate more communicative acts, compared to children with CP±L who are enrolled in verbal training or not involved in any intervention at all; and (2) To explore if caregivers of children with CP±L who are enrolled in infant sign training at the age of 12 months provide more frequent and more complex linguistic input to their child's utterances compared to children with CP±L who are enrolled in verbal training or not involved in any intervention at all.

Methods

This study is approved by the Ethics Committee of the Ghent University Hospital. An informed consent form will be provided to the caregivers. The SLPs who will carry out the assessments will

ensure that the caregivers and participants have understood the information about the study before participation.

Participants

Caregivers from children with CP±L will be invited to participate together with their child via the Ghent University Hospital Craniofacial Center and the Leuven University Hospital Craniofacial Center when their child is 12 months old. This age is chosen because most children have undergone palatal closure at that age and wound healing will be completed. Only children who received palatal closure, have Dutch as mother language and have hearing caregivers will be included. Multilingual children, children with a syndromic cleft, more than mild hearing loss (i.e. > 40dB hearing threshold bilaterally), sensorineural hearing loss, cognitive or motor delay will be excluded.

Sample size. A study by Scherer, et al. [17] included 10 participants per group to explore the effect of early speech intervention in children with CP±L between 15 and 36 months and reached moderate to large effect sizes for all speech-language characteristics (including analyses of PCC-R, true consonants, receptive and expressive language, and complexity of language used by mothers after training). Based on the number of different words used by children with CP±L before and after early speech intervention, a mean difference was reported of 37.2 (SD 33.15 based on SD pre and post and .60 within-subject correlation). 'IBM SPSS SamplePower' was used to calculate the sample size for the current project using an alfa-level of .05 and an estimated power of .80. This resulted in a sample size of at least 8 participants per group to receive a power of 0.78. Taking into account a 25% dropout, the total amount of participants needed in each group will be at least 10.

Design

This trial is a two-center, randomized, parallel-group, longitudinal, controlled trial. Treatment allocation is a 1:1:1: ratio. Children are randomized to either an infant sign training group (IST group), a verbal training group (VT group) or no intervention control group (C group). The aim is to demonstrate superiority of the active intervention (IST group) compared to control (VT group and C group). Baseline assessments will be performed before randomization. Children will be randomly assigned to one of the three groups using a blocked randomization based on age and gender. Children and their caregivers will be followed for 12 months. During this time, a test battery will be completed three times by the child and caregivers, more specifically at T0 (i.e., baseline assessments), T1 (i.e., 5 months after start of the caregiver training), and T2 (i.e., 11 months after start of the caregiver training). Caregivers of children who are assigned to the IST group or VT group will participate in three caregiver training meetings. These meetings will take place 1 month (meeting 1), 2 months (meeting 2) and 3 months (meeting 3) after baseline assessments are performed (T0). Each meeting will take

two hours. Caregivers of children who are assigned to the C group (no intervention) will not participate in any caregiver meeting.

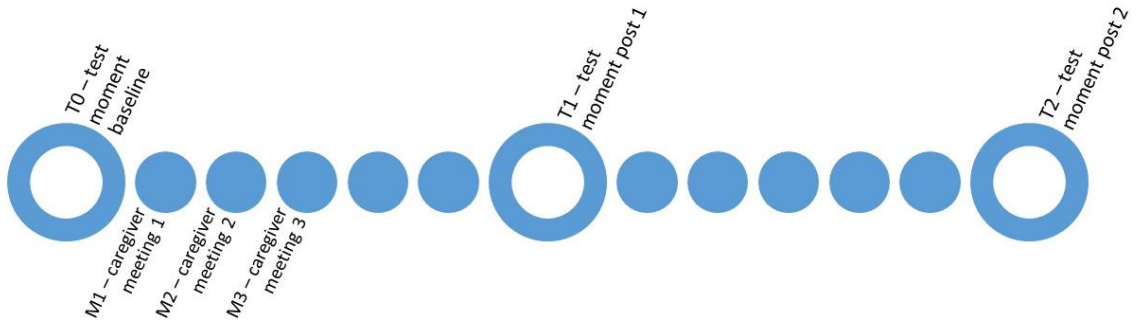

Figure 1 - Study design; M1, M2 and M3 are only applicable for the infant sign training group and the verbal training group

Interventions

Infant Sign Training Group (IST)

The training meetings are based on the caregiver course of Gebarenstem Vlaanderen: 'Baby and child signs for caregivers'[36]. The course is available as a preassembled package for individuals who completed the specialist training of Gebarenstem Vlaanderen and will be adapted to better fit for caregivers of children with CP±L. Training session 1: Information will be given about what infant signs are, how they originated, how speech and (gestural) language develop in young children with CP±L, the possible advantages of using infant signs (i.e., visual-gestural signs) and tips for success. Twelve signs will be chosen to start with: 6 narrative signs (mostly object concepts) and 6 steering signs (mostly non-object concepts) (Table 1). Focus will be on words including oral stop consonants because these sounds are the most difficult to pronounce for children with CP±L. All signs originate from the official Flemish Sign Language and are not adapted. Caregivers will receive a manual with drawings of all learned infant signs and information on how to produce the signs. Training session 2: Experiences (successes and difficulties) with using infant signs at home will be shared, repetition (and correction) of the 12 infant signs and tips for success will be discussed. These tips include: 1) sign before acting; 2) create opportunities to use signs; 3) joint attention: how to create, continue and expand; 4) recognize signs of your child; 5) offer and balance (use of narrative versus steering signs). Another 12 signs will be chosen to add to the repertoire the caregivers can use, based on caregiver input. Training session 3: same as session 2. The content will be based on the input (successes and difficulties) the caregivers experience. Another 12 signs will be chosen to add to the repertoire the caregivers can use, based on caregiver input. Reading aloud while using infant signs will be shown and practiced.

Table 1. First 12 infant signs

Narrative signs	**Steering signs**

poes [pu.s] – ‘cat’	spelen [spe:lən] – ‘playing’
bal [bɑl] – ‘ball’	slapen [sla:pən] – ‘sleeping’
auto [ʌuto:] – ‘car’	eten [e:tən] – ‘eating’
koek [ku.k] – ‘cookie’	gedaan [ɣəda:n] – ‘all done’
boek [bu.k] – ‘book’	kus [kʏs] – ‘kiss’
vogel [vo:ɣəl] – ‘bird’	nog [nɔx] – ‘more’

Words are provided in Dutch together with their transcription and English translation

Verbal Training Group (VT)

The training meetings are based on the caregiver course ‘Language buddies’ to promote speech-language development of young children by training caregivers[37]. Training session 1: Information will be given on how speech and language develop in young children with CP±L and how caregivers can support their child during this development (slow speech, repeating with correct production, focus on oral stop sounds and words that include these sounds). Tips for success and suggestions on how to use these supportive verbal techniques at home will be discussed. Training session 2: Experiences (successes and difficulties) with using supportive verbal techniques at home will be shared and supportive verbal techniques will be repeated. Information will be provided about how children learn new words and tips for success will be expanded. These tips include 1) create opportunities to speak to your child; 2) joint attention: how to create, continue and expand. Training session 3: same as session 2. The content will be based on the input (successes and difficulties) the caregivers experience. Additionally, advances of reading aloud will be discussed and reading aloud will be practiced.

Control Group (C)

Standard clinical care at this moment at the University Hospitals Ghent and Leuven includes providing information to caregivers about speech-language development and encouraging caregivers to communicate with their children. This information will be orally provided by an SLP during a standard clinical appointment at the cleft team at the age of 12 months. A brochure including this information will be provided. Caregivers of children who will be assigned to group C will have the opportunity to receive the most effective intervention (IST or VT) after finishing the study.

Provider

The IST and VT intervention will be provided by an SLP with experience in the diagnosis and treatment of speech-language disorders in children with CP±L. She is officially trained to provide the caregiver courses described above.

Outcome measures

Hearing

Hearing loss may bias intervention outcomes due to distorted speech input. Therefore, a hearing screening based on conditioned orientation reflex audiometry will be performed in every child at T0, T1 and T2 to determine possible hearing loss. More than mild hearing loss (i.e. >40dB hearing threshold bilaterally) and sensorineural hearing loss form exclusion criteria to participate in the study.

Language

To verify receptive and expressive language development, , the Dutch Nonspeech Test[38] will be used at T0 and T1. This standardized test observes, scores and judges communication conditions and first verbal and non-verbal communication in the age range of 12 to 21 months. At T2, the Schlichting Test of Language Comprehension and Language Production[39] will be used. This standardized test measures the receptive and expressive language development starting from 24 months of age. Additionally, caregivers will complete the Dutch version of the MacArthur Communicative Development Inventory[40], 'words and signs' (T0 and T1) or 'words and sentences' (T2). These standardized questionnaires evaluate word comprehension and production, the use of signs by the child, and grammatical development.

Communicative acts

The communicative acts of the child and caregiver will be analyzed based on a video recording of 30 minutes free play with four standardized toy sets (i.e., a farm, a book with pictures of daily objects, cutlery, and vehicles) between the child and caregiver at T0, T1 and T2. Recordings will be made by two static cameras and annotated using ELAN, a free computer software system for multimodal complex annotation of video and audio recorded material[41]. The annotation process will include three steps: the child's communicative acts, the caregiver's contingent responses and a third step where annotations for child and caregiver are controlled following the procedure described by Lieberman, et al. [12]. Each potential communicative act of the child will be annotated by the means of communication (eye contact, gesture or vocalization; vocalization will be identified as non-canonical, canonical or word) following the procedure described by Scherer, et al. [14]. Based on the vocalizations, the percentage of glottal stops, the number of true consonants in the phonetic inventory (i.e., true consonants exclude glide or glottal consonants), and the Percentage Consonants Correct – Revised

(PCC-R)[42] will be determined, following Scherer, et al. [17]. PCC-R is chosen because common (e.g., lateralized production of /s/) and uncommon (e.g., nasal emission on oral consonants) clinical distortions, which are developmentally appropriate for young children, are excluded in this analysis. These parameters provide information about the speech skills of the children. Gestures will be classified as behavior regulation, social interaction, and joint attention following the procedure described by Stewart, et al. [43]. The caregiver contingent responses will be categorized and labelled as acknowledgements, follow-in comments, imitations/expansions or directives following the procedure described by Lieberman, et al.[12]. Based on these annotations, the number and quality of the child's and caregiver's communicative acts will be determined.

All tests and recordings will be performed by two SLPs with experience in the diagnosis and treatment of speech and language disorders in children with CP±L. The annotation, analysis and scoring will be performed by the same SLPs. Both raters will analyze 100% of the video-recordings to calculate inter-rater reliability. To calculate intra-rater reliability, both raters will re-assess 20% of the recordings. The raters will be trained based on previously collected video samples. They first will receive theoretical information about the annotation process and transcriptions. After finishing the analyses of the training videos, they will discuss the results to reach consensus. The raters will not provide intervention to any of the included children and caregivers. They will be blinded for group allocation of the child and caregivers.

Statistical analyses

SPSS version 27 (SPSS Corporation, Chicago, IL) will be used for the statistical analysis of the data. All applicable statistical tests will be 2-sided and will be performed using a 5% significance level. All confidence intervals presented will be 95% and two-sided. The "CONSORT" diagram will be used comprising the number of people screened, eligible, consented, randomized, receiving their allocated treatment, withdrawing/lost to follow-up. The normality of the data will first be assessed using the Kolmogorov-Smirnov test, QQ plots, and histograms. Categorical data will be summarized by numbers and percentages. Continuous data will be summarized by mean, SD and range if data are normal and median, IQR and range if data are skewed. Minimum and maximum values will also be presented for continuous data. Differences between the three groups in terms of age and gender will be assessed using the one-way ANCOVA.

Two-way mixed intraclass single measures correlation coefficients (ICCs) will be calculated to assess inter- and intrarater reliability for the annotation, the analysis of the communicative acts, percentage of glottal stops, phonetic inventory and PCC-R. These ICCs will be interpreted following the classification of Altman [44] (ICC < 0.20: poor, 0.21–0.40: fair, 0.41–0.60: moderate, 0.61–0.80: good, 0.81–1.00: very good).

To compare the mean change from baseline to T1 and from baseline to T2 in continuous outcome measures, generalized linear mixed models (GLMM) will be fitted using the restricted maximum likelihood estimation and a compound symmetry covariance structure. The GLMM will include time, group, a two-way interaction between time and group, and the stratification variables for randomization. To control for type I errors, sequential testing procedures will be applied (group IST vs. group C; group VT vs. group C; group IST vs. group VT). A complete statistical analysis plan will be written before data lock.

Data management

Data will be stored in REDCap, an electronic data capture system [45]. The research will be carried out in accordance with the information security policy of Ghent University. Personal data will be pseudo-anonymized at the level of data collection and anonymized at the level of data analysis. A separate file will be created with the key to the code assigned to each participant. This file will be stored separately from the other databases and will only be accessible to the first and last author or to the appointed replacement. Only anonymized data will be used for analysis and in any type of documentation, reports or publications concerning this study.

Summary and brief discussion

Children with CP±L are known to be at risk for speech-language delays that impact academic and social emotional growth[5,46]. Given the limited scientific prove of the impact of early speech-language intervention, no standardized clinical practice guidelines are available yet for children with CP±L under the age of three years old[15]. Early intervention in this population mostly focusses on improving verbal input via caregivers or professionals without including a multimodal language input.

No evidence is yet available for the effectiveness and feasibility of early intervention based on infant sign training in combination with verbal input to improve speech-language skills in young children with CP±L. To contribute to the evidence-based practice in early speech intervention in children with CP±L, the current project will investigate the effect of infant sign training on the speech-language development in this unique population. Outcome measures will be compared to those of two control groups: verbal training and no intervention. If providing early intervention in the first years of life is effective, there is the potential for improved speech-language outcomes in early childhood, resulting in less need for speech-language therapy on the long-term and a reduced burden of care on children, families and services. Applying a longitudinal randomized controlled trial, including an experimental group and two control groups, is both challenging and unique in this topic and study population. The main challenge of this project will be achieving a sufficiently large sample size. Obtaining large sample sizes is a known issue in speech-language research [47]. A recent systematic

review therefore called for the evaluation of intervention outcomes on an individual level [48]. The authors recommended evaluating the global benefits of speech intervention in children with CP±L, for example, by including outcomes regarding communicative participation in everyday settings. The inclusion of the MacArthur Communicative Development Inventory[40] and the analysis of free play between a child and caregiver meets this recommendation. Another possible limitation will be the amount of home practice as this can bias intervention outcomes. Caregivers need to apply the learned infant signs and techniques at home on a regular basis to create a possible effect on the speech-language development of the children. Three caregiver meetings during three consecutive months will provide the possibility to verify the use of the learned techniques at home and to discuss possible doubts, uncertainties, demotivation but also successes.

In summary, this study meets the need to evaluate the impact of early intervention on speech and language outcomes in children with CP±L as proposed by several researchers based on reviews regarding this topic[15,49,50]. It will contribute to the development of evidence-based clinical practice guidelines regarding early speech-language intervention in children with CP±L under the age of three years.

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