

Review Article

Presurgical orthopedics in cleft lip and palate patients: A systematic review

Amit Kumar¹, Vishwajeet Singh Jamwal², Angad Sharma³

^{1,3}Postgraduate Student, Department Of Orthodontics & Dentofacial Orthopedics, Panjab University, Chandigarh, India;

²BDS, MDS, Oral And Maxillofacial Surgery, Panjab University, Chandigarh, India

ABSTRACT:

Aim: The objective of the study was to systematically summarize current evidence on the effectiveness of pre-surgical infant orthopaedics (PSIO) in cleft lip and palate (CLP) patients. **Methodology:** Electronic and manual searches were conducted, and using specific inclusion and exclusion criteria, data extraction and analysis was performed by two independent investigators. When possible, overall pooled estimates with 95% confidence intervals were obtained using the random-effects model. Twenty-four of 885 original studies met the inclusion criteria and were included in the qualitative synthesis, whereas 10 of them were included in the quantitative synthesis (meta-analysis). **Results:** Except for the variable M-T-C(5) assessing maxillary arch form, which presented an increase at 48 months of follow-up, all other variables concerning craniofacial and dentoalveolar changes demonstrated no significant differences, indicating that PSIO treatment has no effect on CLP patients. **Conclusion:** According to the results of this meta-analysis, only 3 of 13 variables were found to present some significant differences. However, this positive effect was not present at all time points. Thus, existing evidence cannot support the short- or long-term effectiveness of PSIO treatment

Keywords cleft lip; cleft palate; meta-analysis; pre-surgical orthopedics; systematic review

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Corresponding author: Amit Kumar, Postgraduate Student, Department Of Orthodontics & Dentofacial Orthopedics, Panjab University, Chandigarh, India

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INTRODUCTION

Presurgical infant orthopaedics (PSIO) has been part of the treatment protocol of patients with cleft lip and palate since about a half century ago. There are different kinds of PSIO treatment approaches with different mechanics, all seeking and achieving different objectives.¹⁻⁶ Among these, presurgical nasoalveolar moulding (PNAM) appliances have generated considerable interest in recent years and have been in use as a new approach to traditional presurgical infant orthopaedics (TPSIO).⁷⁻¹¹ Some of the major advantages of TPSIO are claimed to be the improvement of arch form, the facilitation of surgical closure, and thus improvement of aesthetic outcome, the facilitation of feeding, and improvement of speech.¹² Advocates of PNAM state that, beside the other advantages of traditional plates, the main objectives of PNAM appliances are improving nasal symmetry and lip aesthetics while elongating the columella and correcting the nasal cartilage.¹³ On the other hand, opponents state that all types of PSIO

approaches are complex and expensive and might have an adverse effect on maxillary growth. None of these claims are evidence based.¹⁴ Therefore, there is not yet a definitive conclusion on the subject, and a systematic review of PSIO seems to be warranted. Cleft lip and palate is one of the most frequent congenital maxillofacial anomalies.¹⁵ It ranks third according to the Latin American Collaborative Study of Congenital Malformations, and its prevalence has increased. The cleft palate rate has increased from 0.4 (1982–1994) to 0.7 (2001–2010) per 1000 births, and the cleft lip rate from 1.2 (1982–1994) to 1.4 (2001–2010) per 1000 births.¹⁶ In Chile, cleft lip and palate prevalence is 1.7 per 1000 newborns: approximately 400 cases each year. Its incidence is 1.8 per 1000 live births. Annually, this amounts to approximately 452 new cases every year.¹⁷ Its aetiology is multifactorial, as it involves genetic and environmental factors that may interfere with the migration of neural crest cells to the first branchial arch. Genetic factors appear in 20% to 25% of cases. Additionally, 20- 25% of

patients present environmental factors such as vitamin A deficiency, corticosteroids, Anticonvulsants, or a viral infection in the first trimester of pregnancy. No precise causes have been found in the remaining cases.¹⁸ Facial development of the foetus occurs between the third and twelfth week of pregnancy.¹⁹ Between the fourth and ninth week, there is an alteration in the migration or fusion of mesenchymal cells, which gives rise to the cleft lip because the frontonasal and maxillary processes fail to fuse. Furthermore, and not necessarily at the same time, a cleft palate occurs when the secondary palate fails to form, and the palatal shelves fail to fuse.¹⁵ This anomaly can be diagnosed in utero with modern technologies: an ultrasound scan in the 16th week of pregnancy or during birth.¹⁸ Cleft lip and palate may occur in association with other syndromic anomalies (20%) or in isolation (80%). It affects various orofacial functions such as feeding, hearing, phonation, breathing, self-esteem, aesthetics, and social adaptation.¹⁹ Therefore, this condition should be addressed from a multidisciplinary perspective to provide comprehensive and long-term rehabilitation from birth to adolescence.¹⁸ Care guidelines have been developed to restore full rehabilitation, improve the appearance of compromised hard and soft tissues, and facilitate the patient's integration into society.²⁰⁻²² Pre dental and paediatric treatment can be divided into three phases: phase 1, from birth to around 3 months of age (before any surgery); phase 2, from 3 to 12 months of age (after lip surgery); and phase 3, from 12 months onwards (after primary palatal repair).²³ The modern school of presurgical orthopaedics in cleft lip and palate treatment started in 1950 with McNeil.²⁴ In 1993, Grayson et al. created an intraoral plate with a nasal stent for alveolar, lip, and nose modelling: nasoalveolar moulding (NAM).²⁵ In unilateral cleft lip and palate cases, the clinician moulds the greater alveolar segment towards the mid-sagittal plane, in the direction of the lesser segment. When the segments are less than 5 mm apart, the nasal component is added, which can be either a stent (acrylic projection or wire extension that runs from the plate to the nose),²⁶ or a conformer, which is positioned in the affected nostril.¹⁷ Presurgical treatment is completed at the age of 5 months approximately, before the closing of the primary palate. Then, the device is removed and the first surgery is performed.²⁷ Berggren et al. subsequently introduced a nasal elevator and paper tape to improve nasal morphology. To avoid using of an intraoral plate and simplify the procedure, the paper adhesive tape is replaced with paper tape with an elastic band.²⁸ This elastic band creates muscular traction, bringing the cleft lip segments together, thus reducing the width of the bone fissure. The treatment lasts for three months in patients with unilateral or bilateral cleft lip.¹⁷

AIM OF THE PRESENT STUDY

Aim of this investigation was to qualitatively and quantitatively assess the currently existing literature by conducting a systematic review and a meta-analysis of randomized controlled clinical trials (RCTs) and prospective controlled clinical trials (pCCTs) in an attempt to provide the best evidence available on the effectiveness of PSIO treatment in CLP patients and more specifically on general developmental measures, as well as on craniofacial and dentoalveolar treatment outcomes in the short and long term.

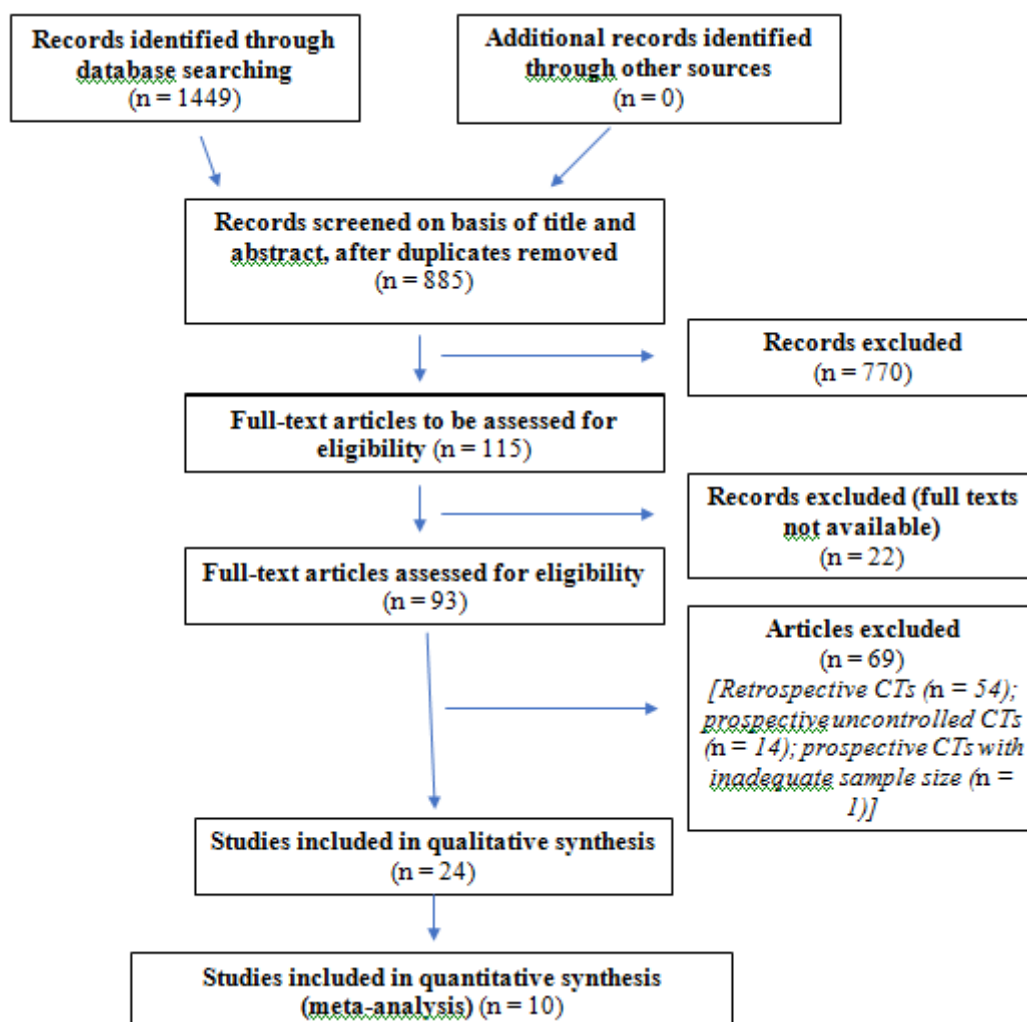
METHODOLOGY

This meta-analysis was conducted following a pre-defined protocol including a search strategy, eligibility criteria for study inclusion, screening methods, quality control, data extraction, and data analysis,²⁹ which was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.³⁰ A computerized literature search of several electronic databases was independently conducted by two authors for the identification of eligible studies published up to July 2021, using key words and their combinations, modified according to the syntax rules of each database. In an attempt to avoid publication bias, grey literature (i.e., articles that have not been formally published) was also searched directly through databases / registers [Google Scholar, UMI Proquest (dissertations and theses), Cambridge Scientific Abstracts (conference proceedings)], ongoing trials (metaRegister of Controlled Trials), and the German National Library of Medicine (technical reports, proceedings, reprints). In addition, publication status was not used as an exclusion criterion. Both English and non-English articles referring to human studies were included. Initially, the titles and abstracts of all identified studies were screened. For studies with insufficient data in the title and/or abstract, as well as for those deemed to meet the inclusion criteria, the full texts of the articles were obtained to make a clear decision. Studies were classified as of low (0–5 points), medium (6–8 points), or high (9 or 10 points) quality. Inter-reviewer agreement on quality analysis was assessed by Cohen's kappa. The mean difference (MD) or the standardized mean difference (SMD) was used as the metric of choice for the continuous variables. Results were stratified as short-term and long-term effectiveness. p-Values were two-tailed with $\alpha = 0.05$, and all presented confidence intervals (CI) were calculated at the 95% level. Heterogeneity among trials was assessed using a chi-square test for heterogeneity, significant at $p < 0.10$ (38), and the I² measure of inconsistency. I² is independent of the number of studies and quantifies heterogeneity on a scale of 0–100%.

RESULTS

The electronic search strategy yielded initially 1449 records. After removing the duplicates, 885 potential studies remained, while no additional records were identified through hand-searching. A total of 770 records did not fulfil the eligibility criteria and were excluded on the basis of their titles and abstracts. The full texts of 22 records were not available and consequently were also excluded. Careful evaluation of the full text of the remaining 93 articles led to the exclusion of 69 trials; 54 were retrospective CTs, 14 were prospective uncontrolled CTs, and one was prospective CT with inadequate sample size. Consequently, although a total of 24 trials were included in this review, meta-analysis was possible to be performed for only 10 of them. The j score for the selection of studies was 0.837, indicating an almost perfect level of inter-reviewer Agreement. In the

majority of the trials, a passive PSIO appliance was used, with the exception of the study by Masarei et al. in which an active appliance was used in infants with complete CLP and a passive one in infants with isolated cleft palate (CP). Control groups in all included trials consisted of infants with CLP that did not receive any type of PSIO (passive or active). Feeding was evaluated using various tools: Neonatal Oral Motor Assessment Scale (NOMAS), Great Ormond Street Measurement of Infant Feeding (GOSMIF), Schedule for Oral-Motor Assessment (SOMA), video fluoroscopy, and anthropometry. Speech development was assessed by speech recordings. PSIO seems to have no effects on weight, height, and feeding, because no significant differences were found for these variables between CLP patients who received PSIO treatment (PSIO+) in comparison with CLP patients who did not receive such treatment.



DISCUSSION

The effectiveness of PSIO treatment remains a subject of controversy in the medical literature. Although PSIO has not been fully established by evidence-based studies, it has become part of the standard care of CLP patients as a preliminary technique included in the treatment protocols of many centers around the

world. In general, according to the results of the current investigation, PSIO treatment seems to have no significant clinical effect in CLP patients. However, certain limitations should be taken into consideration. All comparisons undertaken included a maximum of two compatible studies, thus minimizing the power of the evidence and precluding analyses of

sensitivity or publication bias. Although moderate heterogeneity was present, except for some extreme cases, no actions could be made to eliminate it. Therefore, the summaries provided should by no means be regarded as robust, but only as an insight into existing knowledge, which could serve as a starting point for future studies with more rigorous designs. According to the results of the undertaken meta-analysis, PSIO treatment seems to have little effect on the feeding ability and subsequent growth (investigated through weight and height), as well as on speech (investigated through the number of consonants) of patients with CLP during the first 2 years of life. There seems to be no clinically positive effect of PSIO treatment on facial growth of CLP patients until the age of 6 years. This finding is in agreement with the study of Peat, who examined BCLP patients and assessed their craniofacial outcomes by the SNA, SNB, and SNMP angles up to 9 years of age. The only positive effect of PSIO found in the current investigation was on the maxillary arch form of CLP patients, as measured by one of three variables [M-T-C(5)] included in the analysis. Cost-effectiveness of PSIO+ over PSIO) treatment did not seem to be acceptable with regard to the operating time needed for surgical lip closure. Despite the significant cost of PSIO treatment, the duration of lip surgery was almost the same as in PSIO) patients. However, other variables such as easiness of surgery, appearance or function of the orbicularis oris after lip closure were not included in their analysis.

CONCLUSION

According to the results of this meta-analysis, only 3 of 13 variables were found to present some significant differences. However, this positive effect was not present at all time points. Thus, existing evidence cannot support the short- or long-term effectiveness of PSIO treatment in CLP patients. In the future, well-designed RCTs with long-term follow-up should be undertaken in order to provide additional evidence to confirm or reject

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