



Feasibility of CareToy Early Intervention in infants with Down Syndrome

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Background. CareToy (CT) System has been recently developed and validated in preterm infants with positive effects at short-term both on visual and motor development.

Objective. We aimed to assess the feasibility of CT training in infants with Down Syndrome (DS) and to evaluate the effects of the CT training in promoting their neurodevelopment.

Methods. 10 infants with DS aged 6.16 ± 1.54 months were recruited and allocated in two groups: CareToy (CT) or Standard Care (SC). 5 infants of the CT group performed CT Intervention in the clinical setting for 5 weeks; other 5 infants were followed as SC for the same period. Data about the feasibility of the intervention were collected. Moreover, all recruited infants performed motor and visual assessment at baseline (T0) and in the week after the CT or SC periods (T1; 5 weeks after T0).

Results. All infants allocated in the CT group performed the CT training with good compliance. In all outcome measures the mean delta changes (T1-T0) showed promising positive effects of the training in the CT group, compared to SC.

Conclusions. CT demonstrated its feasibility for providing EI also in infants with DS and its effects seems promising. However, further large RCT studies are needed.

Keywords : Down syndrome; Early Intervention; CareToy intervention, Feasibility, Information and Communication Technologies, Medical device.

I. INTRODUCTION

Down Syndrome (DS) is characterized by abnormalities on chromosome 21, usually related to an additional chromosome

(trisomy 21). The DS is the most common genetic cause for the presence of intellectual disability with an incidence of more than 1 in 1000 new births in the world [1]. The over-expression of the chromosome 21 results in a delay of myelination, a dysregulation of cell cycles and neurotransmission anomalies. The syndrome is characterized by an alteration in developmental process involving motor, language, cognitive, self-care and personal-social dimensions [2]-[5]. Regarding motor development, infants with DS, compared to typical developing infants, acquire motor skills later in the age, mainly due to hypotonia and ligamentous laxity and poor balance [6]-[7]; these conditions in general lead to a reduction in the exploration of the environment, crucial experience to promote the development of language, cognition and socialization [8].

EI programs for infants at risk of neurodevelopmental disabilities (NDDs) are usually focused on stimulation of developmental skills (motor, cognitive, language and/or social), as well as on facilitating parent-child interactions with some positive effects on development. The program of EI are mainly based on the concept of environmental enrichment (EE), which is a promising and non-invasive strategy to enhance brain plasticity in infants at risk for developing neurodevelopmental disorders [9].

The effects in relation to the EI programs have been broadly assessed in preterm infants while, at our knowledge, there are only few studies on infants with DS albeit, the effects on their developmental skills are of great interest to researchers. In this framework, CareToy (CT) system, recently developed and validated as a tool for providing, in infants born preterm, EI telerehabilitation, has shown positive effects at short-term both on motor and visual development [10]-[13] and also on reducing the parental stress [14]. We hypothesized that the CT intervention, with some adaptation, could provide a tailored, intensive and incremental challenging family-centered EI also for infants with DS.

The aim of this pilot study was to assess, in the clinical setting, the feasibility and acceptability of CT intervention in a group of infants with DS. In particular we aimed to evaluate the feasibility of CT for the three main end-users i.e. i) for the infants, in terms of compliance and suitability to the CareToy activities (i.e type of activities, duration of the daily training), ii) for parents, in terms of system management and iii) for the rehabilitation staff for the customization of the CT training in infants with DS. An exploratory and secondary goal of the study was to evaluate the effects, in relation to the promotion of both motor and visual development in infants with DS. of the CT Intervention compared to performing standard care.

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II. METHODS

A. Participants

In this pilot study, the participation was proposed from January 2016 to August 2016, to families of eligible infants already longitudinally followed by the clinical staff of IRCCS Fondazione Stella Maris (Calambrone, Pisa; Italy).

The Inclusion criteria were the following: 1) confirmed genetic diagnosis of DS, 2) age at recruitment between 3 and 9 months and iii) gross motor ability ranging from an initial head control to a partial trunk control.

The exclusion criteria were: 1) severe sensory deficits (blindness or deafness); ii) progressive neurological disorder and iii) severe non neurological malformation or other medical conditions (e.g. percutaneous endoscopic gastrostomy or bowel derivation, recent cardiac surgery).

Specific study information were provided to the families explaining that the allocation to CT or SC group was open and based on their availability to come to the clinical center: either at least 3 times per week for 5 weeks to be allocated in the CT group; or only 2 times, at distance of 5 weeks, to be allocated in the SC group. The infants were enrolled, only after obtaining the parental written consent. Clinical data (demographic, medical and developmental data) were collected at the time of enrolment. At the beginning of the study (baseline, T0) and after 5 weeks (T1), all infants were assessed with standardized clinical tools by clinicians and therapists, blind to group allocation. Moreover, all the clinical outcomes were videotaped by a therapist blind to group assignment. Videotapes were then randomised and scored by assessors blind to group allocation and order of assessments. The study was approved by Pediatric Ethics Committee of the Tuscan Region.

B. CareToy system

The CareToy System (Fig 1), as described in Cecchi et al. [10], is a biomechatronic gym that, thanks to a tele-rehabilitation architecture, is used at home with remote monitoring by the rehabilitation staff. Briefly, it is inspired to common gyms for infants and it is composed by: i) sensorized toys with various features and affordances for promoting various grasping abilities, ii) two walls embedded with lights, buttons and speakers, iii) a large monitor (screen wall), iv) a wall for the sitting position, equipped with a sensorized pillow, v), four cameras, vi) an arch equipped with lights vii) a mat with sensors and viii) 3 wearable sensors, 2 used for the upper limb as bracelets and one in the trunk as chest strap. The combined activation of the modules and the feedbacks setting allow to provide a customized home-based and family-centered EI. In fact, during the CT activities, the infant, while playing actively at home with his parents, inside the system is promoted to increase his trunk control, manual abilities (as reaching and grasping) and visual function.

The CareToy is connected to a laptop which receives and sends data from/to the clinical center (tele-rehabilitation module) and parents have a user manual (both printed and inside the software) for the management of the training. Sensors embedded in the system are able to acquire and process data about infant's behavior while playing [15]-[16]. A post processing elaboration creates an organized and readable report about infant's behavior for the clinical staff.

Even if the CT system is designed to be used at home, in

this pilot study the system was installed and used in clinical environment. However, it was mainly managed by the parents under the supervision of a child therapist.



Figure 1: The CareToy (CT) system with the examples of some modules and activities. Upper left: the sensorized Ring toy for the manipulation of toys while supine. Upper right: the sensorized mat for the prone position. Lower left: the belt for the video observation. Lower right: the sensorized U-Toy for the manipulation of toys while sitting.

C. CareToy intervention

Clinical staff created a wide library of tailored and multi-axial goal-directed activities, called scenarios, projected on the basis of the most common developmental needs of infants and highly customizable not only in terms of CT active modules (e.g. one toy on a wall, two toys on the arch, the screen etc.) but also for other little features, as activity length, volume regulation, lights colors, type of videos and pictures presented on the screen.

CareToy training consists in a set of scenarios, selected by the rehabilitation staff in relation to particular infant's needs and capabilities. The length of each scenario is from 2 to 10 minutes and it has a main goal and several sub-goals. CareToy training could promote many motor abilities such as visual fixation and gaze movements, postural control, rolling, pivoting, manual function as reaching, grasping and eye-hand coordination. The training can be designed with a high amount of increasing complexity and variability.

The management of CareToy intervention followed in general the guidelines described in [12]. According to them, first training days were planned on the basis of baseline assessment. The training was proposed for 5 weeks, at least 3 times per week, for 30-45 minutes of activity each day and it was mainly managed by parents. A child therapist was present during the whole CT training and her role was to observe and monitor infants' behavior, parents' ability in interacting with infants and in using the system providing only minimum facilities to families (e.g. cleaning, turn on-off the system) and ensure the right system functioning.

In the planning of the training, a minimum amount of executed training, for considering the intervention intensive, has been established and it was defined as at least 15 days of training in which infant performed a minimum of 20 minutes of training each day.

D. Standard Care

Standard Care consisted in follow-up visits, i.e. a monthly visit in which multidisciplinary staff of IRCCS Fondazione Stella Maris provided personalized advices to support parents and to promote play activities and infant's neurodevelopment.

If the infant underwent to specific interventions (i.e. physical therapy), the number of sessions per week was registered through a diary.

E. Outcome measures - Feasibility measures

CT training data and Scenario feasibility

Data of CT intervention in terms of differences between planned and executed days, minutes of training per day and the total training were computed to assess the general feasibility of CT training. In addition, caregivers were asked to complete the CT questionnaire that investigated the infant's participation (excellent: > 75%; good: 50-75%; sufficient: 25-50%; insufficient: < 25%) and his/her mood (angry – neutral - happy), to record the feasibility and acceptability of each scenario.

Parents' point of view about usability and acceptability of CT training

A semi-structured interview, using the CareToy Questionnaire Parent-infant Experience (CQPE) [17]; has been carried out with parents of children allocated to the CT group. The CQPE questionnaire is composed by 68 questions grouped into 9 macro-categories, aimed to explore different domains: 1) Parent's expectations regarding the CT training; 2) Parent's opinion on infant's skill before the training 3) General opinions about the CareToy System, 4) Management of the system, 5) Time spent in the training, 6) Parent's opinion about changes on infant's skills after the training, 7) Parent' s participation during the activities, 8) Infant' s participation during the activities and 9) Parent-infant interactions and home environment after training with CareToy. As recommended when using ICT devices [18], end users' opinion need to be considered and for this purpose the CQPE has been used.

F. Outcome measures - Motor assessment

According to previous studies [12-13], the Infant Motor Profile (IMP) has been chosen as primary outcome measure. IMP is a qualitative tool that is based on the scoring of videorecording for the evaluation of the quality of motor performance and motor behavior in infants with an age range from 3 to18 months. It is composed of 80 items, that are based on the evaluation of the child's motor abilities and behavior [19]-[21]. In addition, it has been also used the Alberta Infant Motor Scale (AIMS). AIMS is a widely used standardized scale aimed to assess infants with an age range from at term to18 months, which allows to identify motor delays and/or abnormal motor development [22]. Both scales were performed at T0 and T1.

G. Outcome measures - Visual assessment

For evaluating the visual acuity, Teller Acuity Cards were used. They are a behavioral validated test for infant and children, based on forced-choice preferential looking and used for the evaluation of infant's looking behaviour. The subject has to look a set of grey cards with different grating targets, differentiated for distinct spatial frequencies. The examiner observes movements of the subject's eye, judging whether the infant can or cannot orient his gaze to the target on each card of the set. The level of acuity is the highest spatial frequency that the infant is able to see [23],[24]. In the present study the visual assessment was performed at T0 and T1.

H. Data analysis

For each infant allocated in the CT group, total days of training, mean of planned and executed training (in minutes for each day and in hours for the total amount of training) were calculated. In addition, a percentage ratio between the total of executed and of the planned CareToy training was calculated, with the aim of evaluating the compliance to the CareToy intervention.

Mean and standard deviation (SD) of the main infant characteristics and the results of the outcome measures at baseline for both groups were computed. Mean delta changes between T0 (baseline) and T1 (soon after the CT intervention) were calculated for all the outcome measures. Potential trends due to intervention were qualitatively discussed in the results section. In relation to the small sample and to the exclusively exploratory aim of the study, statistical analysis was not carried out.

III. RESULTS

A. Feasibility results - Study sample and characteristics

As shown in the figure 1, 13 infants with DS were evaluated for eligibility. Two infants were excluded because they didn't meet inclusion criteria (gastro-intestinal and cardiac malformation with severe medical complications) and one family declined to participate. Ten infants were recruited between December 2015 and May 2016.

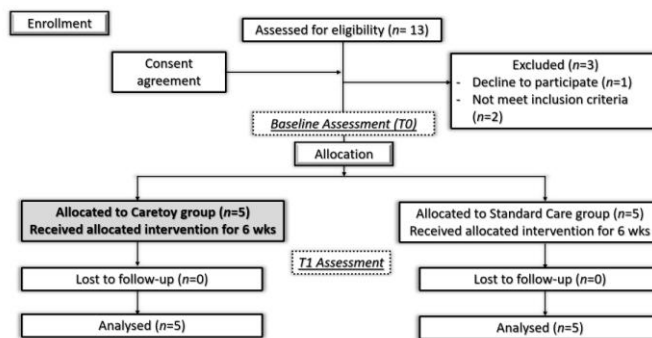


Figure 2: Flow chart of the study

All infants whose families requested to be allocated in the CT groups lived near the IRCCS Fondazione Stella Maris, with exception of one family (infant #3) who lived far.

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Five infants (age range: 4.15–9.5 months, mean age 6.64 ± 1.99 months) were allocated to CareToy group and 5 (age range 4–7.5 months, mean age 5.6 ± 1.43 months) to Standard Care group (Table 1). The baseline participant's features are reported in Table 1. In CT group none of the infants received additional special rehabilitation sessions; while in SC Group one infant received physical therapy sessions (two times per week).

Table 1: Baseline (T0) main features of the two groups (CareToy and Standard Care).

Characteristics	CareToy group (n=5)	Standard Care group (n=5)
Gender M/F	1/4	4/1
ASQ-3 Gross Motor Area (median)		
Form 4	n= 2/5	n= 4/5
Form 6	n= 3/5	n= 1/5
Age at T0	6.64 (1.99)	5.6 (1.43)
Infant Motor Profile, mean (SD)		
Total	69.32 (6.02)	66.76 (1.98)
Performance	48.83 (10.2)	45.92 (5.93)
Variation	62.31 (4.48)	59.50 (0.25)
Fluency	73.33 (3.72)	75.00 (0.00)
Symmetry	96.19 (8.51)	90.95 (6.10)
AIMS Total, mean (SD)	12.60 (4.72)	10.2 (3.11)
Prone	4.40 (2.07)	3.80 (1.48)
Supine	4.60 (1.94)	4.00 (1.41)
Sit	2.60 (2.5)	1.40 (.89)
Standing	1	1
Teller Acuity Card (cy/degree), mean (SD)	5.82 (2.72)	4.76 (1.58)

Abbreviations M : male, F : female, n : number; SD : standard deviation, AIMS: Alberta Infant Motor Scales. ASQ-3 : Ages & Stages Questionnaires

B. Feasibility results - CT Training data

The 5 infants allocated in CT group performed CT intervention for 5 weeks (daily planned mean in minute: 39.2 ± 4.02). 4/5 infants overcame the minimum of the 15 training days, while one of infants (#3) performed only 9 days (Table 2). The time of executed training per day ranged from 25 to 39 minutes and the total time of the training ranged from 5.16 to 17.54. The ratio between planned and executed training ranged from 66.31 to 99.62 %.

Table 2: Mean duration (± SD) of the CareToy training in days; mean daily planned and executed training in minutes, total executed training in hours and the ratio between the total of the executed and the planned training in percentage.

User	Training days (n ^o)	Mean planned per day (min)	Mean of executed per day (min)	Total executed (hrs)	Ratio (%) planned/ executed training
#1	23	40	27	10,23	66,31
#2	21	39	30	10,32	74,85
#3	9	45	34	5,16	47,76
#4	27	39	39	17,54	99,62

#5	18	33	25	7,06	76,67
mea	19,4 ± 6,84	39,2 ± 4,02	31 ± 5,61	10,06 ± 4,71	73,04 ± 18,75
n ± SD					

Abbreviations: SD: standard deviation, N: number, min: minutes; h: hours

C. Feasibility results - CT scenarios feasibility

Based on the answers of scenario's short-questionnaires it emerged that, in total, infants had an excellent (more than 75%) participation for the 30% of executed scenarios; a good participation (between 50–75%) for the 65% of scenarios and a sufficient one (25–50%) only in the 5% of executed scenarios. Moreover, a mean of 90% of scenarios were carried out with good grade of system acceptance and playing activity (happy mood of infant), 9% were carried out with a medium grade of acceptance (neutral mood infant) and just 1% of executed scenarios were not enjoyed by the infants (angry mood during activity).

D. Feasibility results - CareToy Questionnaire Parent-infant Experience (CQPE)

Four of the 5 families involved in the CT training accepted to be interviewed. Their expectations (Domain 1) were that the CT training could mainly improve the psychomotor development of their infant. In addition, all of them judged CareToy experience as positive (Domain 3), mainly because the CT intervention allowed to improve the attention, gross motor skills (i.e. rolling) and manual abilities (i.e. grasping) of their infants (Domain 2 and 6). The system management (Domain 4) was evaluated as "rather simple". Training activities were evaluated as "enough personalized" (1/4) for infants' needs or "well personalized" (3/4). The infant's participation (Domain 8) was deemed, by all parents, as generally good by saying that (4/4) "the child was quiet for most of the time" and "he/she was interested to most activities".

The reported more appreciated activities were those mainly involving the use of screen or toys (especially when they were hanged on the arch); on the contrary, less interesting scenarios were those involving lights (on the walls or on the arch). Concerning parents participation (Domain 7) during the training, CQPE data indicated that all parents felt free to interact and participate during play activities of the CT training. Finally, (Domain 9) parents stated that after training they changed the way they play with their infant "in large part" (3/4) or "completely" (1/4).

E. Clinical results - Motor outcome measure

Delta changes (T1-T0, mean ± SD) of IMP Total score were higher in CT group (3.05 ± 4.52) than in SC group (2.13 ± 1.62; Table 3). Moreover, in IMP Performance domain after the intervention period a higher delta change difference was found between the two groups (CT vs SC; 7.16 ± 5.35 vs 3.90 ± 4.77). After the intervention period a difference was found also in the AIMS Total: CT group (4.40 ± 3.78) reached higher values of delta changes compared to SC group (2.6 1.51; Table 3).

F. Clinical results - Visual outcome measure

After the intervention period, delta changes (T1-T0, mean ± SD) in the visual acuity increased more in CT group compared to SC (1.50 ± 1.62 vs 0.80 ± 1.39; Table 3).

Table 3: Mean of delta changes (T1-T0) of the two groups.

Characteristic	CareToy group (n=5)	Standard Care group (n=5)
Infant Motor Profile, mean (SD)		
Total	3.05 (4.52)	2.13 (1.62)
Performance	7.16 (5.35)	3.90 (4.77)
Variation	2.68 (5.77)	1.93 (2.28)
Fluency	0.00 (0.00)	0.00 (0.00)
Symmetry	0.00 (0.00)	2.48 (5.95)
AIMS Total, mean (SD)		
Prone	1.60 (1.34)	0.80 (0.84)
Supine	0.80 (0.84)	1.60 (1.34)
Sitting	1.60 (2.5)	0 (0)
Standing	0.40 (3.78)	0.20 (0.45)
Teller Acuity Card (cy/degree), mean (SD)	1.50 (1.62)	0.80 (1.39)

Abbreviations: M: male, F: female, n: number, SD: standard deviation, ASQ-3: Ages & Stages Questionnaires, AIMS: Alberta Infant Motor Scales.

IV. DISCUSSION

This is the first study providing an EI program in children with DS using an ICT system, as the CT. This trial was mainly devoted to test the feasibility and the acceptability of CT training and secondarily to explore the changes in motor and visual development compared to standard care.

A. Feasibility and acceptability of CareToy in Down Syndrome

The CT system, firstly validated in a large sample of children born preterm, has been designed and developed to have a high modularity and wide variability of the possible scenarios, allowing to plan, for each infant, a tailored and multi-axial training.

Thanks to the modularity of CareToy scenario library and to the possibility to customize also minor features of scenarios, some modifications of activities were made at the beginning of the study and also during the experimental trial, in order to adapt CareToy intervention also to infants with DS taking into account their specific developmental needs. In general, scenarios already present in the library of CT system demonstrated to be suitable and useful also for the training of infants with DS.

In some occasions, scenarios were slightly adapted to the new population. In fact, the global duration of the daily training was maintained, but the single scenario duration demonstrated to need a change (increasing of the length). It is known that infants with DS often present cognitive delay and their time of response to stimuli or their initiative could be delayed, for this reason scenario's length has been increased, in order to give them more time for perceive the visual and/or audio stimuli and orientate to it, or to organize the motor activity. In addition, as in the previous project, scenarios duration has been calibrated to each single infant. An interesting data about the DS infant training regarded also the variability of the proposed activities: they were interested for

much time in the same scenario and demonstrated to appreciate and need more repetitions of the same scenario, showing during the repetition a higher attention to stimuli and a better organization of their motor activity.

Moreover, another characteristic of infants with DS is their global hypotonia, that could influence the postural development; based on this issue, feedback events have been set at lower values, which means that the requested pressure for activating the response was lower than the one planned for the population of preterm infants. Thanks to these small adjustments of scenarios, the training was suitable for DS infants' needs and this permitted to guarantee a high quantity of daily training in this new population of infants.

Finally, after the first sessions, the intervention of the therapist was never required by the parents, meaning that the training was feasible also in relation to the management by parents. Concerning the amount of training executed by the sample of DS infant, four of them overcame the minimum number of training days fixed in this study; only infant #3 performed only 9 days of training and in total less than 50% of the training, but this data could be related to high morbidity of the infant (frequent fever). However, to reach the cut off, families spent a much time and energy to do the intervention and this finding points out the advantage of providing home-based intervention, especially in the early age of development, increasing the time of intervention and thus the intensity. Data obtained from CT questionnaire, filled in by parents immediately after each CT scenario, reported encouraging data about the compliance of infants, because the majority of scenarios were played and enjoyed by the infants and were participated for more than 50% of the duration. CQPE data also highlighted that all parents considered CareToy experience as positive, commenting the scenarios activities as "well personalized" or "enough personalized". All these data support that also in infants with DS there is a good acceptability and the feasibility of CareToy training.

B. Effects of CareToy Intervention

All recruited infants carried out all the planned assessments and interventions on the basis of their allocation. Regarding the characteristics of sample, the baseline (T0) data were in general slightly different between the two groups (CareToy and Standard Care), mainly due to high variability confirmed by the wide clinical pictures of the DS (Table 1). In all outcome measures, the mean delta changes (T1-T0) showed promising results highlighting positive effects in CareToy group compared to those of Standard Care group, resulting in higher changes in CT group. Moreover, results could be, in part, limited by the used motor measures. In fact the IMP, used as a primary outcome measure and chosen to follow the same approach of previous studies, is not already a validated tool to assess motor development in infants with DS. On the contrary, AIMS has been validated also in DS, but differently to the IMP, it measures mainly gross-motor development and it could not be able to evaluate changes in short period.

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In general, the small size of the sample and the variety of SD determined a wide variation in the results, which appeared promising but not conclusive and need further confirmation with a more extensive sample and a higher quality study.

V. LIMITATIONS

This study has some limitations. In particular, the sample was small and infants' allocation was not randomized but related to the possibility of the family to attend the trial and the follow-up at the clinical center. A home-based intervention and tele-rehabilitation approach, that is well applicable with CT technology, can overcome this issue enlarging the access of infants to EI programs. Moreover, outcome measures need to be adjusted for this population and follow-up evaluations should be added to evaluate medium and long-term effects. These data were out of our principal aim and there will be overcome in the future study with CareToy in infants with DS.

VI. CONCLUSIONS

This preliminary study confirmed feasibility and suitability of CareToy intervention also in infants with Down Syndrome. Results appear promising but need to be confirmed by more extensive studies. The use of new evidence-based technologies for providing home rehabilitation in the context of early intervention, not only in infants at risk for developing cerebral palsy, but also in genetic disorders could open new frontiers in the care of these groups of infants and their families.

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