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Review Article

Long term outcome of presurgical infant orthopaedics in patients with cleft lip and palate: A systematic review and meta-analysis

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ABSTRACT

Objectives: To evaluate the long term outcome of Presurgical Infant Orthopaedics (PSIO) in patients with Cleft Lip and Palate (CLP).

Materials and Methods: A systematic literature search was performed according to PRISMA guidelines of articles from Jan 2011 till Feb 2021, using PubMed, Cochrane database and manual searching in the institutional library. Fifteen articles which met the inclusion and exclusion criteria were ranked according to the Oxford Centre for Evidence based Medicine – Levels of Evidence. The quality assessment of selected systematic reviews was done with ROBIS tool. Studies included for meta-analysis were analyzed with Q statistic methods, I^2 index, fixed-effects, DerSimonian-Laird Random effects and Begg-Mazumdar bias indicator.

Results: Selected fifteen articles were qualitatively assessed for various parameters on long term outcome of PSIO (minimum of 5 years), showed a positive outcome in nasolabial and pharyngeal airway parameters. Due to heterogeneity in the studies, meta-analysis was carried out for five studies in which nasolabial aesthetics parameters showed a significant improvement in PSIO group compared to control group (Q Statistic : 569.52523, P-value<0.001).

Conclusions: The PSIO in patients with CLP shows significant positive changes in nasolabial aesthetics and pharyngeal airway on a long term. These results should be considered with caution as the heterogeneity of included studies cannot be denied. Hence, more controlled and well conducted studies should be performed, focussing on the individual parameters for long term outcome of PSIO.

1. Introduction

Cleft lip and palate (CLP) is the most common congenital malformation caused due to variation in development of facial structure during gestation resulting in discrepancy in form and function with varied severity.[1] The maxillary component in patients with CLP is segmented by the cleft involving palate and alveolus. The extraoral clinical features in unilateral cleft defect are characterised by wide base of the nostril and clefting of the upper lip on the affected side. The nasolabial deformities are a major challenge for the initial surgical procedures and affect the final aesthetic outcome.

Presurgical Infant Orthopaedics (PSIO) is defined as "use of forces to reposition tissues secondarily displaced due to a cleft deformity".[2] The aim of PSIO is to decrease the width of the cleft gap, to achieve a favourable alignment in the cleft segments within the initial few months of infancy prior to cheiloplasty, and to allow surgical repair with minimal tension.[3,4]

PSIO has been used in treatment of patients with CLP for centuries, however it was Hoffmann in the year 1689, who demonstrated that the cleft can be narrowed with the usage of facial binding and thereby prevent

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postsurgical dehiscence.[5,6] Adhesive tape binding usage[7] and strapping the premaxilla[8,9] gradually evolved. The modern school of PSIO using a series of plate system was introduced by McNeil.[10–12] followed by Latham's appliance, Hotz plate.[13,14] Matsuo's (1988-91) series of research on neonatal molding on nasal cartilage and nostril with help of silicone tubes was the gateway to invent newer modern methods.[15–17] The paradigm shift in PSIO treatment in patients with CLP was with introduction of Nasoalveolar molding (NAM) by Grayson and Cutting in 1993, a novel technique in which presurgical molding of the alveolus, lip and nose is done in infants born with CLP.[18]

The ultimate goal of PSIO is to reduce the cleft width so to ease soft tissues under tension, thus helping in surgical repair of lip for better aesthetic results. The other added benefits are improvement and ease in feeding, increased volume of fluid intake, subsequently weight gain, improvement in functioning of tongue, reduced risk of aspiration, nasal symmetry, improvement in airway, and reduction in severity of dental & skeletal deviations.[19–21]

The aim of present systematic review is to thoroughly evaluate clinical evidence necessary to critically appraise and systematically summarize the long term outcome of PSIO in patients with CLP.

1.1. Focused question

Does PSIO have long term positive outcome in patients with CLP?

2. Objective

The objective is to evaluate the long term outcome of PSIO in patients with CLP.

3. Materials and Methods

3.1. Protocol development and eligibility criteria

A comprehensive protocol was considered and accordingly Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines were followed.[22] Study protocol was registered on International Prospective Register of Systematic Reviews (CRD42020195879). The following focused question formulated in the Patient, Intervention, Comparison and Outcome format was developed: "Does PSIO have long term positive outcome on patients with CLP?"

3.2. Information sources and search strategy

The evidences were searched using internet sources and manual search for suitable papers, cross references satisfying eligibility criteria of study. The electronic database of National Library of Medicine (MEDLINE PubMed), Cochrane, and manual search using institutional library resources was carried out. The keywords or the Medical subject headings (MeSH) that were used to recognize pertinent articles and full electronic search strategy for each database are illustrated in Table 1 respectively.

4. Study Records and Selection Criteria

4.1. Inclusion criteria and exclusion criteria

PICOS format was utilized for formulating inclusion and exclusion criteria (Table 2).

4.2. Inclusion criteria

1. Full text English articles published till Feb 2021
2. Studies from January 2011 to 2021 were included (previous systematic review published in 2011 included articles from 1963 to 2010.[23]
3. Randomised Control Trails (RCT) that reported data on treatment outcome of PSIO with controls without PSIO.
4. Prospective and retrospective controlled clinical trials (CCTs) that reported data on treatment outcome of PSIO with controls without PSIO.
5. Studies with follow-up period of minimum of 5 years

4.3. Exclusion criteria

1. Reviews, case reports, abstracts, editorials, letters, and historical reviews
2. CCTs without control group and comparing different types of PSIO
3. Studies related exclusively on cost factor analysis
4. Studies with follow-up period less than 5 years

5. Study Selection and Data Collection Process

The selection of articles at each stage is presented in Figure 1 in which the flow diagram is adapted from PRISMA -2009.[22] A positive exclusion method was used, whereby publications that did not meet one or more of inclusion criteria were excluded. In step 1, only titles and abstracts were collected from the records from Jan 2011 till Jul 2020. Step 2 involved removal of duplicated articles. In step 3, the copies of full articles were reviewed from those selected in step 1 and the ones which did not qualify inclusion criteria were excluded. Both steps of the review process were done twice by author AB.15 articles which satisfied the selection criteria were included in the present study[24–37]. The distribution of the journals in which these articles are published is tabulated in Table 4.

5.1. Exclusion of studies

Twenty four studies were excluded from the review because they did not satisfy the selection criteria [A1-A24].(Table 5 and reference as per Appendix A).

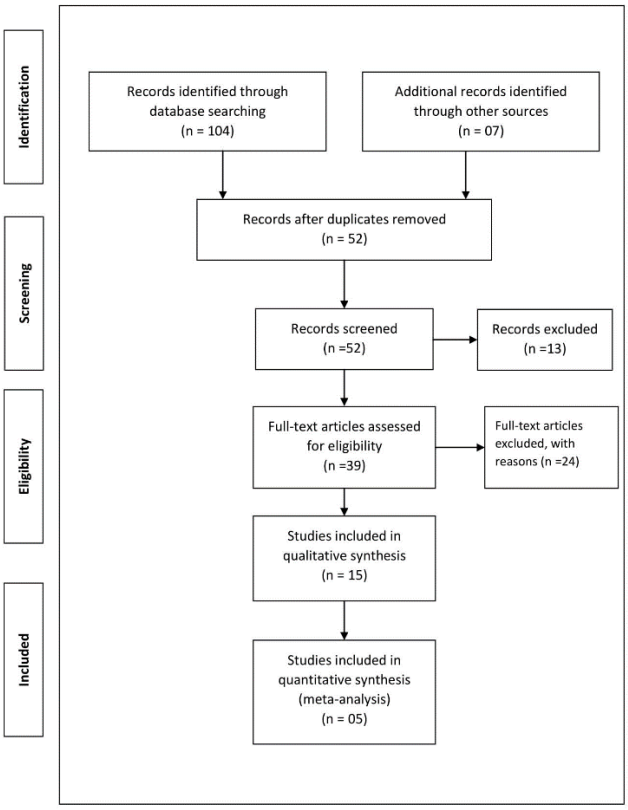

Figure 1: The PRISMA flow diagram

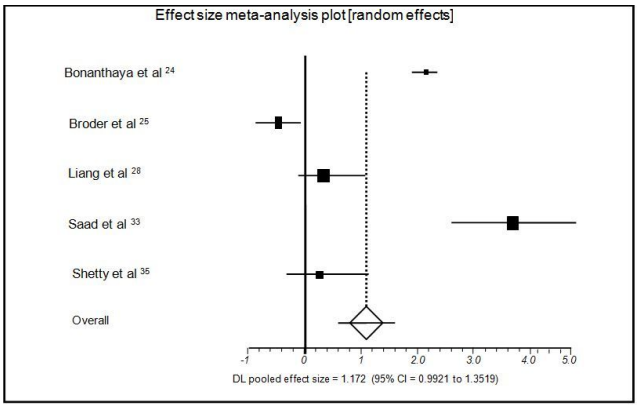

Figure 2: Forest plot showing the effect sizes with 95% confidence interval (CI) found in the studies for Mean difference included in the meta-analysis

5.2. Data extraction and quality analysis

The data in the form year of publication, study design, materials (study sample, control sample), type of presurgical appliance, methods of measurement, outcome and authors' conclusions were summarised. (Table 5) A quality evaluation of the methodological soundness of each article was performed for the studies according to "The Oxford Centre for Evidence-Based Medicine Levels of Evidence" criteria.[38] The following characteristics were used to evaluate accordance with the standards: study design, sample selection description, blinding in measurements, and provision of adequate statistics (Table 6).

5.3. Assessment of risk of bias of the studies

Each article has been ranked according to the Oxford Centre for Evidence-based Medicine-Level[38] and the quality assessment of systematic reviews was done with ROBIS tool (Risk of Bias in Systematic reviews)[39] by two reviewers AB and SD. (Tables 6 and 7).

6. Results

The search strategy resulted in 111 articles, of which 15 were qualified for the final analysis. The studies included in this review, characteristics of participants, type of interventions, outcome measures are summarized in Table 5.

6.1. The meta-analysis

Although a total of 15 studies were included in this review, meta-analysis was possible to be performed for only 05 of them due to heterogeneity of material, method and type of PSIO used. Figure 2 shows the Meta-analysis for mean difference of parameters (Study group versus control group). In the meta-analysis, a statistical test of heterogeneity was performed.[40,41] The test of heterogeneity seeks to determine whether there are genuine differences underlying the results of the studies (heterogeneity), or whether the variation in the published findings is compatible with chance alone (homogeneity). From the results obtained through meta analysis, it is clear that there is a significant heterogeneity reported in the literature in terms of mean difference between study group and control group being included in this review study (Q Statistic : 569.52523, P-value<0.001, I^2 99.3% (Table 8). A forest plot (blobbogram) of estimated results using 5 selected studies addressing the same question, along with the overall results was formulated (also called pooled effect). Forest plot, that includes the effect-sample size with 95% CI found in the studies included in the meta-analysis. The funnel plot along with Begg-Mazumdar's statistically non-significant Kendall tau value shows clear evidence of non-existence of publication bias (P-value>0.05).

Table 1: Search strategy database

S. No	Search strategy	No of Articles searched	No of Articles selected	Reason for exclusion
1	Presurgical infant orthopaedics	24	3	Case reports, unclear results
2	PSIO	03	1	Case reports, comparing 2 PSIO methods
3	Cleft palate and infant orthopaedics	18	1	Case reports, unclear results
4	Infant orthodontics	09	1	Case reports, unclear results
5	Nasoalveolar molding	39	8	Case reports, comparing 2 PSIO methods
6	NAM	11	1	Case reports
	Total	104	15	

Table 2: PICOS criteria for selection of studies

Category	Criteria for selection
Participant Characteristics	Patients with Cleft lip and palate
Intervention/ Exposure	PSIO appliances
Comparison	No treatment with PSIO appliances
Outcome	Studies providing Long term outcome of PSIO
Study design	Randomised Control Trails (RCTs), Prospective and retrospective Controlled Clinical Trials(CCTs) , Studies with follow up with a minimum of 5 years

Table 3: Distributionof the journals in which the 15 selected articles were published

Name of the Journal	Number of studies
International Journal of Oral and Maxillofacial Surgery	2
Plastic and Reconstructive Surgery	2
The Cleft Palate-Craniofacial Journal	2
Clinical Oral Investigations	1
JDR Clinical & Translational Research	1
Journal of Craniofacial Surgery	1
Journal of Evidence-Based Dental Practice	1
Journal of Oral & Maxillofacial Research	1
Journal of Oral and Maxillofacial Surgery	1
Oral diseases	1
Orthodontics & Craniofacial Research	1
PLOS One	1

Table 4: Referencesof excluded studies with rationale for exclusion

S. No	References	Rationale for exclusion
1	Abbott et al A1	Short term follow up
2	Abhinav et al A2	Comparing different types of PSIO
3	Bekisz et al A3	Different surgical methods
4	Botticelli et al A4	PSIO not received
5	Chang et al A5	Comparing different types of PSIO
6	Dubois et al A6	Different surgical methods
7	El Ashmawi et al A7	Comparing different types of PSIO
8	El-Ashmawi et al A8	Short term follow up
9	El-Ghafour et al A9	Short term follow up
10	El-Ghafour et al A10	Comparing different types of PSIO
11	Funayama et al A11	Short term follow up
12	Jahanbin et al A12	Short term follow up
14	Kamble et al A13	Short term clinical report
15	Kornbluth et al A14	Short term follow up
16	Monasterio et al A15	Comparing different types of PSIO
17	Kinouchi et al A16	Comparing different types of PSIO
18	Ritschl et al A17	Short term follow up
19	Saad et al A18	Short term follow up
20	Sasaki et al A19	Comparing different types of PSIO
21	Shen et al A20	Short term follow up
22	Shetty et al A21	Short term follow up
23	Sischo et al A22	Comparing different types of PSIO
24	Zapta et al A23	Comparing different types of PSIO
25	Zhong et al A24	Short term follow up

Table 5: ClinicalSummaries of the selected articles

Author and year of publication	Study design	Study sample	Appliance	Outcome	Conclusion
Astani et al[23]	Cross-sectional retrospective study	40 patients with CLP 26 with NAM, 14 without NAM	NAM	Pharyngeal Airway	There is an effective enlargement in nasopharyngeal airway size in patients with CLP after NAM, more apparent in BCLP than UCLP individuals after NAM
Bonanthaya et al[24]	Cross-sectional retrospective study	121 patients with CLP 59 with NAM 62 without NAM	NAM	Nasolabial aesthetics	Nasolabial aesthetics at post cheiloplasty were significantly better in patients who had undergone NAM in infancy.
Broder et al[25]	Nonrandomized, prospective, multicenter Study	110 infants with CLP 62 with NAM 48 without NAM	NAM	Nasolabial aesthetics	Infants who underwent NAM were perceived by caregivers to have better post surgical outcomes than those who underwent lip repair without NAM
Hosseini et al[26]	A systematic review and meta-analysis of randomized controlled trials	118 patients with unilateral complete CL/P and 16 with cleft of the soft and at least two thirds of the hard palate.	PSIO	Feeding, general body growth, facial esthetics, speech and language evaluation, caregiver-reported outcomes, economic evaluation, as well as, adverse effects and problems	No significant effect of investigated PSIO protocol on outcome
Jodeh et al[27]	Meta analysis	1241 patients with CLP from 15 studies	PSIO	Development of oronasal fistula	Multiple benefits in relation to facial and nasal form with PSIO in patients with CLP .

Continued on next page

Table 5 continued

Liang et al[28]	Prospective, randomized clinical trial	84 patients with CLP 42 with NAM 42 without NAM	NAM	Nasolabial aesthetics	NAM is beneficial when used as an early-stage adjunctive therapy during nasal deformity correction before primary cheiloplasty; however it is lacks long-term nostril symmetry maintained after primary cheiloplasty.
Liu et al[29]	Systematic review of Cohort studies and RCT	756 patients with CLP	NAM	Surgical, esthetic, functional, and socioeconomic effects	NAM appliance therapy can offer positive outcome on patients with UCLP when performed before primary repair surgeries
Maillard et al[30]	Systematic review of RCTs, prospective , retrospective studies	1893 patients with CLP	PSIO	Surgical, esthetic, functional, and socioeconomic effects and the three-dimensional technology	NAM appliance therapy can offer positive outcome on patients with UCLP before the primary repair surgeries. Three-dimensional technology results in a more efficient and predictable NAM treatment.
Noverraz et al[31]	Prospective two-arm randomized controlled trial (DUTCHCLEFT)	43 patients with CLP wearing Passive plate, 46 patients with CLP not wearing plate	Passive maxillary plate	Maxillary transverse arch relation	Passive maxillary plate does not show significant changes in transverse dental arch relationships in patients with CLP.
Papadopoulos et al[32]	Systematic review and meta-analysis of randomized controlled trials	200 patients with CLP	PSIO	Feeding, general body growth, facial esthetics, speech and language evaluation, caregiver-reported outcomes, economic evaluation, as well as, adverse effects and problems	Evidence cannot support the short or long-term effectiveness of PSIO treatment in patients with CLP

Continued on next page

Table 5 continued

Saad et al[33]	Prospective randomized controlled clinical trial	40 infants with nonsyndromic UCLP 20 NAM-treated group 20 non–NAM treated group	NAM	Maxillary arch dimensions	NAM in patients with CLP minimizies cleft severity, and realigns the maxillary arch segments with no worsening in transverse and vertical arch growth. .
Shetty et al[34]	Nonrandomized, prospective, Study	150 patients with CLP	NAM	Nasolabial dimensions	Improvement in Nasolabial dimensions was seen with the NAM protocol. .
Shetty et al[35]	RCT	60 patients with CLP	NAM	Maxillary arch dimensions	PNAM aids in improving the maxillary arch symmetry as well as stability, and helps in preventing arch collapse in the long term.
Thierens et al[36]	Systematic review	587 patients with CLP	Labial adhesion and lip strapping	Alveolar and palatal cleft width	There is an effective reduction in alveolar and palatal cleft width with usage of labial adhesion with or without infant orthopedics. However the long term effect on nasolabial esthetics remains uncertain
Van der Heijden et al	Systematic review	212 patients with CLP	NAM	Nasal symmetry	Positive effect is appreciated in respect to nasal symmetry with the usage of NAM.

7. Discussion

PSIO concept for treating the patients with CLP has been integrated as the standards of care in many treatment protocols teams around the world. The definitive treatment for patients with CLP is followed after the development of face.[24] The PSIO treatment being one of the first approaches in treatment protocol (NAM being the commonest method), it is imperative to study the long term outcome of the procedure keeping in mind the variation of growth in the face of the individual. Thus, the focused question of this systematic review was about the long-term outcome of PSIO in patients with CLP, which require a relevant, evidence-based evaluation in various outcome parameters like feeding, general body growth, facial and nasolabial aesthetics, airway, maxillary arch dimension, speech as well as adverse effects and problems. The studies included in the present review were with the long term effect of PSIO on various parameters. The longest follow up period among the studies selected was an RCT with follow up of 12 years.[31] However the selection of a large sample of untreated control group is not easy and comparing the true effect of PSIO is very difficult.

7.1. Feeding and general body growth

PSIO in the form of active or passive appliances seems to have no evident positive effects on feeding function and successive effect on growth and development outcomes in the form of height and weight. There seems to be no considerable differences between patients with CLP who received PSIO treatment in comparison with patients with CLP who did not receive such treatment.[26,32]

7.2. Facial and nasolabial aesthetics

The long term effect of PSIO seems to have no lasting effect on facial aesthetics when assessed by full-face and nasolabial photographs.[32] Treatment of patients with CLP with PSIO performed before primary repair in infancy enhances nasolabial aesthetics by improving its symmetry due to active nasal molding of the lower lateral nasal cartilage.[24,26,29,30,34] Better results in facial appearance and aesthetics were reported after primary cleft lip and nasal repair in the infants who underwent PSIO compared with the control group.[25] The repositioning and approximation of cleft segments benefited surgeons in marking and dissection during the operation, with a less invasive surgery leading to reduction in recovery time[28,37]

7.3. Airway

The patients with CLP who underwent PSIO treatment during infancy were assessed for the long term outcome in relation to upper airway parameters. Nasopharyngeal, oropharyngeal, and total airway volumes of all the patients with CLP were calculated with the help of 3D CBCT. There were statistically significant differences in nasopharyngeal volume in PSIO group compared to control group. The oropharyngeal and total pharyngeal airway were not statistically significant. The amount of nasopharyngeal, oropharyngeal, and total pharyngeal airway size in patients with BCLP of PSIO group was significantly more than that of patients with BCLP of control group. Thus it was concluded that PSIO can effectively enlarge the nasopharyngeal airway size in patient with CLP.[21]

7.4. Maxillary arch dimension

The patients with CLP who underwent PSIO treatment with passive maxillary plate during infancy showed that the long term transverse dental arch relationships at 9 and 12 years of age had no statistically significant difference between children with UCLP treated with or without PSIO [32]. It was concluded that the orthodontic requirement to perform PSIO in infants with UCLP with an aim for maxillary transverse expansion is not necessary. However PSIO improves arch symmetry and stability by reducing the cleft width, minimizing cleft severity, realigning maxillary segments without the deterioration of the transverse and vertical arch growth. Thus, it may prevent arch collapse in the long term.[33,35,36]

7.5. Speech

The patients with CLP who underwent PSIO treatment had positive effects on speech and further associated language development. In comparison to patients who were not treated with PSIO, treated infants had a considerable normal phonetics development, improved production of alveolar contoids & oral plosives, superior intelligibility, and longer utterances in their speech. The improvement changes in speech were temporary as the effects faded away in long term. The long term assessment of speech at the age of 6 years did not show any significant effects when compared to no treatment.[26,32]

7.6. Adverse effects /unfavourable/ pitfalls and problems

The patients with CLP undergoing PSIO treatment generally do not present significant adverse effects when compared to each other or to no treatment. However minor reports of tissue and skin ulceration due to application of pressure by intra oral appliances, irritated mucosa and skin over the cheek region, dislodgement of intra oral plates, excessive

Table 6: ROBI Sassessment of systematic reviews

Study	Study eligibility criteria	**Data collection and study appraisal**	**Synthesis and findings**	**Risk of bias in the review**
Hosseini et al[26]	High	High	High	Low
Papadopoulos et al[32]	High	High	Low	Low
Maillard et al[30]	High	High	Low	Low
Liu et al[29]	Low	Low	Low	Low
Thierens et al[36]	High	Low	Low	Low
Van der Heijden et al[37]	Low	High	Low	Low

Table 7:

Article	**Study Design**	**Selection Description**	**Blinding in Measurements**	**Adequate Statistic Provided**	**Oxford Centre Level of Evidence-2010**
Astani et al[23]	Retrospective study	Adequate	Mentioned	Yes	2b
Bonanthaya et al[24]	Retrospective study	Adequate	Mentioned	Yes	2b
Broder et al[25]	Prospective study	Adequate	Mentioned	Yes	2b
Hosseini et al[26]	Systematic review and meta-analysis	Adequate	-	Yes	1a
Jodeh et al[27]	Meta analysis	Adequate	Mentioned	Yes	1a
Liang et al[28]	RCT	Adequate	Mentioned	Yes	1b
Liu et al[29]	Systematic review	Adequate	-	Yes	1a
Maillard et al[30]	Systematic review	Adequate	-	Yes	1a
Noverraz et al[31]	RCT	Adequate	Mentioned	Yes	1b
Papadopoulos et al[32]	Systematic review and meta-analysis	Adequate	-	Yes	1a
Saad et al[33]	RCT	Adequate	Mentioned	Yes	1b
Shetty et al[34]	Prospective, Study	Adequate	Mentioned	Yes	2b
Shetty et al[35]	RCT	Adequate	Mentioned	Yes	1b
Thierens et al[36]	Systematic review	Adequate	-	Yes	1a
Van der Heijden et al[37]	Systematic review	Adequate	-	Yes	1a

Table 8: Meta-analysis of Effect sizes of Mean difference ofpost-op parameters (PSIO Group vs Control Group).

Author Year of publication	**Study**	**Control**	**Mean difference (d)**	**Approximate Interval(CI)**	**95%**	**Confidence**
				Lower		Upper
Bonanthaya et al 24	59	62	2.1000	1.886182		2.13818
Broder et al 25	62	48	-0.7300	-1.10376		-0.35624
Liang et al 28	42	42	0.3000	-0.55541		1.155414
Saad et al 33	20	20	3.8400	2.290484		5.389516
Shetty et al 35	60	60	0.3500	-0.54461		1.244614

Non-combinability of studies
Cochran Q = 569.52523(df = 4) P< 0.0001I^2 (inconsistency) = 99.3% (95% CI = 99.0% to 99.5%)
Randomeffects (DerSimonian-Laird)
Pooled d+ = 1.17200 (95% CI = 0.992138 to 1.351862)
Z (test d+ differs from 0) : P <0.001
Bias indicators
Begg-Mazumdar:Kendall's tau = -0.5840 P = 0.3453
(Lowpower)

alar expansion leading to mega nostril are also documented. Sometimes due to the poor and unmonitored molding process, wherein the greater segment of cleft moves more rapidly, without the change in position of the lesser segment, resulting the lesser segment to get locked out behind the greater segment known as locked-out segments. [26]

7.7. Strengths and limitations

The strengths of the present review include systematic approach using standard protocol and guidelines of search strategy, risk of bias, and summarizing the evaluation of various PSIO outcome parameters like feeding, general body growth, facial and nasolabial aesthetics, airway, maxillary arch dimension, speech as well as adverse effects & problems. Limitations of the review included the heterogeneity of the level of study in various parameters for outcomes of PSIO.

8. Recommendations

The definitive long-term outcomes of PSIO protocols are of utmost importance in patients with CLP; however it can only be recognized after completion of facial development. The level of evidence varies in long term outcomes of various parameters of PSIO. Further research with equal selection of level of evidence can justify the different parameters for long term outcome of PSIO.

9. Conclusions

1. The zeal for PSIO is increasing among orthodontists working on patients with CLP, so as to look for better surgical outcomes with minimal requirement of surgery.
2. The PSIO in patients with CLP shows significant positive changes in nasolabial aesthetics and pharyngeal airway in long term.
3. These results should be considered with caution as the heterogeneity of included studies cannot be denied.
4. Hence, more controlled and well conducted studies should be performed, focussing on the individual parameters for long term outcome of PSIO.

10. Source of Funding

None.

11. Conflict of Interest

None.

References

1. Thronton JB, Nimer S, Howrd P. Incidence, classification, etiology and embryology of oral clefts. *Semin Orthod*. 1996;2(3):162–70.
2. Jaeger M, Silva JB, Gehlen D, Sato Y, Zuker R, Fisher D. Correction of the alveolar gap and nostril deformity by presurgical passive orthodontia in the unilateral cleft lip. *Ann Plast Surg*. 2007;59(5):489–94.
3. Braumann B, Keillig L, Bourauel C, Jager A. 3D analysis of morphological changes in the maxilla of patients with cleft lip and palate. *Cleft Palate Craniofac J*. 2002;39(1):1–11.
4. Berkowitz S. Cleft lip and palate diagnosis and management. 3rd ed. Germany: Springer; 2006. p. 381–92.
5. Yang S, Stelnicki EJ, Lee MN. Use of nasoalveolar molding appliance to direct growth in newborn patient with complete unilateral cleft lip and palate. *Pediatr Dent*. 2003;25(3):253–9.
6. Millard D. Cleft craft: The evolution of its surgery. Bilateral and rare deformities. Boston: Little Brown: Lippincott Williams and Wilkins; 1976. p. 52.
7. Goldwyn RM, Hullihen SP. Pioneer oral and plastic surgeon. *Plast Reconstr Surg*. 1973;52(3):250–7.
8. Millard D, Berkowitz S, Latham RA. A discussion of presurgical orthodontics in patients with clefts. *Cleft Palate J*. 1988;25(4):403–15.
9. Brophy TW. Cleft lip and cleft palate. *J Am Dent Assoc*. 1927;14:1108–17.
10. Mcneil C. Orthodontic procedures in the treatment of congenital cleft palate. *Dent Records*. 1950;70(5):126–58.
11. Millard DA. A primary camouflage of the unilateral harelook. In: Skoog T, Ivy R, editors. Transactions of the International Society of Plastic Surgeons; 1957. p. 160.
12. Burston WR. The early orthodontic treatment of cleft palate conditions. *Dent Pract*. 1958;22(5):435–76.
13. Georgiade NG, Latham RA. Maxillary arch alignment in the bilateral cleft lip and palate infant, using pinned coaxial screw appliance. *Plast Reconstr Surg*. 1975;56(1):52–60.
14. Hotz M, Perko M, Gnoinski W. Early orthopaedic stabilization of the premaxilla in complete bilateral cleft lip and palate in combination with the Celesnik lip repair. *Scand J Plast Reconstr Surg*. 1987;21:45–51.
15. Matsuo K, Hirose T. Nonsurgical correction of cleft lip nasal deformity in the early neonate. *Ann Acad Med Singapore*. 1988;17(3):358–65.
16. Matsuo K, Hirose T, Otagiri T, Norose N. Repair of cleft lip with nonsurgical correction of nasal deformity in the early neonatal period. *Plast Reconstr Surg*. 1989;83(1):25–31.
17. Matsuo K, Hirose T. Preoperative non-surgical over-correction of cleft lip nasal deformity. *Br J Plast Surg*. 1991;44(1):5–11.
18. Grayson BH, Cutting C, Wood R. Preoperative columella lengthening in bilateral cleft-lip and palate. *Plast Reconstr Surg*. 1993;92(7):1422–5.
19. Millard DR, Latham RA. Improved primary surgical and dental treatment of clefts. *Plastic Reconstr Surg*. 1990;86(5):856–71.
20. Radhakrishnan V, Sabarinath VP, Thombare P, Hazarey PV, Bonde R, Sheorain A, et al. Presurgical nasoalveolar molding assisted primary reconstruction in complete unilateral cleft lip palate infants. *J Clin Pediatr Dent*. 2010;34(3):267–74.
21. Astani SA, Yilmaz HN, Nevzatoglu S, Demirkaya A, Acar ZA. Evaluation of airway volume in cleft lip and palate following nasoalveolar molding. *J Craniofac Surg*. 2018;29(8):2143–50.
22. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*. 2015;349:7647.
23. Uzel A, Alparslan ZN. Long-term effects of presurgical infant orthopedics in patients with cleft lip and palate: a systematic review. *Cleft Palate Craniofac J*. 2011;48(5):87–95.
24. Bonanthaya K, Nayak T, Bitra S, Rachwalski S, Shetty PN. An assessment and comparison of nasolabial aesthetics in bilateral clefts using the anatomical subunit-based scale: A nasoalveolar moulding versus non-nasoalveolar moulding study. *Int J Oral Maxillofac Surg*. 2019;48(3):298–301.
25. Broder HL, Roberto L, Garfinkle JS, Clouston S, Kirschner RE. Surgeon's and caregivers' appraisals of primary cleft lip treatment with and without nasoalveolar molding: A prospective multicenter pilot

study. *Plast Reconstr Surg*. 2016;137(3):938–83.
26. Hosseini HR, Kaklamanos EG, Athanasiou AE. Teatment outcomes of pre-surgical infant orthopedics in patients with non-syndromic cleft lip and/or palate: A systematic review and meta-analysis of randomized controlled trials. *PLoS One*. 2017;12(7):181768. doi:10.1371/journal.pone.0181768.
27. Jodeh DS, Buller M, Rottgers SA. The Impact of presurgical infant orthopedics on oronasal fistula rates following cleft repair: A meta-analysis. *Cleft Palate Craniofac J*. 2019;56(5):576–85.
28. Liang Z, Chen Y, Zheng KT, Yang C. Effect of presurgical nasoalveolar Molding on nasal symmetry in unilateral complete cleft lip/palate patients after primary cheiloplasty without concomitant nasal cartilage dissection: early childhood evaluation. *Cleft Palate Craniofac J*. 2018;55(7):935–75.
29. Liu Y, Hua F, He H. Nasoalveolar molding therapy may offer positive effects on unilateral clefts of lip and/or palate. *J Evid Based Dent Pract*. 2018;18(3):252–6.
30. Maillard S, Retrouvey J, Ahmed MK. Correlation between nasoalveolar molding and surgical, aesthetic, functional and socioeconomic outcomes following primary repair surgery: a systematic review. *J Oral Maxillofac Res*. 2017;8(3):e2. doi:10.5037/jomr.2017.8302.
31. Noverraz RL, Disse MA, Ongkosuwito M, Kuijpers-Jagtman AM, Prahl C. Transverse dental arch relationship at 9 and 12 years in children with unilateral cleft lip and palate treated with infant orthopedics: a randomized clinical trial (DUTCHCLEFT). *Clin Oral Investig*. 2015;19(9):2255–65.
32. Papadopoulos MA, Koumpridou EN, Vakalis ML, Papageorgiou SN. Effectiveness of pre-surgical infant orthopedic treatment for cleft lip and palate patients: a systematic review and meta-analysis. *Orthod Craniofac Res*. 2012;15(4):207–43.
33. Saad MS, Fata M, Farouk A, Habib A, Gad M, Tayel MB, et al. Early progressive maxillary changes with nasoalveolar molding: randomized controlled clinical trial. *JDR Clin Trans Res*. 2019;5(4):319–31.
34. Shetty V, Thakral A, Sreekumar C. Comparison of early onset nasoalveolar molding with patients who presented for molding up to 1 year of age. *J Oral Maxillofac Surg*. 2016;74(4):811–38.
35. Shetty V, Agrawal RK, Sailer HF. Long-term effect of presurgical nasoalveolar molding on growth of maxillary arch in unilateral cleft lip and palate: randomized controlled trial. *Int J Oral Maxillofac Surg*. 2017;46(8):977–87.
36. Thierens L, Brusselaers N, Roo D, Pauw N. Effects of Labial adhesion on maxillary arch dimensions and nasolabial esthetics in cleft lip and palate: a systematic review. *Oral Dis*. 2017;23(7):889–96.
37. Heijden PD, Dijkstra PU, Astrid GW, Meijer K, Sieneke M, Brouwer G. Limited evidence for the effect of presurgical nasoalveolar molding in unilateral cleft on nasal symmetry: a call for unified research. *Plast Reconstr Surg*. 2013;131(1):62–71.
38. The Oxford Centre for Evidence-Based Medicine Levels of Evidence; 2009. Available from: https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-evels-evidence-.
39. Whiting P, Savović J, Higgins JP, Caldwell DM, Reeves BC, Shea B. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol*. 2016;69:225–9.
40. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–60.
41. Borenstein M, Hedges LV, Higgins JPT. Introduction to meta-analysis. HR R, editor. Chichester, UK: Wiley; 2009. p. 107–32.

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