

Review Paper:

Effect of Nasoalveolar Molding on Nasal Symmetry in Patients With Cleft Lip and Palate: A Systematic Review



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ABSTRACT

Context: One of the main types of nasal deformity is the unilateral cleft lip or palate, which affects breathing and smelling. It is supposed that nasoalveolar molding (NAM) has a positive effect on the reduction of the tension in lips and helps to simplify or even eliminate the subsequent orthodontic treatment.

Objective: This systematic review of papers focused on the effectiveness of NAM in patients with unilateral cleft lip or palate.

Data Sources: The databases of Google Scholar, PubMed, Web of Science, and Medline were searched.

Study Selection: A total of 1282 relevant articles published up to 2018 were identified. The selected papers were screened based on the eligibility criteria after the thorough investigation of their titles and abstracts. In the next step, the inconsistent articles with our objectives were removed. Afterward, the papers were thoroughly studied, and data related to our study goals were extracted and recorded in predetermined extraction forms. After the full-text evaluation of the articles, 22 articles were finally selected.

Data Extraction: The search process was performed with the following keywords in combination with nasoalveolar molding or pre-surgical nasoalveolar molding or pre-surgical orthopedic appliances: "unilateral cleft lip or palate", "UCL/P", "Cleft lip", "Cleft palate".

Results: Based on the literature, many studies have supported the effectiveness of NAM appliance therapy on nasal symmetry in the unilateral cleft of the lip and or palate treatment.

Conclusions: The NAM therapy is effective in decreasing the severity of the initial cleft deformity, as well as repositioning of deformed nasal cartilage and alveolar process. It has many beneficial results in surgical outcomes. However, the long-term effect of this approach has remained unclear.

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1. Context

The nasal deformity is an abnormality in the structure and appearance of the nose, which involves the displacement of lower lateral nasal cartilage, oblique and short columella, depressed dome, overhanging nostril apex, and deviated septum. Difficulties in breathing and smelling are the main problems of this deformity. One of the main types of nasal deformity is unilateral cleft lip or palate (UCL/P). The reconstruction of facial soft tissue is the most challenging issue in these patients (1).

The worldwide prevalence of the UCL/P is 0.5-3 cases per 1000 births (2). Genetic and local factors are the etiology of this problem (2). Moreover, the frequency of this deformity differs among people in terms of gender, population, and maternal features. The female/male ratio in children with UCL/P is 1:2, and it is more common in the Caucasian population (2). The cleft of lip or palate is the fourth most common craniofacial abnormalities in Iranian children with a rate of 2.14 patients per 1000 births (3).

Rhinoplasty for UCL/P patients is very complicated and should be performed with caution due to the complex nature of the unilateral cleft nasal deformity. There are several surgical approaches to correct the cleft lip tissue; however, wide and bilateral clefts have remained a remarkable challenge (4). For this reason, presurgical infant orthopedics were introduced to manage the floating premaxilla and align the alveolar bone of maxilla (5). Grayson et al. introduced presurgical nasoalveolar molding (PNAM) in 1999 in which the alveolar segments and deformed lower lateral cartilages are repositioned via active molding prior to the primary cheiloplasty. The main goals of PNAM therapy are the correction of the normal arc of alveolar segments and decrease the cleft gap.

The PNAM helps to gradually shift nasal tissues to their normal positions (5). It is supposed that nasoalveolar molding (NAM) has a positive effect on lowering the tension on the lip and helps to simplify or even eliminates the subsequent orthodontic treatment (4, 6). This approach was considered as the early intervention for UCL/P children in the 1960s and 1970s (7, 8).

The use of nasoalveolar molding has increased over the past two decades. So far, several attempts have been made to assess the efficacy of PNAM for the nasal deformity (9-12). Although the use of NAM increased to improve UCL/P patients, its effect is still a matter

of discussion. The reason for this is a small number of long-term randomized, double-blind controlled trials, which drew a comparison between the patients with NAM therapy and those without it or the comparison of the effectiveness of this approach with other presurgical neonatal orthopedics. Moreover, there is insufficient scientific evidence on the long-term effect of NAM.

2. Objective

This study aimed to evaluate the literature regarding the effectiveness of NAM in patients with UCL/P, compared to those who did not undergo NAM therapy. The main issues in the assessment of the articles were the objectives, instruments, and short-term and long-term effects of this technique on patients with UCL/P. This study also addressed the prospect of this approach. We focused on answering the following questions:

Does NAM therapy before primary repair surgeries have positive outcomes in UCL/P patients compared to those with no experience of this approach?

Does NAM therapy have better outcomes in UCL/P patients compared to other instruments?

3. Data Source

This study is a systematic review with comprehensive search strategies on the articles addressing the effectiveness of NAM therapy in UCL/P patients. We searched four databases of Google Scholar, PubMed, Web of Science, and Medline for the published articles up to 2018. In this study, the researchers applied the recommendation stages of Cochrane Handbook (asking a question, determining the eligibility criteria, searching process, selecting papers, exclusion of inappropriate articles, determining the features of article assessment, extracting data, as well as explaining and presentation) (13). We used PICO elements (population, intervention, comparison, and outcome) of the PRISMA-P protocol (2015), which is suggested to create systematic reviews (14).

4. Study Selection and Data Extraction

The selected papers were screened based on the eligibility criteria after a complete reading of their titles and abstracts. For the study, two researchers were continuously in contact with each other to exchange information and select the necessary papers. In the next step, the inconsistent article with our objectives were removed from the current study. Afterward, the papers

were thoroughly studied, and data related to our study goals were extracted and recorded in predetermined extraction forms. The selection process of the papers is shown in the PRISMA flow diagram (Figure 1).

Eligibility criteria

This systematic review entailed all parallel randomized, quasi-randomized, prospective studies performed on human subjects focused on the effectiveness of NAM therapy in UCL/P patients. However, only the articles with a clear description of the treatment protocol and objective results measurements were entered in this review. The exclusion criteria included the non-English papers, in vitro studies,

and those with insufficient data, and animal samples. The use of presurgical infant orthopedics other than NAM, sample size smaller than 10 subjects, bilateral clefts of the lip and or palate and articles with no control group were the other exclusion criteria. Moreover, retrospective studies, non-clinical studies, meta-analyses, expert opinions, editorial letters, case reports, or case series, consensus statements, and qualitative studies were removed from this study.

Risk of bias in individual trials

We followed the Cochrane tool to assess the risk of bias in the included trials (15). This study focused solely

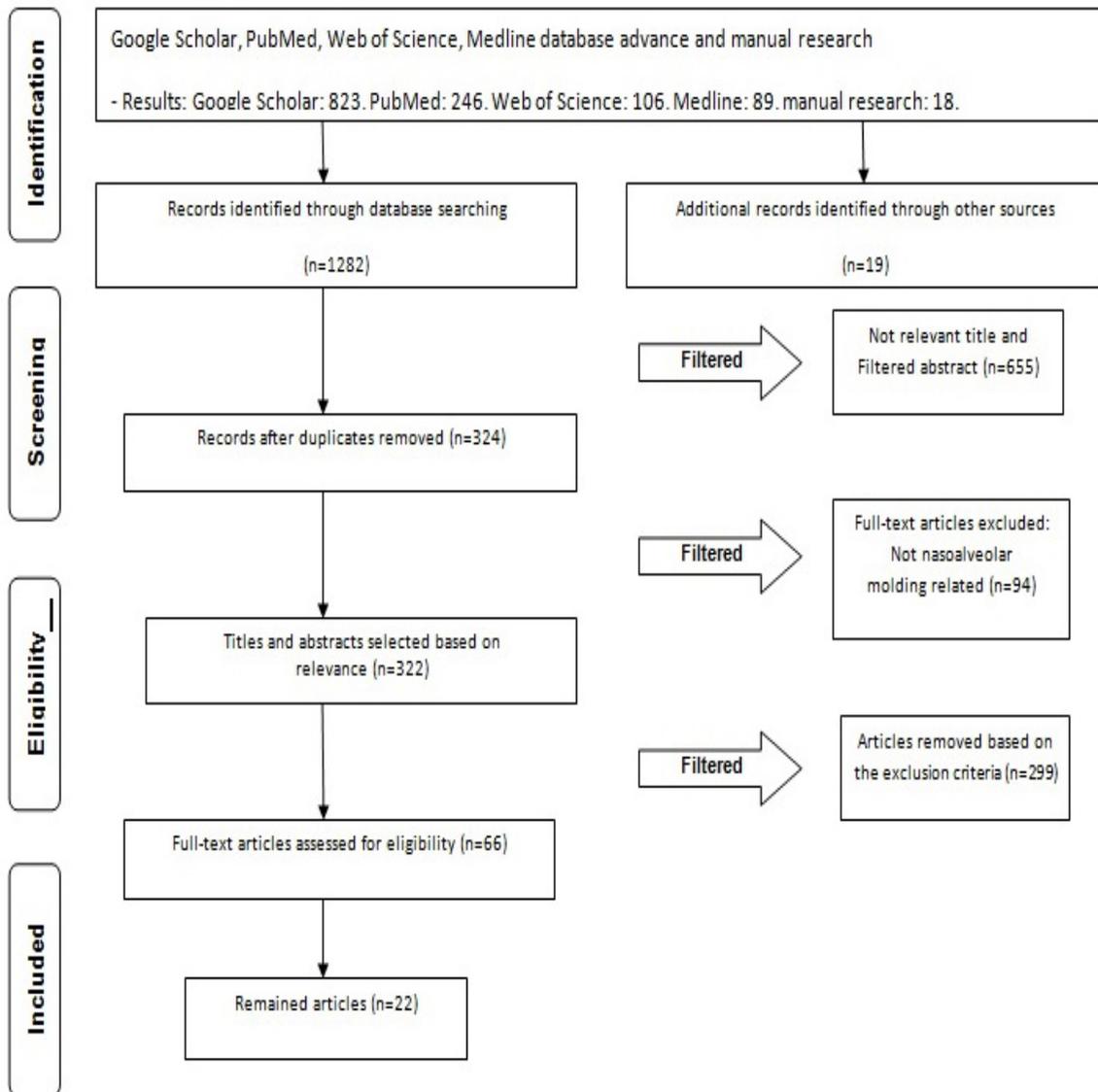


Figure 1. Flow chart of study selection

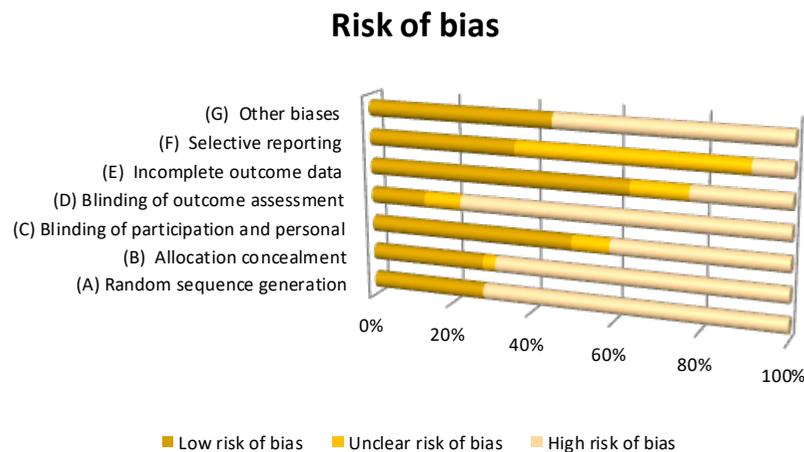


Figure 2. Quality assessment of the articles included in the review process

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on randomized clinical trials. [Figure 2](#) shows the quality assessment of the selected articles.

published in non-English languages ($n=10$) were excluded too.

Quality assessment

To improve the quality of the study, two researchers performed the search process. They agreed on the inclusion and exclusion criteria and resolved their disagreement through discussion sessions. To decrease the risk of bias, they applied Cochrane recommendations (16).

This study involved the assessment of the manuscripts adopting randomized control trials or prospective comparative studies. These studies were performed in 11 different countries: 5 in North America, 3 in South America, and 5 in the Far East. Furthermore, 7, 2, and 1 studies were performed in India, Germany, and Taiwan, respectively. Also, one study was conducted in Iran. Approximately, these studies were performed on 1099 subjects ([Table 1](#)). [Table 2](#) presents the risk of bias assessment for the included trials.

5. Results

The search process identified 1282 articles, of which 960 papers were removed after the initial evaluation due to duplications and relatedness. Accordingly, 322 papers were selected to further the evaluation; however, 299 eligible articles were screened based on the inclusion and exclusion criteria. After a detailed assessment of the full texts of the articles, 22 were selected for the final analysis ([Figure 1](#)).

6. Discussion

The excluded articles were selected in the following process: studies focused on the other presurgical infant orthopedics ($n=53$), studies addressing the NAM therapy of patients with bilateral cleft ($n=10$), studies focused on the animals ($n=1$), papers providing techniques other than NAM ($n=30$), non-comparative articles ($n=27$), experimental studies ($n=2$), descriptive and cross-sectional studies ($n=10$), inaccessibility of the full-text version ($n=4$), and insufficient data ($n=5$). Moreover, retrospective studies ($n=42$), editorial letters ($n=11$), survey of previous experiences ($n=3$), books ($n=2$), case reports ($n=30$), case series ($n=19$), qualitative and narrative articles ($n=26$), systematic reviews ($n=14$), and papers

The decrease in the severity of the initial cleft deformity is the primary purpose of NAM (39). Moreover, this approach paves the way for the repositioning of deformed nasal cartilage and alveolar process. Also, this approach aimed to place lip segments on their proper side without any lip adhesion and scar, as well as to decrease the need for secondary alveolar bone grafts and surgical procedures (39, 40). In the present review, we focused on the two main questions of whether NAM therapy before primary repair surgeries has positive outcomes in UCL/P patients compared with those with no experience of this approach and whether NAM therapy has better results in UCL/P patients compared with other instruments.

Effectiveness of NAM therapy on nasal symmetry and maxillary arch

Several articles confirmed the efficacy of NAM on initial surgeries. Presurgical orthopedics such as NAM is

Table 1. Variables evaluated in the reviewed studies

Authors (Year) References	Country	Sample Size	Type of Study	Technique	Method Assessment	Follow-up	Outcomes
Singh et al. (2007) (17)	USA	N=25 NAM:15 No cleft: 10	Prospective study	Three-dimensional analysis (CAD)	Digital stereophotogrammetry used to capture three-dimensional facial image	37 weeks after CAD 4 weeks after surgery	The three-dimensional facial morphology virtually was indistinguishable from the non-cleft.
Nakamura et al. (2009) (18)	Japan	N=30 NAM:15 Hotz:15	Prospective comparative	Nasal stent impact on nasal and alveolar molding	Two-dimensional photographs casts	1-5 years	The nostril height and width ratio and the height of the top of the alar groove in the correction group were better in NAM, compared with the controls.
Bennun et al. (2009) (19)	Argentina	N=93 NAM:46 No-NAM:48	Prospective comparative	Aesthetic and functional impacts	--	6 years	The nasal morphology differences were less in the NAM group than non-presurgically treated cases.
Mishra et al. (2010) (20)	India	N=34 NAM: 17 No-NAM: 17	Prospective comparative	Nasal stent impact on nasal and alveolar molding	Two-dimensional photographs	1 year	Nasoalveolar molding is a useful approach for the treatment of cleft lip nasal deformity.
Clark et al. (2011) (21)	USA	N=25 NAM:20 No-NAM: 5	Prospective study	Nasal and alveolar molding	Three-dimensional scanner	5 years	There was more improvement in nasal and lip anatomy in the PNAM group.
Isogawa et al. (2010) (22)	Japan	N=10 NAM: 5 Hotz: 5	Prospective study	Nasal stent impact on nasal and alveolar molding	Casts	4 months	The method was effective in nasal molding and alveolar molding in the PNAM group.
Sasaki et al. (2012) (23)	Japan	N=28 NAM:13 Hotz:15	Prospective study	Nasal stent impact on nasal and alveolar molding	Two-dimensional photographs casts	--	Naris morphology was improved, and the cleft gap was smaller in the NAM group.
Yu et al. (2013) (24)	China	N=30 NAM: 15 CAD/CAM: 15	Randomized control study	Three-dimensional analysis (CAD) and printing (CAM)	Measurement on scanned cast	--	There was a difference before and after CAD-NAM therapy in terms of arch length, cleft gap, labial frenum deviation, anteroposterior relation of the cleft to non-cleft segment, and alveolus height.
Liang et al. (2015) (25)	Taiwan	N=84 NAM: 42 No-NAM: 42	Two-group, parallel, retrospective, randomized clinical trial	Nasal stent impact on nasal and alveolar molding	Two-dimensional photographs casts	--	The improvement of the nasal and alveolar of PNAM group was observed before primary cheiloplasty, which facilitated less invasive surgical repair. However, to maintain long-term nostril symmetry, there was no significant difference between the two groups.
Shetty et al. (2012) (26)	India	N=45 NAM:30 No-NAM:15	Prospective study	Nasal and alveolar molding improvement with NAM	Two-dimensional photographs, dentofacial impression	18 months before surgery	There was an improvement in nasal measurements in the NAM group.

Authors (Year) References	Country	Sample Size	Type of Study	Technique	Method Assessment	Follow-up	Outcomes
Monasterio et al. (2010) (27)	Chile	N=40 Grayson: 20 Nasal elevator: 20	Prospective study	Nasal stent impact on nasal and alveolar molding	Two-dimensional photograph casts	3 months before surgery	Two approaches improved nasal asymmetry and reduction of the cleft width.
Chang et al. (2014) (28)	Taiwan	N=15 Grayson:15 Figuroa:15	Randomized prospective, single blind trial	Evolution of the NAM procedure	Two-dimensional photographs	6 months after surgery	Similar results were found in NAM approaches in terms of the nasal outcome.
Rubin et al. (2015) (29)	USA	N=20 NAM: 10 No-NAM: 10	Quasi-experimental study	Impact on primary repair surgeries	Two-dimensional photographs	Before the surgery	The necessity of secondary nasal revision surgery was 3% and 21% in the NAM group and in the non-NAM group, respectively.
Shetty et al. (2016) (30)	India	N=150 1 month: 50 1 - 6 months: 50 6 months to 1 year: 50	Prospective study	Nasal and alveolar molding improvement with NAM	Cast landmark	1 year	There was a decrease in the nasal height, nasal dome height, columella height, and intersegment distance after NAM therapy.
Broder et al. (2016) (31)	USA	N=100 NAM: 62 No-NAM: 48	Non-randomized, prospective multicenter study	Impact on primary repair surgeries	Two-dimensional photographs	13 months	The better post-surgery outcome was reported in the NAM group compared to the non-NAM group, especially concerning the appearance of the nose.
Ritschl et al. (2016) (32)	Germany	N=12 CAD NAM: 6 traditional NAM: 6	Prospective comparative	Compare traditional NAM with CAD technology	--	--	There were similar outcomes in the two groups.
Cerón et al. (2016) (33)	Colombia	N=32 NAM: 16 Hotz: 16	Prospective comparative	Evolution of the NAM procedure	Three-dimensional laser scanning	Yes	Cleft depth was highly improved in the NAM group at the larger segment. The deeper cleft was observed in children treated with Hotz compared to PNAM.
Rachwalski et al. (2017) (34)	India	N=80 NAM: 40 No-NAM: 40	Prospective comparative	Evolution of the NAM procedure	Digital three-dimensional laser scanning	Yes	There was an increase in nasal height, nasal width. Moreover, the columellar length was closer to a natural columellar angle in patients who underwent PNAM therapy, compared to those without PNAM.
Shetty et al. (2017) (35)	India	N=120 NAM: 60 No-NAM: 60	Prospective comparative analysis	Evolution of the NAM procedure	Digital three-dimensional laser scanning	Long-term	Reduced intersegment distance following PNAM improves arch symmetry and stability and prevents an arch collapse in the long-term.
Astani et al. (2018) (36)	Iran	N=40 NAM: 26 No-NAM: 14	Prospective comparative analysis	Evolution of the NAM procedure	Two-dimensional photographs	--	There was a difference in the nasopharyngeal volume of the NAM group. There was no significant difference in oropharyngeal and total pharyngeal airway.

Authors (Year) References	Country	Sample Size	Type of Study	Technique	Method Assessment	Follow-up	Outcomes
Singh et al. (2018) (37)	India	N=22 Grayson:11 Figueroa:11	Prospective analysis	Evolution of the NAM procedure	Digital three-dimensional laser scanning	--	There were similar results on the increase of nostril height and nostril width in the NAM group. The reduction of the alveolar gap and expansion of the arch width was better in Figueroa's approach.
Grill et al. (2018) (38)	Germany	N=14 CAD/ CAM:170 Rapid- NAM:7	Prospective analysis	Evolution of the NAM procedure	Digital three-dimensional laser scanning	--	There was an increase in the cleft-side nasal height and better nose symmetry towards symmetry after the application of the two approaches.

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NAM: nasoskeletal molding; CAD: computer-aided design; CAM: computer-aided manufacturing; PNAM: pre-surgical nasoskeletal molding.

Table 2. Quality assessment of the study articles

Publication	Adequate Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Outcome Assessors	Incomplete Outcome Data Addressed	Free of Selective Reporting	Free of Other Biases
Singh et al. (2007) (17)	No	No	No	No	No	No	Unclear
Nakamura et al. (2009) (18)	No	No	Unclear	No	No	Unclear	Unclear
Bennun et al. (2009) (19)	No	Unclear	No	No	Unclear	No	Unclear
Mishra et al. (2010) (20)	Yes	Yes	No	No	Yes	Yes	Unclear
Clark et al. (2011) (21)	No	No	Yes	No	No	Unclear	Yes
Isogawa et al. (2010) (22)	No	No	No	No	Unclear	Unclear	Unclear
Sasaki et al. (2012) (23)	No	No	Unclear	Unclear	Yes	Unclear	Unclear
Yu et al. (2013) (24)	No	No	No	No	Yes	Unclear	Unclear
Liang et al. (2015) (25)	Yes	Yes	Yes	No	No	Unclear	Yes
Shetty et al. (2012) (26)	Yes	Yes	Yes	No	Yes	Unclear	Yes
Monasterio et al. (2010) (27)	No	No	No	No	Yes	Unclear	Unclear
Chang et al. (2014) (28)	Yes	Yes	Yes	No	No	Unclear	Yes
Rubin et al. (2015) (29)	No	No	No	No	Unclear	Yes	Unclear
Shetty et al. (2016) (30)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes

Publication	Adequate Sequence Generation	Allocation Concealment	Blinding of Participants	Blinding of Outcome Assessors	Incomplete Outcome Data Addressed	Free of Selective Reporting	Free of Other Biases
Broder et al. (2016) (31)	No	No	Yes	No	Yes	Yes	Yes
Ritschl et al. (2016) (32)	Yes	Yes	No	No	Yes	Yes	Unclear
Cerón et al. (2016) (33)	No	No	Yes	No	Yes	Unclear	Yes
Rachwalski et al. (2017) (34)	No	No	Yes	No	Yes	Unclear	Yes
Shetty et al. (2017) (35)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Astani et al. (2018) (36)	Yes	Yes	Yes	No	Yes	Yes	Yes
Singh et al. (2018) (37)	Yes	Yes	Yes	No	Yes	Yes	Yes
Grill et al. (2018) (38)	No	No	No	No	Unclear	Yes	Unclear

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used to improve facial symmetry before the operation in patients with UCL/P (11). Following a 12-month or longer observation, Matsuo et al. showed that using NAM during the first week of life (for three months) leads to superior nasal shape symmetry in comparison with traditional surgeries (41). A study conducted by Clark et al. indicated the improvement in the long-term nasal symmetry in patients who had NAM in combination with alveolar molding, compared with those without NAM. Moreover, they showed long-term clinical improvement in nasal and lip anatomy but not in dental arch configuration, as well as occlusion of patients who underwent NAM, compared with those without NAM. A remarkable improvement in nasal symmetry and normalization of the dental arch was demonstrated in a short-time study conducted by Ezzat et al. (42).

Based on a study performed by Jaeger et al., NAM therapy may lead to nostril overexpansion (43). Therefore, orthodontic force should be kept low enough to prevent the extension of soft tissues constituting the nasal cavity during the longitudinal correction. Sasaki et al. showed a remarkable decrease in the alveolar cleft after NAM therapy. The improvement in the naris morphology is due to the modification of the position of the maxillary bone and the elevation of cartilage by stent insertion (23).

Deficient columella, overhanging nasal apex, and depressed dome have remained as the main problems after cheiloplasty (44, 45). Based on one study, a reduc-

tion in the deficient columella, depressed dome, wide alar width, and deviated nasal septum were reported after using PNAM (46). A comparative study conducted by Liang et al. on the long-term effect of the nasal contour between patients underwent NAM and those without NAM revealed that NAM improved nasal symmetry after cheiloplasty (25). A normal anatomical position in the columella, philtral column, the apex of the nose, and nasal ala were reported three months after using PNAM. The main advantages of PNAM include lengthening of the deficient columella, repositioning of the deformed nasal cartilage, and decreasing the intra-alveolar gapless, limitation of invasive surgery, and reducing recovery time. Nasoalveolar molding decreased cleft width, premaxillary protrusion, and deviation, and increased the arch circumference, columellar length, and width. Moreover, it can improve maxillary midline and nasal symmetry (10, 24, 42, 47-50)

The slight overcorrection of the alar dome on the cleft direction is suggested by Singh et al. (48), which is the short-term positive effect of nasoalveolar molding reported in many studies (10, 24, 42, 47-50). However, the long-term impact of this approach is still challenging. According to one study, an increase in nose symmetry would remain until early childhood (48), while other studies indicate a relapse of columella length in some cases after three years of follow-up (47) and relapse of nostril shape (10).

According to a study conducted by Baek and Son, NAM leads to positive effects in the anterior and posterior alveolar segments in cases with UCL/P (50). Based on another study, alveolar height decreased in UCL/P neonates who were treated with computer-aided design-as alveolar molding (CAD-NAM). This result was indicative of the inhibitory impact of the traction force of the appliance on the vertical development of the alveolar bone (24).

In the NAM approach, anterior alveolus in the non-cleft position is moved inward, and both sides of alveolar segments shape the normal arc form. Due to the vertical component forces of the retention tapes, the alveolar height and canine segments decrease after NAM therapy. This means that this process prevents the vertical growth of alveoli. However, presurgical orthopedics by intraoral devices are still challenging due to an unclear effect of NAM therapy on the alveolar growth inhibition and upper alveolar growth.

The growth process may affect the nasal structure and even the shape of the nose after the operation. There is no available parameter for digitizing the results of the surgery. Therefore, the investigation of the relationship between the cleft jaw and the shape of the nasal cavity is challenging. There are various measures to evaluate the nasal morphology (47, 48); however, when the deformities are complex, the results of surgery cannot be assessed by simple estimation of the ratio of height to width of the alar groove or angles. Hausdorff distance is a parameter determining the geometrical resemblance between two objects that provides an accurate value even for complicated graphics. A high correlation between Hausdorff distance and the human visual assessment of symmetry is reported by Sasaki et al., which is very important in analyzing the aesthetics of the nose (23).

Cerón-Zapata et al. showed a reduction in the interior dimension of the cleft in all UCL/P patients who underwent NAM in comparison with patients with no experience of NAM (33). This finding was in line with a study conducted by Mishima et al. (51). A reduction in the width of the cleft in the anterior segment after treatment with active plates was observed in another study (52). In a study performed by Cerón-Zapata et al., anterior width mainly decreased using the PNAM approach compared with the Hotz appliance, which may be due to the lip adhesion with the use of the tape. The decrease in the width of the alveolar cleft could be considered a positive predictor of the surgical outcome. However, there was no significant difference between PNAM

and Hotz appliance regarding the changes in intercanine width. The decrease in width at the canine area distance was larger using the Hotz plate than PNAM, which can be due to the soft material of the plate (33). However, Mishima et al. study showed contradictory results (51). Moreover, both PNAM and Hotz increased the length and depth of the cleft, which indicated the potential of maxillary segments in the neonatal period (33).

Stable reduction in the width of the mid-part of the larger and smaller segments due to the treatment with the plate was reported by another study (50). Age is another main predictor of treatment success. The main goal of presurgical orthopedics in UCL/P neonates is the alignment of maxilla segments and premaxilla into a normal form. The efficacy of NAM in the repositioning of maxillary segments and facilitating the surgical repair of nasal deformities is reported in many studies (53-55). The NAM therapy helps to create a better outcome by reforming the lower lateral cartilages, decreasing the gap, and aligning the gingiva. The correction of the gap may prevent a step deformity, and the lip repair is performed under less tension with the possibility of acquiring enough closure to allow a more straightforward repair (21).

According to Shetty et al., alveolar clefts were narrowed using PNAM before cheiloplasty. Moreover, PNAM can facilitate the surgery procedure to primary cleft lip closure (56, 57). Quan et al. indicated that CAD-NAM therapy could decrease the alveolar cleft gap and arch length as well as correcting upper denture midline deviation. Moreover, there was a decrease in the outward rotation of the maxillary arch in the non-cleft side and improvement in the contour of the alveolus (24). Other studies also reported the decreased width of the alveolar cleft and the sagittal arch length of the anterior arch after NAM therapy (21, 58).

The CAD-NAM approach is designed for alveolar growth in each modality and maintenance of the maxilla width. Quan et al. showed slight growth in arch width after CAD-NAM therapy. Besides, there was a report of the decrease in the anteroposterior relation of the cleft to non-cleft segment and anteroposterior maxillary alveolar length of the non-cleft side after CAD-NAM therapy for the sagittal dimension, which showed that CAD-NAM could improve the protrusion of the anterior upper alveolus (24).

Moreover, Astani et al. evaluated the morphometrics of pharyngeal airway in patients with a cleft lip and palate, which showed nasopharyngeal volume was dif-

ferent between patients undergoing NAM group compared with the control group. However, there was no confirmation of volumetric differences in oropharyngeal and total pharyngeal airway. Therefore, NAM can enlarge the nasopharyngeal airway size in patients with a cleft lip and palate (36).

Three-dimensional technology

Three-dimensional technology (CAD-CAM) is one of the advanced techniques for medical imaging in which laser surface scanning is applied for obtaining three-dimensional images and providing high-accuracy measurements from the defined sites. This study was an evaluation of the presurgical cleft treatment using a CAM system (36). We found two prospective comparative studies confirming CAD systems as reliable techniques for the assessment and quantification of the nasal and alveolar improvement following NAM therapy (17, 24).

Yu et al. assessed the efficiency of computer-aided design–nasalveolar molding (CAD-NAM) on maxillary alveolar morphology. Rapidform XOR3 software was used to analyze the maxillary morphology and all pre- and post-CAD-NAM variables. They indicated a trend toward morphological improvement in maxillary alveoli. In other words, these findings revealed the obstructive effects of the traction force of CAD-NAM appliance on the vertical growth of the alveolar bone (24).

Another study was performed by Singh et al. to assess three-dimensional (3D) facial morphology in UCL/P patients following NAM. They showed that 3D facial morphology in UCL/P patients was indistinguishable from that in the control group (17). Yilmaz et al. performed a study to evaluate the effects of NAM therapy on 3D nasolabial morphology in UCL/P neonates. They reported an increase in all measurements before and after NAM therapy except for the lip gap, nostril floor width, and nostril diameter, which showed improvement in the nasal and lip symmetry. Three-dimensional technology helps the diagnosis and measurement of the UCLP upper alveolar morphology using laser scanning. With regard to this approach, the treatment procedure could be visible on the computer, and the final treatment goals could be simulated. However, this technology is recently developed and there are not enough prospective comparative studies in this regard. Therefore, it is recommended to conduct future studies with larger sample size and longer follow-up.

Comparison of nasalveolar molding therapies

The researchers found 4 prospective studies comparing the different approaches toward NAM. In Singh et al. study, the effectiveness of the Grayson technique and Figueroa modified presurgical nasalveolar technique were compared with the treatment of UCL/P patients. Based on the obtained results, there was an increase in the nostril height of the cleft side. Also, the nostril width on the cleft side decreased, while there was no difference between the efficacy of Grayson and Figueroa approaches. The reduction of the alveolar gap and increase of the arch width were better in Figueroa technique compared with the Grayson technique (37), which was confirmed by another similar study (27). Besides, the effectiveness of the Grayson approach on the alveolar cleft using adhesive tape tractions across the cleft lip was confirmed by other studies (53, 59). The decreased cleft width likely resulted in the combined impact of redirecting the growth of the alveolar segments by molding plate and active molding (37).

Ritschl et al. compared CAD-NAM with traditional NAM in a study. The findings revealed similar outcomes in the two approaches (32). Another study conducted by Grill et al. aimed to compare two methods of CAD/CAM-NAM and RapidNAM approaches. The results showed an increase in the cleft-side nasal height and better nose symmetry after applying the two approaches (38). In another study conducted by Chang et al., the modified Figueroa and the modified Grayson techniques were compared. The obtained results revealed no significant difference between these two techniques regarding total costs, nostril height, or nostril area ratio (28). Therefore, future studies are recommended in this regard.

Application of nasalveolar molding appliances

McNeil described the modern concept of presurgical maxillary orthopedics in 1950. This approach is still preferred and applied in various types of neonatal maxillary orthopedic appliances. Active, semi-active, and passive devices are the main types of this approach. In active appliances, some force applies to the alveolar segments and move them in a specified side by some appliances, such as spring or screw. In semi-active appliances, the dental cast is divided into sections, and the position of maxillary segments is changed to a more favorable place and forces the palatal segments in a predetermined position when the pre-made plate is placed in the oral cavity (60). In passive appliances, certain regions of the palate are exposed to grinding away acrylic material. The reason for this is to induce arch alignment during

growth, which focused on the correct spontaneous development of the segments and prevented the collapse of cleft segments (60, 61). In nasoalveolar molding, the stent is inserted into the affected nostrils and helps to reform, expand, and reposition the external nasal structures. Accordingly, the palatal segments are repositioned by the intraoral plate. This act is performed when the baby is sleeping (61).

Complications

Because of the imposition of excessive force by the applied appliance of NAM, it is essential to assess and correct the adjustment of the appliance carefully. Irritation of the oral mucosa, gingival tissue, and nasal mucosa are the main complications of this approach (62). Moreover, the lack of oral hygiene or fulltime wear of molding plate may lead to the fungal infection, which can be managed by local nystatin or systemic amphotericin (4).

Short-term and long-term effects

The PNAM is applied widely in patients with cleft lip or palate. Although the short-time effectiveness of PNAM before cheiloplasty is supported, its long-term impacts are still unclear. In this regard, the experience of surgeons plays an important role in the efficacy of this surgery. Based on Shaw et al., the experience of surgeons should be considered as the main factor in the success of the surgery and its outcome (63). The evaluation of the long-term effect of Hotz and Gnoinski revealed that concomitant surgical intervention should be performed with the same technique, at the same timing, and by the same surgeon (64). Therefore, it is recommended to conduct future studies on the long-term effects of nasoalveolar molding.

Since the presurgical orthopedic treatment occurs in the neonatal period, the evolution and estimation of its long-term effects are difficult. Sasaki et al. assessed the impact of NAM therapy in patients aged 3-18 years. The NAM therapy was commonly performed until the end of the primary cleft palate surgery in all reported cases by Sasaki et al. (23).

Research limitations

In this study, we followed the Cochrane tool to assess the risk of bias in the included trials and focused solely on randomized clinical trials. However, data insufficiency and lack of homogeneity among studies were the main limitations of our research, which may lead to bias in our outcome. Besides, the use of different nasoalveo-

lar molding techniques and lack of follow-up in some of the reviewed studies may have affected our findings.

7. Conclusions

Based on the literature review, various studies supported the positive effect of NAM appliance therapy on nasal symmetry in unilateral clefts of the lip and or palate treatment. The NAM therapy is effective in decreasing the severity of the initial cleft deformity, as well as repositioning of deformed nasal cartilage and alveolar process, which has many beneficial results in the surgery outcome. However, the long-term effects of this approach have remained unclear.

Disclaimer

It should be noted that the present study is informative; therefore, the described strategies might not be suitable for other conditions or purposes.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article.

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Conflict of interest

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References

1. Massie JP, Bruckman K, Rifkin WJ, Runyan CM, Shetye PR, Grayson B, et al. The effect of nasoalveolar molding on nasal airway anatomy: A 9-year follow-up of patients with unilateral cleft lip and palate. *The Cleft Palate-Craniofacial Journal*. 2018; 55(4):596-601. [DOI:10.1177/1055665617744062] [PMID]
2. Akcam MO, Evirgen S, Uslu O, Memikoğlu UT. Dental anomalies in individuals with cleft lip and/or palate. *The European Journal of Orthodontics*. 2010; 32(2):207-13. [DOI:10.1093/ejo/cjp156] [PMID]

3. Vig K, Mercado A. The orthodontist's role in a cleft palate-craniofacial team: Orthodontics: Current Principles and Techniques 5th ed. St Louis: Mosby Co; 2012.
4. Murthy PS, Deshmukh S, Bhagyalakshmi A, Srilatha K. Pre surgical nasoalveolar molding: Changing paradigms in early cleft lip and palate rehabilitation. *Journal of International Oral Health*. 2013; 5(2):70-80. [PMCID] [PMID]
5. Moetamedi AK, Feizbakhsh M, Mortazavi M, Derakhshanfar H, Hasheminasab M. Nasoalveolar molding in cleft lip and palate: A review of literature. *Journal of Craniomaxillofacial Research*. 2015; 1(3-4):32-6.
6. Khosla RK, McGregor J, Kelley PK, Gruss JS. Contemporary concepts for the bilateral cleft lip and nasal repair. *Seminars in Plastic Surgery*. 2012; 26(4):156-63. [DOI:10.1055/s-0033-1333885] [PMID] [PMCID]
7. Georgiade NG, Mason R, Riefkohl R, Georgiade G, Barwick W. Preoperative positioning of the protruding premaxilla in the bilateral cleft lip patient. *Plastic and Reconstructive Surgery*. 1989; 83(1):32-40. [DOI:10.1097/00006534-198901000-00008] [PMID]
8. Georgiade NG, Latham RA. Maxillary arch alignment in the bilateral cleft lip and palate infant, using the pinned coaxial screw appliance. *Plastic and Reconstructive Surgery*. 1975; 56(1):52-60. [DOI:10.1097/00006534-197507000-00011] [PMID]
9. Liou EJ-W, Subramanian M, Chen PK, Huang CS. The progressive changes of nasal symmetry and growth after nasoalveolar molding: A three-year follow-up study. *Plastic and Reconstructive Surgery*. 2004; 114(4):858-64. [DOI:10.1097/01.PRS.0000133027.04252.7A] [PMID]
10. Pai BCJ, Ko EWC, Huang CS, Liou EJW. Symmetry of the nose after presurgical nasoalveolar molding in infants with unilateral cleft lip and palate: A preliminary study. *The Cleft Palate-Craniofacial Journal*. 2005; 42(6):658-63. [DOI:10.1597/04-126.1] [PMID]
11. Barillas I, Dec W, Warren SM, Grayson BH. Nasoalveolar molding improves long-term nasal symmetry in complete unilateral cleft lip-cleft palate patients. *Plastic and Reconstructive Surgery*. 2009; 123(3):1002-6. [DOI:10.1097/PRS.0b013e318199f46e] [PMID]
12. Keçik D, Enacar A. Effects of nasoalveolar molding therapy on nasal and alveolar morphology in unilateral cleft lip and palate. *Journal of Craniomaxillofacial Surgery*. 2009; 20(6):2075-80. [DOI:10.1097/SCS.0b013e3181be88cf] [PMID]
13. Green S, Higgins J. *Cochrane handbook for systematic reviews of interventions*. Hoboken: John Wiley & Sons; 2005.
14. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*. 2015; 4(1):1. [DOI:10.1186/2046-4053-4-1]
15. Higgins JP, Green S. *Cochrane handbook for systematic reviews of interventions*; version 5.1.0 [updated March 2011]. Manchester: The Cochrane Collaboration; 2011.
16. Deeks J, Higgins JP, Altman DG, Green S. *Cochrane handbook for systematic reviews of interventions*; version 5.1.0 [updated March 2011]. Manchester: The Cochrane Collaboration; 2016.
17. Singh GD, Levy-Bercowski D, Yáñez MA, Santiago PE. Three-dimensional facial morphology following surgical repair of unilateral cleft lip and palate in patients after nasoalveolar molding. *Orthodontics & Craniofacial Research*. 2007; 10(3):161-6. [DOI:10.1111/j.1601-6343.2007.00390.x] [PMID]
18. Nakamura N, Sasaguri M, Nozoe E, Nishihara K, Hasegawa H, Nakamura S. Postoperative nasal forms after presurgical nasoalveolar molding followed by medial-upward advancement of nasolabial components with vestibular expansion for children with unilateral complete cleft lip and palate. *Journal of Oral and Maxillofacial Surgery*. 2009; 67(10):2222-31. [DOI:10.1016/j.joms.2009.04.098] [PMID]
19. Bennun RD, Langsam AC. Long-term results after using dynamic presurgical nasoalveolar remodeling technique in patients with unilateral and bilateral cleft lips and palates. *Journal of Craniomaxillofacial Surgery*. 2009; 20(Suppl. 1):670-4. [DOI:10.1097/SCS.0b013e318193d5f0] [PMID]
20. Mishra B, Singh AK, Zaidi J, Singh G, Agrawal R, Kumar V. Presurgical nasoalveolar molding for correction of cleft lip nasal deformity: Experience from northern India. *Eplasty*. 2010; 10:e55. [PMCID] [PMID]
21. Clark SL, Teichgraeber JF, Fleshman RG, Shaw JD, Chavarria C, Kau CH, et al. Long-term treatment outcome of presurgical nasoalveolar molding in patients with unilateral cleft lip and palate. *The Journal of Craniomaxillofacial Surgery*. 2011; 22(1):333-6. [DOI:10.1097/SCS.0b013e318200d874] [PMID] [PMCID]
22. Isogawa N, Ochiai S, Mito T, Kindaichi J, Ishibashi N, Takagi Y, et al. Three-dimensional comparison in palatal forms between modified presurgical nasoalveolar molding plate and Hotz's plate applied to the infants with unilateral cleft lip and palate. *Singapore Dental Journal*. 2010; 31(1):36-42. [DOI:10.1016/S0377-5291(12)70008-1]
23. Sasaki H, Togashi S, Karube R, Yanagawa T, Nakane S, Tabuchi K, et al. Presurgical nasoalveolar molding orthopedic treatment improves the outcome of primary cheiloplasty of unilateral complete cleft lip and palate, as assessed by naris morphology and cleft gap. *Journal of Craniomaxillofacial Surgery*. 2012; 23(6):1596-601. [DOI:10.1097/SCS.0b013e31825196dc] [PMID]
24. Yu Q, Gong X, Shen G. CAD presurgical nasoalveolar molding effects on the maxillary morphology in infants with UCLP. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2013; 116(4):418-26. [DOI:10.1016/j.oooo.2013.06.032] [PMID]

25. Liang Z, Yao J, Chen PK, Zheng C, Yang J. 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. *The Cleft Palate-Craniofacial Journal*. 2018; 55(7):935-40. [DOI:10.1597/14-296] [PMID]
26. Shetty V, Vyas H, Sharma S, Sailer H. A comparison of results using nasoalveolar moulding in cleft infants treated within 1 month of life versus those treated after this period: Development of a new protocol. *International Journal of Oral and Maxillofacial Surgery*. 2012; 41(1):28-36. [DOI:10.1016/j.ijom.2011.09.002] [PMID]
27. Monasterio L, Ford A, Gutiérrez C, Tastets ME, García J. Comparative study of nasoalveolar molding methods: Nasal elevator plus DynaCleft® versus NAM-Grayson in patients with complete unilateral cleft lip and palate. *The Cleft Palate-Craniofacial Journal*. 2013; 50(5):548-54. [DOI:10.1597/11-245] [PMID]
28. Chang CS, Wallace CG, Pai BCJ, Chiu YT, Hsieh YJ, Chen JJ, et al. Comparison of two nasoalveolar molding techniques in unilateral complete cleft lip patients: A randomized, prospective, single-blind trial to compare nasal outcomes. *Plastic and Reconstructive Surgery*. 2014; 134(2):275-82. [DOI:10.1097/PRS.0000000000000361] [PMID]
29. Rubin MS, Clouston S, Ahmed MM, Lowe K, Shetye PR, Broder HL, et al. Surgeons' assessment of presurgical clefts and predicted surgical outcome in patients treated with and without nasoalveolar molding. *The Journal of Craniofacial Surgery*. 2015; 26(1):71-5. [DOI:10.1097/SCS.0000000000001233] [PMID] [PMCID]
30. Shetty V, Thakral A, Sreekumar C. Comparison of early onset nasoalveolar molding with patients who presented for molding up to 1 year of age. *Journal of Oral and Maxillofacial Surgery*. 2016; 74(4):811-27. [DOI:10.1016/j.joms.2015.08.004] [PMID]
31. Broder HL, Flores RL, Clouston S, Kirschner RE, Garfinkle JS, Sischo L, et al. Surgeon's and caregivers' appraisal of primary cleft lip treatment with and without nasoalveolar molding: A prospective multicenter pilot study. *Plastic and Reconstructive Surgery*. 2016; 137(3):938-45. [DOI:10.1097/01.prs.0000479979.83169.57] [PMID] [PMCID]
32. Ritschl LM, Rau A, Güll FD, Wolff KD, Schönberger M, Bauer FX, et al. Pitfalls and solutions in virtual design of nasoalveolar molding plates by using CAD/CAM technology-A preliminary clinical study. *Journal of Cranio-Maxillofacial Surgery*. 2016; 44(4):453-9. [DOI:10.1016/j.jcms.2016.01.008] [PMID]
33. Cerón-Zapata A, López-Palacio A, Rodríguez-Ardila M, Berrio-Gutiérrez L, De Menezes M, Sforza C. 3D evaluation of maxillary arches in unilateral cleft lip and palate patients treated with nasoalveolar moulding vs. Hotz' s plate. *Journal of Oral Rehabilitation*. 2016; 43(2):111-8. [DOI:10.1111/joor.12350] [PMID]
34. Rachwalski M, Pullan S, Parmar R, Shetty P, Sharma P, Bonanathaya K. Nasal aesthetics in unilateral cleft lip and palate with and without presurgical nasoalveolar molding: A preliminary assessment. *International Journal of Oral and Maxillofacial Surgery*. 2017; 46(1):68. [DOI:10.1016/j.ijom.2017.02.246]
35. Shetty V, Agrawal R, Sailer H. Long-term effect of presurgical nasoalveolar molding on growth of maxillary arch in unilateral cleft lip and palate: Randomized controlled trial. *International Journal of Oral and Maxillofacial Surgery*. 2017; 46(8):977-87. [DOI:10.1016/j.ijom.2017.03.006] [PMID]
36. Astani SA, Yilmaz HN, Nevzatoglu S, Demirkaya AA, Acar ZA. Evaluation of airway volume in cleft lip and palate following nasoalveolar molding. *Journal of Craniofacial Surgery*. 2018; 29(8):2143-7. [DOI:10.1097/SCS.00000000000004681] [PMID]
37. Singh A, Thakur S, Singhal P, Diwana VK, Rani A. A comparative evaluation of efficacy and efficiency of grayson's presurgical nasoalveolar molding technique in patients with complete unilateral cleft lip and palate with those treated with figueroa's modified technique. *Contemporary Clinical Dentistry*. 2018; 9(Suppl 1):S28-33. [DOI:10.4103/ccd.ccd_820_17] [PMID] [PMCID]
38. Grill FD, Ritschl LM, Dikel H, Rau A, Roth M, Eblenkamp M, et al. Facilitating CAD/CAM nasoalveolar molding therapy with a novel click-in system for nasal stents ensuring a quick and user-friendly chairside nasal stent exchange. *Scientific Reports*. 2018; 8(1):12084. [DOI:10.1038/s41598-018-29960-z] [PMID] [PMCID]
39. Grayson BH, Maull D. Nasoalveolar molding for infants born with clefts of the lip, alveolus and palate. *Clinics in Plastic Surgery*. 2004; 31(2):149-58. [DOI:10.1016/S0094-1298(03)00140-8] [PMID]
40. Yang S, Stelnicki E, Lee M. Use of nasoalveolar molding appliance to direct growth in newborn patient with complete unilateral cleft lip and palate. *Pediatric Dentistry*. 2003; 25(3):253-6. [PMID]
41. Matsuo K, Hirose T, Otagiri T, Norose N. Repair of cleft lip with nonsurgical correction of nasal deformity in the early neonatal period. *Plastic and Reconstructive Surgery*. 1989; 83(1):25-31. [DOI:10.1097/00006534-198901000-00006] [PMID]
42. Ezzat CF, Chavarria C, Teichgraeber JF, Chen JW, Stratmann RG, Gateno J, et al. Presurgical nasoalveolar molding therapy for the treatment of unilateral cleft lip and palate: A preliminary study. *The Cleft Palate-Craniofacial Journal*. 2007; 44(1):8-12. [DOI:10.1597/06-009] [PMID]
43. Jaeger M, Braga-Silva J, 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. *Annals of Plastic Surgery*. 2007; 59(5):489-94. [DOI:10.1097/01.sap.0000259001.98869.d8] [PMID]

44. Chang CS, Por YC, Liou EJW, Chang CJ, Chen PKT, Noordhoff MS. Long-term comparison of four techniques for obtaining nasal symmetry in unilateral complete cleft lip patients: A single surgeon's experience. *Plastic and Reconstructive Surgery*. 2010; 126(4):1276-84. [DOI:10.1097/PRS.0b013e3181ec21e4] [PMID]
45. van der Heijden P, Dijkstra PU, Stellingsma C, van der Laan BF, Korsten-Meijer AG, Goorhuis-Brouwer SM. Limited evidence for the effect of presurgical nasolabial molding in unilateral cleft on nasal symmetry: A Call for Unified Research. *Plastic and Reconstructive Surgery*. 2013; 131(1):62e-71e. [DOI:10.1097/PRS.0b013e318267d4a5] [PMID]
46. Maull DJ, Grayson BH, Cutting CB, Brecht LL, Bookstein FL, Khorrambadi D, et al. Long-term effects of nasolabial molding on three-dimensional nasal shape in unilateral clefts. *The Cleft Palate-Craniofacial Journal*. 1999; 36(5):391-7. [DOI:10.1597/1545-1569_1999_036_0391_tleonn_2.3.co_2]
47. Liou EJW, Subramanian M, Chen PK. Progressive changes of columella length and nasal growth after nasolabial molding in bilateral cleft patients: A 3-year follow-up study. *Plastic and Reconstructive Surgery*. 2007; 119(2):642-8. [DOI:10.1097/01.prs.0000239600.79638.6f] [PMID]
48. Singh GD, Levy-Bercowski D, Santiago PE. Three-dimensional nasal changes following nasolabial molding in patients with unilateral cleft lip and palate: Geometric morphometrics. *The Cleft Palate-Craniofacial Journal*. 2005; 42(4):403-9. [DOI:10.1597/04-063.1]
49. Spengler AL, Chavarria C, Teichgraber JF, Gateno J, Xia JJ. Presurgical nasolabial molding therapy for the treatment of bilateral cleft lip and palate: A preliminary study. *The Cleft Palate-Craniofacial Journal*. 2006; 43(3):321-8. [DOI:10.1597/05-093R.1] [PMID]
50. Baek SH, Son WS. Difference in alveolar molding effect and growth in the cleft segments: 3-dimensional analysis of unilateral cleft lip and palate patients. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2006; 102(2):160-8. [DOI:10.1016/j.tripleo.2005.09.009] [PMID]
51. Mishima K, Sugahara T, Mori Y, Sakuda M. Three-dimensional comparison between the palatal forms in complete unilateral cleft lip and palate with and without Hotz plate from cheiloplasty to palatoplasty. *The Cleft Palate-Craniofacial Journal*. 1996; 33(4):312-7. [DOI:10.1597/1545-1569(1996)0332.3.CO; 2] [PMID]
52. Ross RB. Treatment variables affecting facial growth in complete unilateral cleft lip and palate; Part 1: Treatment affecting growth. *The Cleft Palate Journal*. 1987; 24(1):5-77. [PMID]
53. Grayson BH, Santiago PE, Brecht LE, Cutting CB. Presurgical nasolabial molding in infants with cleft lip and palate. *The cleft palate-Craniofacial journal*. 1999; 36(6):486-98. [DOI:10.1597/1545-1569_1999_036_0486_pnmiiw_2.3.co_2]
54. Honda Y, Suzuki A, Ohishi M, Tashiro H. Longitudinal study on the changes of maxillary arch dimensions in Japanese children with cleft lip and/or palate: Infancy to 4 years of age. *The Cleft Palate-Craniofacial Journal*. 1995; 32(2):149-55. [DOI:10.1597/1545-1569(1995)0322.3.CO; 2] [PMID]
55. Grayson BH, Cutting CB. Presurgical nasolabial orthopedic molding in primary correction of the nose, lip, and alveolus of infants born with unilateral and bilateral clefts. *The Cleft Palate-Craniofacial Journal*. 2001; 38(3):193-8. [DOI:10.1597/1545-1569_2001_038_0193_pnomip_2.0.co_2]
56. Huddart A. Presurgical changes in unilateral cleft palate subjects. *The Cleft Palate Journal*. 1979; 16(2):147-57. [PMID]
57. Weil J. Orthopaedic growth guidance and stimulation for patients with cleft lip and palate. *Scandinavian Journal of Plastic and Reconstructive Surgery*. 1987; 21(1):57-63. [DOI:10.3109/02844318709083581] [PMID]
58. Sabarinath V, Thombare P, Hazarey P, Radhakrishnan V, Agrekar S. Changes in maxillary alveolar morphology with nasolabial molding. *Journal of Clinical Pediatric Dentistry*. 2010; 35(2):207-12. [DOI:10.17796/jcpd.35.2.f80u21362566qr34] [PMID]
59. Deng X, Zhai J, Jiang J, Li F, Pei X, Wang H. [A clinical study of presurgical nasolabial molding in infants with complete cleft lip and palate (Chinese)]. *Chinese Journal of Stomatology*. 2005; 40(2):144-6. [PMID]
60. Kuijpers-Jagtman AM. Cleft lip and palate: Role of the orthodontist in the interdisciplinary management team. In: Krishnan V, Davidovitch ZE (editors). *Integrated Clinical Orthodontics*. Hoboken: John Wiley & Sons; 2012. [DOI:10.1002/9781118702901.ch9]
61. Peterson-Falzone SJ, Hardin-Jones MA, Karnell MP. *Cleft palate speech*. St Louis: Mosby Co; 2001.
62. Grayson BH, Shetye PR. Presurgical nasolabial moulding treatment in cleft lip and palate patients. *Indian Journal of Plastic Surgery*. 2009; 42(Suppl. 1):S56. [DOI:10.1055/s-0039-1699377]
63. Shaw WC, Dahl E, Asher-McDade C, Brattstrom V, Mars M, McWilliam J, et al. A six-center international study of treatment outcome in patients with clefts of the lip and palate; Part 5: General discussion and conclusions. *The Cleft Palate-Craniofacial Journal*. 1992; 29(5):413-8. [DOI:10.1597/1545-1569(1992)0292.3.CO; 2]
64. Hotz MM, Gnoinski WM. Effects of early maxillary orthopaedics in coordination with delayed surgery for cleft lip and palate. *Journal of Oral and Maxillofacial Surgery*. 1979; 7(3):201-10. [DOI:10.1016/S0301-0503(79)80041-7]