DynaCleft® Effects on Soft Tissues and on Quality of Life for Incomplete Unilateral Cleft Lip Infants

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Protocol Title:	DynaCleft® Effects on Soft Tissues and on Quality of Life for Incomplete Unilateral Cleft Lip Infants
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Population:	Prospective study of 10 infants with non-syndromic unilateral incomplete cleft lip; retrospective chart review of infants with non-syndromic unilateral incomplete cleft lip without any presurgical interventions
Number of Sites:	University of Texas Health Science Center at Houston (UTHealth) Advanced Education in Pediatric Dentistry and UTHealth Texas Cleft-Craniofacial Clinic
Study Duration:	Two Years
Subject Duration:	Prospective study – four months

General Information

- This prospective study will investigate soft tissue changes of the DynaCleft® + Nasal Elevator system (CranioRehab, Denver, CO) on infants with non-syndromic incomplete unilateral cleft lip. The retrospective aspect of the study will examine records of infants who had or will have surgery without presurgical interventions and will provide as the control group. A comparison will be performed to analyze the effectiveness of DynaCleft® on soft tissues and on the quality of life for these infants and that of their families. Factors such as general physical appearances, overall development, behavioral differences, feeding improvements, and social functions will be evaluated. The study aims to use these collected data to establish the effectiveness of DynaCleft® for orofacial clefts at a university-based postdoctoral pediatric dentistry clinic.

Background Information

- Cleft lip and palate is globally the most common form of congenital craniofacial anomalies[1]. It is generally reported to affect approximately 1 in 700 live births[2] and may be isolated or associated with a syndrome. Children born with clefts are faced with many complicated issues that need to be addressed to ensure successful rehabilitation. A combination of factors such as functional, psychological, and sociological issues make this a challenging condition overall to manage. It has also been reported that this anomaly decreases the quality of life of the infant and that of their families due to the long road of costly operations and life adjustments[1].

- Even a mild incomplete cleft lip without involvement of the palate can produce significant nasal deformities. These deformities include separated lip segments, widen nostril base, flattened nasal tip, flared alar rim, rotated premaxilla, deviated and deficient columella[3].
- Due to the complexity of this craniofacial birth defect, it has been found that early interventions prior to surgery may achieve improved esthetic and functional outcomes. Nasal, lip, and maxillary tissue can be expanded and malpositioned structures can be guided into a more anatomical position with presurgical orthopedics. This may allow for less invasive surgeries by minimizing the deformities[4]. This movement is facilitated by circulating maternal estrogens that are present in the first month or two of life. Presurgical cleft orthodontics take advantage of these estrogens as they increase hyaluronic acid in the tissue, causing greater pliability and plasticity, in the infant cartilage for recontouring[3]. Cheiloplasty usually occurs within the first few months of life at approximately 3-6 months of age depending on severity of the cleft lip. Palatal cleft surgical repair is often recommended later on between the 9-18 months of life.
- Throughout the past decades, many methods have been formulated to address orofacial clefts nonsurgically. DynaCleft® was introduced and approved by the Federal Drug Administration recently in 2013[4]. The kit consists of premade approximation tape with an elastomeric core that has been successfully used to bridge cleft segments and mold the upper lip. Tension from the band distributes passively over the cleft lip tissue and provides gentle guidance. A nasal stent is suspended from the forehead by an adhesive to support and reshape the developing affected nasal tissues prior to surgical repair. Parents are then instructed to continue replacing the tape with take home instructions up to the date of surgery[5].
- When compared with the widely accepted nasoalveolar molding technique (NAM) developed by Grayson in 1993[4], DynaCleft® showed equivocal results in bridging cleft lip segments closer in proximity, reducing palatal cleft width distance, decreasing nostril width while increasing its height, and improving the columellar angle[5] in infants with complete cleft lip and palate.
- Though studies have shown an overall efficacy of the DynaCleft® therapy, more research is necessary to establish the potential of this modality and to enhance its acceptance as a presurgical orthopedic molding alternative for infants with clefts[4, 6]. No studies have yet examined the effectiveness of DynaCleft® to treat patients with incomplete cleft lip, who due to the reduced severity of defect, do not receive presurgical infant orthopedic appliance therapy.

Objectives

- The primary objective of this study is to examine the effectiveness of the DynaCleft® system on soft tissues of infants with unilateral incomplete cleft lip.
- The secondary objective of this study is to assess influences on quality of life for infants who underwent DynaCleft® and that of their families.

Purpose

- Evaluate soft tissue changes of the oral and nasal regions in infants born with incomplete unilateral cleft lip from the initial time of examination with a craniofacial team to the time of

cheiloplasty and to determine if the DynaCleft® + Nasal Elevator system (CranioRehab, Denver, CO) changes presurgical positioning of craniofacial soft tissues.

- Analyze the effect on quality of life for families that complete the prospective DynaCleft® study.

Outcome Measures (Endpoints) and Time Points

Primary Outcome Measures:

- Soft tissue changes as indicated by columellar angle measured from extraoral clinical photographs
  - Time points: initial time of examination with study team, time of surgery ○ Soft tissue changes as indicated by nostril width measured from extraoral clinical photographs
  - Time points: initial time of examination with study team, time of surgery ○ Soft tissue changes as indicated by nostril height measured from extraoral clinical photographs
  - Time points: initial time of examination with study team, time of surgery ○ Soft tissue changes as indicated by width of the cleft lip measured from extraoral clinical photographs
  - Time points: initial time of examination with study team, time of surgery

Secondary Outcome Measures:

- Quality of life assessment utilizing an Infant and New Parent Quality of Life questionnaire
  - Time points: initial time of examination with study team, time of surgery

Study Design

Newborns with incomplete cleft lip and parents that consent to presurgical intervention of DynaCleft® + Nasal Elevator system will be compared to a retrospective group of infants born with incomplete cleft lip treated by the UTHealth Texas Cleft-Craniofacial Team that have received surgical intervention and have existing presurgical photographs available for examination. The primary outcome will be to compare craniofacial soft tissue changes measured from extraoral clinical photographs obtained at the initial examination to the ones obtained prior to surgery. The child's guardian who completed the DynaCleft® therapy will also be asked to complete an infant quality of life assessment survey.

Retrospective:

- The control group for this study will be obtained from a retrospective chart review of electronic health records of patients with incomplete cleft lip who underwent surgery without any presurgical interventions. These records will be obtained from the Texas Cleft-Craniofacial Team. Only records of infants with non-syndromic unilateral incomplete cleft lip will be qualified for this study. To eliminate variability, only patients treated by one pediatric plastic surgeon (Matthew Greives, MD) will be included. All patients with complete cleft lip, or diagnosed with a syndrome, or had any surgeries not provided by the same plastic surgeon (prior to the initial cheiloplasty) will be excluded. Any records with incomplete data or necessary photographs will also be excluded.

- Necessary photographs are to include those taken at the initial visit soon after birth and those at the visit immediately prior to lip surgery. Photographs need to include those taken in the standard anterior-posterior view, profile view, and worms-eye view.
- Linear measurements will be obtained with a ruler and registered in millimeters. A goniometer will be used to measure angles.

Prospective:

- The study population for the prospective aspect will include recruited newborns with untreated unilateral incomplete cleft lip. Patients whose clefts are associated with a syndrome will be excluded. DynaCleft® + Nasal Elevator therapy will be discussed with parent(s) as a presurgical orthopedic option while awaiting primary cleft lip surgical repair that typically occurs between the ages of 3 to 6 months. Informed consent for participation in the study must be obtained from the patients' parents.
- Study duration will be up to three months of presurgical intervention (similar to the existing nasoalveolar molding NAM appliance protocols).
- Patients will be recruited by the Texas Cleft-Craniofacial team. ○ Infants that match the inclusion criteria will be invited to participate in this study.
- Photographs are to be taken at initial visit prior to presurgical intervention and later at completion of the DynaCleft® therapy immediately prior to lip surgery. Angles to be pictured are to include the standard anterior-posterior, profile, and worms-eye view.
- Linear measurements will be obtained with a ruler and registered in millimeters. A goniometer will be used to measure angles.
- The parents of infants enrolled in the DynaCleft® study will be asked to complete an Infant and New Parent Quality of Life survey at the initial and final visits. Components from this survey were adopted from the Infant and Toddler Quality of Life Questionnaire and the CDC Breastfeeding and Infant Practices Questionnaire (see attachments).

Study Population

Previous studies have examined similar number of patients and identified significant findings on presurgical infant orthopedic appliances[4, 5, 7]. To reduce the variability in this study, patient inclusion and exclusion criteria are strict.

Retrospective:

- The Texas Cleft-Craniofacial Team photo database will be queried for patients with incomplete unilateral cleft lip who have undergone cleft lip repair from 2015-2020.
    - Inclusion criteria
        - Unilateral cleft lip with or without cleft palate
        - Patients of a single surgeon (Matthew Greives, MD)
        - Patients with complete photographs: After birth, first visit

- At cleft lip repair (3-4 months)
- Post-operative cleft repair (about 1 year of age)
    - Exclusion criteria
        - Bilateral cleft lip or complete unilateral cleft lip
        - Patients operated on by other primary surgeons

- Patients with incomplete photo records will be evaluated to determine if the patient should be excluded

Prospective:

- Patients will be approached at their first visit to the Texas Cleft-Craniofacial Team starting in 2020.
    - Inclusion Criteria:
        - Patients with incomplete unilateral cleft lip with or without cleft palate
        - Patients of any surgeon ○ Exclusion Criteria:
        - Patients with bilateral cleft lip or complete unilateral cleft lip
        - Patients whose parents refuse to consent to inclusion
        - Patients with tape allergies to the adhesive of the DynaCleft®
        - Patients with syndromic craniofacial conditions or Tessier type facial clefts

Study Procedures

Retrospective:

- Electronic health records of infants with unilateral incomplete cleft lip and/or palate who underwent or is undergoing surgery within the University of Texas Health Science Center will be reviewed. Patients whose clefts are associated with a syndrome will be excluded along with those that have had any other presurgical interventions. Qualifying participants must have had surgical repair after January 2015 or will have surgery before January 2021. Charts with incomplete patient data, inaccessible contact of caregiver, inadequate records or both pre- and post-op photographs in the necessary angles will be excluded.

Prospective:

- One evaluator will obtain all photographs to be evaluated in this study, examine Electronic Health Records, and collect necessary data and measurements onto a password protected Microsoft Excel Spreadsheet. Measurements to be recorded may include columellar angles, nostril width, nostril height, width of the lip cleft, etc. While most of the information can be gathered directly from the photographs, some factors may require calculations such as soft tissue ratios if need be. The primary investigator will be blinded to whether or not subject has participated in the DynaCleft® study. Data are to be measured twice and results compared to account for accuracy. Participants are identified on the spreadsheet solely by an assigned code. Factors to be recorded will also include general biographical and physical information (age, gender, weight, etc.), duration of treatment and compliance of caregivers. ○ Interaction with

participants in the DynaCleft® study will involve one monthly visit up until date of surgery, usually between 3 to 6 months of age. Each appointment is estimated to be

an hour long to allow for assessment of the orthopedic, recording of information, and addressment of any concerns. The initial and last visits may require more time due to obtainment of necessary photographs. Participants will be required to receive DynaCleft® treatment for at least 2 months before lip surgery to qualify. Additionally, parents of infants with incomplete unilateral cleft lip that choose not to use the DynaCleft® + Nasal Elevator system but are willing to complete the infant quality of life assessment at time of surgery will be allowed to complete the survey. All images obtained in this study will be stored in a password protected and encrypted computer. Prospective patient images will be stored in the Electronic Health Record. Images will be de-identified.

- Parents will be asked to complete the Infant and New Parent Quality of Life questionnaire at both the initial visit and date of surgery.

Data and Safety Monitoring

- There are no adverse events expected as there is no direct risk involved with the participants. All patient information will be unidentifiable and stored in password protected devices.
- The DynaCleft® + Nasal Elevator system is an FDA approved medical device. Adverse events can include skin irritation from the adhesive tape. In the event of skin irritation, parents will be offered suggestions to limit irritation (including use of duoderm as a barrier between the skin and tape) or will be allowed to terminate their participation in the study.
- Unanticipated problems will be reported to the Center for the Protection of Human Subjects.
- Periodic assessment of research progression and data collection will be reviewed within the pediatric dental department through presentations and research committee meetings. Any deviations from protocol will be addressed with the research committee and appropriate authorities as necessary.

Statistics

- Each individual patient will be monitored for changes during either participation in the experimental group or control group. A paired Student's t-test will be used to compare changes within the individual patient.
- Comparisons between the experimental and control group will be made with an appropriate statistical test depending on the distribution of data points (parametric or non-parametric).
- Up to 20 patients will be approached for recruitment for the prospective portion of this study. After the 10th patient is enrolled in the study, no other patients will be approached.
- We plan to enroll 10 subjects. This sample size collection was determined as an appropriate amount for a pilot study to test the effectiveness of this treatment. Similar studies using DynaCleft® have utilized similar sample sizes. Additionally, this number was based on the number of potential patients we can enroll within a twelve-month period.
- P-values less than 0.05 will be considered significant.

- Termination of the pilot trial will occur after the 10th patient completes treatment.

Ethics

- IRB approval will not need to be sought from another IRB.
- The prospective aspect of this study will include a request for consent while the retrospective aspect will require a waiver of consent. To protect the privacy of participants, charts will only be accessed with a protected password on encrypted computers within a secure network, participants will be unidentifiable, any data stored will be on an encrypted computer, and individual information will solely be used for the purpose of this study.
- No risks to the safety of the patient or parent/guardian are anticipated with participation in this study. There is potential risk associated with the DynaCleft® + Nasal Elevator system, including skin irritation/allergy to the adhesive used in the system. If a skin allergy is encountered, participation in the study will be discontinued and appropriate care given. There is potential risk of breach of confidentiality with participation in this study, though all personal identifiers will be removed. Additionally, there is the risk that participants may tire or lose interest while completing the DynaCleft® + Nasal Elevator protocol.

Data Handling and Record Keeping

- The source documents will only be accessed with passwords within the University of Texas Health Science Center secure network on an encrypted computer. All data stored will be password protected on an encrypted, password protected computer.
- Human participants will be immediately reassigned to an unidentifiable code and any information collected will be linked solely to this code for confidentiality. Access to any information will be restricted to only the primary evaluator and co-investigators. The recorded data will be destroyed after the completion of the study following the protocols set by the IRB.

Quality Control and Assurance

- There will be a single evaluator collecting any and all data, a single pediatric dentist overseeing the DynaCleft® procedure, and a single plastic surgeon performing all surgical repairs. Evaluator will be blinded to whether or not the participant has had DynaCleft® intervention when reviewing photographs for data collection.
- All data are to be blindly measured and assessed at two separate times to ensure consistency.
- There are no plans to have any third-party monitoring of the collected information.

Publication Plan

- The research results are to be submitted to appropriate journal for publication and will be published as a Master's Thesis in Pediatric Dentistry.
- Results will not be returned to research participants. Additionally, results will hopefully be presented at appropriate national, state, and local meetings.

ATTACHMENTS

1. Schematic of Study Design
2. Study Schedule
3. Consent Document
4. Linking Log
5. Infant and New Parent Quality of Life Survey

References

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