Dental developmental stage affects the treatment outcome of maxillary protraction in skeletal Class III children: A systematic review and metaanalysis

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Background: The aim of this study was to investigate the effect of the stage of dental development on the treatment outcome of maxillary protraction in skeletal Class III children.

Materials and methods: The Medline, Web of Science, Embase, Cochrane Library, CMB and CNKI database were searched to identify all of the relevant articles published prior to 30 August 2019. The grey literature was also searched. Human controlled clinical trials in which patients with a skeletal Class III malocclusion were treated by maxillary protraction (facemask with or without rapid maxillary expansion) were considered. The quality of the included studies was assessed using ROBINS-I. Meta-analysis was performed using RevMan 5.3.

Results: A total of 19 trials were included in the systematic review and 16 trials were included in the meta-analysis, of which three studies were assessed as low risk of bias (high quality), eight were assessed as having a moderate risk of bias, and five were assessed as a high risk of bias. The treatment effect of maxillary protraction in skeletal Class III children was greater in the primary dentition than that in the early mixed dentition with respect to an increase in SNA, ANB and SN/GoGn. The treatment effect was greater in the early mixed dentition than in the late mixed dentition, with an evident decrease in SNB. The treatment effect was greater in the early mixed dentition than that which occurred in the early permanent dentition, with an increase in SNA and ANB. The treatment effect was not significantly different, either between the primary dentition and late mixed dentition, or between the late mixed dentition and early permanent dentition. No study compared the treatment effect between the primary dentition.

Conclusion: The dental developmental stage affects the treatment effect of maxillary protraction in skeletal Class III children. The treatment effect at an early dentition stage may be more effective than that at a late dentition stage in improving a skeletal Class III relationship. Although the variations in effectiveness between the various dental stage groups were generally statistically significant, most variations were small, with unclear clinical significance.

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Introduction

A skeletal Class III malocclusion may involve maxillary hypoplasia, or mandibular hyperplasia, or a combination of both. It has been found that approximately two-thirds of subjects presenting with a skeletal Class III malocclusion have maxillary hypoplasia,¹ which negatively affects orofacial aesthetics and function.

Maxillary protraction therapy using a facemask (reverse headgear) is invariably used for the treatment of skeletal Class III malocclusion as a result of maxillary hypoplasia in growing patients.²⁻⁴ The principle of maxillary protraction includes opening the maxillary sutures, increasing cartilagenous and subperiosteal osteogenesis, promoting a favourable clockwise rotation of the mandible in low angle cases, and inhibiting unfavourable forward and downward growth of the mandible.^{5,6}

The optimal timing for maxillary protraction therapy is still cause for debate. A number of studies have found that maxillary protraction therapy carried out at an early age is more effective than that performed at a later age in improving a skeletal Class III relationship.^{2,3,7-9} For example, a study using pubertal growth to select and group patients found that maxillary protraction applied at a pre-pubertal or mid-pubertal age showed greater orthopaedic effects than at late-puberty.7 An additional study using chronological age to group patients showed that maxillary protraction therapy is more effective in patients under 10 years of age than in patients older than 10 years.¹⁰ In contrast, further studies have found that a patient's age had little influence on the effectiveness of maxillary protraction therapy.¹¹⁻¹⁴ For example, a study in patients with mixed dentitions (deciduous and permanent dentitions were not included) reported similar therapeutic responses when maxillary protraction began either before or after eight years of age.¹¹ An additional study also found no statistical difference in the treatment outcome of maxillary protraction in patients aged between seven and 12 years, and the amount of skeletal change between the protraction groups subdivided by age was not statistically significant.¹² The controversy regarding the optimal timing of maxillary protraction therapy was mainly due to the inconsistencies within the participants and the different methodologies used in the reported studies that did not include the deciduous dentition.

Therefore, the aim of this systematic review was to investigate the effect of the stage of dental development (i.e., primary dentition, early mixed dentition, late mixed dentition and early permanent dentition) on the treatment outcome of maxillary protraction in skeletal Class III children.

Materials and methods

This systematic review followed the ROBINS-I (Risk Of Bias In Non-randomised Studies of Interventions) guidelines, as a tool for assessing the risk of bias in non-randomised studies of interventions.^{15,16}

Search strategy and databases

A systematic search to identify all of the relevant studies was conducted within the following databases: MEDLINE (via PubMed; no restrictions were employed regarding language or year of publication), Web of Science, EMBASE, CENTRAL (The Cochrane Library), CBM (Chinese Biological Medical) database and CNKI (Chinese National Knowledge Infrastructure) database. A supplemental manual search was conducted by reviewing the reference lists of the related papers and review articles. The search strategy included controlled vocabulary and free terms. It was developed for MEDLINE and adapted for the other databases (Table I). The grey literature was searched on SIGLE (System for Information on Grey Literature in Europe), Clinicaltrial.gov, OpenGrey and the World Health Organization's International Clinical Trial Registry Platform. The grey literature consists of papers that have not been published or have been published informally or non-commercially, such as government reports, statistics, patents, and conference papers and posters. All searches were conducted on 30 August 2019.

Eligibility criteria

The inclusion criteria for the studies were participants who were patients presenting with a skeletal Class III malocclusion caused by maxillary hypoplasia from the period of the primary dentition to the early permanent dentition whose intervention involved maxillary protraction therapy using a facemask (with or without rapid maxillary expansion). A comparison was provided by untreated Class III patients who were

	Search history	Number of results
#1	Maxillary protraction OR facemask OR face mask OR facial mask OR reverse headgear	6340
#2	Class III OR Class 3	189199
#3	Malocclusion, Angle class III [Mesh]	3528
#4	#2 OR #3	189199
#5	Primary dentition OR deciduous dentition	15204
#6	Early mixed dentition OR late mixed dentition OR mixed dentition OR early permanent dentition	3589
#7	#5 OR #6	17327
#8	#1 AND #4 AND #7	78

Table I. Search strategy used for PubMed.

matched for age and gender and whose outcomes were skeletal and dentoalveolar variables measured on lateral cephalometric radiographs. The study designs were randomised clinical trials (RCTs), controlled clinical trials (CCTs) or cohort studies and the published papers provided the original data or the data could be obtained from a primary source. The exclusion criteria of the studies were identified by case reports, review articles, conference papers, patients treated with other orthodontic or orthopaedic appliances, and patients affected by cleft lip/palate and/or other craniofacial syndromes.

Data extraction

Two calibrated reviewers (W.M. and D.Z.) independently screened the titles and abstracts of the identified studies. Consensus was obtained by discussion and consultation with the third reviewer (Y.P.) to resolve any disagreements during study selection and data extraction. The two reviewers (W.M. and D.Z.) independently extracted data from the studies using a data extraction form. The following information was collected: author and year of publication, country of origin, study design, number and age of participants, details of interventions and controls, assessment methods, and cephalometric outcomes.

Methodological quality appraisal

Each study was assessed using the evaluation method recommended by the ROBINS-I.^{15,16} Bias domains included bias due to confounding, bias due to the selection of participants into the study, bias due to intervention classification, bias due to deviations from intended interventions, bias due to missing data, bias

due to outcome measurement and bias due to the selection of the reported result. The overall risk of bias of each study was assessed as low, moderate, serious, critical risk of bias or no information. In the present review, studies assessed at low risk of bias were defined as 'high quality', whereas others were considered as 'low quality'.^{15,16}

Statistical analysis

Review Manager version 5.3 (The Cochrane Collaboration, 2012) was used for the metaanalysis.^{17,18} Mean differences (MD) and standard mean differences (SMD) with 95% confidence intervals (95% CI) were calculated for all of the evaluated variables. SMD were used when the calculation of identical effects differed between the studies. P < 0.05was considered statistically significant for pooled MD or SMD determined by two-tailed Z-tests. Statistical heterogeneity between the studies was evaluated by the Cochrane Chi-square test based on the Q-test and the I² static. When I² < 50%, a fixed-effects model was applied, and when $I^2 > 50\%$, a random-effects model was applied. A fixed-effects model was applied when only two studies met the inclusion criteria and deemed sufficient to perform a meta-analysis. The publication and other reporting biases were assessed using the Begg's test if at least six studies were included in a meta-analysis. Egger's test was used to quantify the small study effects or publication bias by Stata 14.0 (STATA Corp., TX, USA).¹⁸

Results

Study selection

A total of 136 articles were screened for relevance (Figure 1). After applying inclusion and exclusion



Figure 1. Flow Diagram.

criteria, 97 studies did not meet the inclusion criteria and were excluded. A total of 39 full papers were retrieved and reviewed, among which 20 articles were excluded for the reasons given in Figure 1. Finally, 19 studies^{2-4,7-9,11-14,19-27} were included in the systematic review.

Characteristics of the included studies

The 19 trials included in the present review were published between 1993 and 2017 (12 studies were conducted in Asia, four in Europe, and three in North America), describing a total of 767 participants who were evaluated and grouped into primary dentition

Study	Location	Study design	Dentition (year of age)	Sample size	Appliance
Kajiyama 2004	Japan	CCT	Primary (5.6) Early mixed (8.7)	Primary (N=34) Early mixed (N=29)	FM
Lee 2010	South Korea	CCT	Primary (6.1) Early mixed (8.4)	Primary (N=26) Early (N=23)	FM
Saadia 2000	Mexico	CCT	Primary (3-6) Early mixed (6-9) Late mixed (9-12)	Primary (N=38) Early mixed (N=55) Late mixed (N=19)	FM+RME
Saadia 2001	Mexico	CCT	Primary (3-6) Early mixed (6-9) Late mixed (9-12)	Primary (N=38) Early mixed (N=55) Late mixed (N=19)	FM+RME
Fareen 2017	Malaysia	CCT	Early mixed (8-9) Late mixed (10-11)	Early mixed (N=20) Late mixed (N=26)	FM
Atalay 2010	Turkey	CCT	Early mixed (8.18) Late mixed (11.75)	Early mixed (N=15) Late mixed (N=15)	FM
Cha 2003	South Korea	CCT	Early mixed (9.82) Late mixed (11.31) Early permanent (13.07)	Early mixed (N=34) Late mixed (N=32) Early permanent (N=19)	FM+RME
Wang 2002	China	CCT	Early mixed (7.3) Late mixed (11.7)	Early mixed (N=32) Late mixed (N=11)	FM+RME
Baccetti 2000	Italy	CCT	Early mixed (5.5-7.8) Late mixed (7.8-10)	Early mixed (N=16) Late mixed (N=13)	FM+RME
Baccetti 1998	Italy	CCT	Early mixed (6.9) Late mixed (10.3)	Early mixed (N=23) Late mixed (N=23)	FM+RME
Merwin 1997	Hong Kong	CCT	Early mixed (6.8) Late mixed (10.2)	Early mixed (N=15) Late mixed (N=15)	FM+RME
Liu 2013	China	CCT	No information (8-15)	Late mixed (N=14) Early permanent (N=15)	FM
Yuksel 2001	Turkey	CCT	Late mixed (9.8) Early permanent (12.6)	Late mixed (N=17) Early permanent (N=17)	FM
Takada 1993	Japan	CCT	Early mixed (7.8) Late mixed (10.3) Early permanent (12)	Early mixed (N=20) Late mixed (N=22) Early permanent (N=19)	FM
Baik 1995	South Korea	CCT	Early mixed (<10) Late mixed (10-12) Early permanent (>12)	Early mixed (N=11) Late mixed (N=21) Early permanent (N=15)	FM+RME
Kapust 1998	America	CCT	Primary dentition (4-7) Early mixed (7-10) Late mixed (10-14)	Primary dentition (N=15) Early mixed (N=32) Late mixed (N=16)	FM+RME

Table II. Characteristics of the included studies.

CCT = Controlled clinical trial; FM = Facemask; RME = Rapid maxillary expansion.

(N = 98), early mixed dentition (N = 325), late mixed dentition (N = 244), and early permanent dentition (N = 85) (Table II).

The interventions used in the included studies were FM (facemask) and FM+RME (facemask and rapid maxillary expansion). The studies of Saadia et al.^{13,21} appeared to be the same research with different

cephalometric measurements, therefore these two studies were merged into one in the quantitative meta-analysis.

The treatment outcomes assessed in the included studies included SNA, SNB, ANB, SN/GoGn, ANS-Me, overjet and the Wits appraisal.

Quality assessment of the included studies

After a quality assessment, three of the included studies^{2,8,27} were assessed as low risk of bias (high quality), eight studies^{3,4,7,14,20,24-26} were assessed as having a moderate risk of bias, and five studies^{11,13,21-23} were assessed as having a high risk of bias (Table III). When assessing bias due to confounding factors, the severity of the maxillary retrusion was considered as the most important factor influencing intergroup comparability. When assessing bias due to deviations from intended interventions, the timing and force of maxillary protraction that might affect the treatment outcomes and prognosis were considered as the most important factors.

The Egger's tests (Table IV) showed no publication bias in most of the measurements, except the SN/ GoGn (P = 0.022) and ANS/Me (P = 0.001) in the

comparison between the early mixed dentition and late mixed dentition.

Meta-analysis between the primary dentition and early mixed dentition

Five studies were included in the meta-analysis between the primary dentition and early mixed dentition (Figure 2). The treatment outcomes of maxillary protraction involved in the meta-analysis included SNA, SNB, ANB, SN/GoGn and ANS-Me. The treatment effect was significantly greater in the primary dentition than that produced in the early mixed dentition with respect to an increase in SNA (MD = 1.23° , 95% CI = 0.19 - 2.27, P = 0.02), ANB (MD = 1.80° , 95% CI = 0.39 - 3.20, P = 0.01), SN/GoGn (MD = 0.82° , 95% CI = 0.29 - 1.34, P

Table III. Risk of bias of the included studies assessed by ROBINS-I (Risk Of Bias In Non-randomized Studies of Interventions).

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
Kajiyama 2004	Moderate	Moderate	Low	Low	Low	No information	Low	Moderate
Lee 2010	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Saadia 2000	Serious	Moderate	Low	Low	Low	No information	Low	Serious
Saadia 2001	Serious	Moderate	Low	Low	Low	No information	Low	Serious
Fareen 2017	Low	Low	Low	Low	Low	Low	Low	Low
Atalay 2010	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Cha 2003	Moderate	Serious	Low	Low	Low	Low	Low	Serious
Wang 2002	Serious	Serious	Low	Low	Low	Low	Low	Serious
Baccetti 2000	Moderate	Low	Low	Low	Low	No information	Low	Moderate
Baccetti 1998	Low	Low	Low	Low	Low	No information	Low	Low
Merwin 1997	Serious	Serious	Low	Low	Low	Low	Low	Serious
Liu 2013	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Yuksel 2001	Moderate	Moderate	Low	Low	Low	No information	Low	Moderate
Takada 1993	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Baik 1995	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
Kapust 1998	Low	Low	Low	Low	Low	Low	Low	Low

Table IV. Egger's test for the analysis of small study effects on publication bias.

	SNA	SNB	ANB	SN/GoGn	ANS/Me	Overjet
Primary dentition vs early mixed dentition	0.539	0.704	0.639	0.054	N/A	N/A
Early mixed dentition vs late mixed dentition	0.099	0.217	0.195	0.022*	0.001*	0.313
Late mixed dentition vs early permanent dentition	0.764	0.144	0.576	0.207	N/A	0.220

* P < 0.05; N/A = Not applicable.

= 0.002), and ANS-Me (MD = 1.57 mm, 95%CI = 0.65–2.49, P < 0.001). No significant differences were found in SNB (MD = -0.61°, 95% CI = -1.76 – 0.54, P = 0.30) between the two groups.

Meta-analysis between the early mixed dentition and late mixed dentition

Twelve studies were included in the meta-analysis between the early mixed dentition and late mixed dentition (Figure 3). The treatment outcomes of maxillary protraction involved in the meta-analysis included SNA, SNB, ANB, SN/GoGn, overjet and ANS-Me. The treatment effect was greater in the early mixed dentition than that produced in the late mixed dentition with respect to an increase in overjet (MD = -0.74 mm, 95% CI = -0.98 - -0.50, P < 0.001) and ANS-Me (MD = -1.13 mm, 95%CI = -1.45 - -0.80, P < 0.001), and a decrease in SNB (MD = -0.45°, 95% CI = -0.85 - -0.06, P = 0.03). No significant difference was found in the changes of SNA (MD = -0.39° , 95% CI = -0.82-0.05, P = 0.08), ANB (MD) = 0.01°, 95% CI = -0.47 - 0.48, P = 0.98), and SN/ GoGn (MD = -0.21° , 95%CI = -0.42 - 0.00, P = 0.05) between the two groups.

Meta-analysis between the late mixed dentition and early permanent dentition

The meta-analysis included five studies conducted between the late mixed dentition and early permanent dentition (Figure 4). The treatment outcomes of maxillary protraction involved in the meta-analysis included SNA, SNB, ANB, SN/GoGn, overjet and Wits. There was no statistically significant difference between the two groups in all outcomes, including SNA (MD = 0.61°, 95% CI = -0.16 - 1.38, P = 0.12), SNB (MD = -0.10° , 95% CI = -0.79 - 0.59, P = 0.78), ANB (MD = 0.75° , 95% CI = -0.48 - 1.99, P = 0.23), SN/GoGn (MD = 0.67° , 95% CI = -0.83 - 2.18, P = 0.38), overjet (MD = 0.38 mm, 95% CI = -0.45 - 1.22, P = 0.37), and Wits (MD = -0.37 mm, 95% CI = -2.07 - 1.32, P = 0.67).

Meta-analysis between the early mixed dentition and early permanent dentition

The meta-analysis included three studies conducted between the early mixed dentition and early permanent dentition (Figure 5). The treatment outcomes of maxillary protraction involved in the meta-analysis included SNA, SNB and ANB. The treatment effect was greater in the early mixed dentition than that produced in the early permanent dentition with respect to an increase in SNA (MD = 1.02° , 95% CI = 0.05 - 2.0, P = 0.04) and ANB (MD = 1.89° , 95% CI = 1.27 - 2.50, P < 0.001). No significant difference was found in SNB (MD = -0.69° , 95% CI = -2.08 - 0.70, P = 0.33) between the two groups.

Meta-analysis between the primary dentition and late mixed dentition

The meta-analysis included two studies conducted between the primary dentition and late mixed dentition (Figure 6). The treatment outcomes of maxillary protraction involved in the meta-analysis included SNA, SNB and ANB. The treatment effect was significantly greater in the primary dentition than that produced in the late mixed dentition with respect to an increase in SNA (MD = 0.62° , 95% CI = 0.03–1.21, P = 0.04) and ANB (MD = 1.21° , 95% CI = 0.51 - 1.92, P < 0.001). No significant difference was found in SNB (MD = -0.44° , 95% CI = -0.91 - 0.04, P = 0.07) between the two groups.

Meta-analysis between the primary dentition and early permanent dentition

No study comparing the treatment effect of maxillary protraction between the primary dentition and the early permanent dentition was included in this review.

Discussion

Maxillary protraction using a facemask is applied for the treatment of a skeletal Class III malocclusion. An important factor influencing the treatment effect of protraction therapy is considered by many to be the timing of treatment. Maxillary protraction has been carried out in growing patients at a variety of ages and dental stages, ranging from the primary dentition to the early permanent dentition. The optimal timing for maxillary protraction, however, is still unclear. The findings of the present systematic review suggest that the dental stage affects the treatment outcome of maxillary protraction for a hypomaxillary skeletal Class III malocclusion. The treatment effect at an early dental stage was more effective than that undertaken at a late dental stage in improving a skeletal Class



Figure 2. Meta-analysis between primary dentition and early mixed dentition.

The efficacy assessment of the primary dentition group for Class III malocclusion versus the early mixed dentition group. The comparison was performed using five indices. 1: Angle SNA. The primary dentition group presented a greater increase in SNA than the early mixed dentition group (MD = 1.23, 95% Cl = 0.19 - 2.27, P = 0.02). 2: Angle SNB. There were no significant differences in SNB between the primary dentition group and the early mixed dentition group (MD = -0.61, 95% Cl = -1.76 - 0.54, P = 0.30). 3: Angle ANB. The primary dentition group presented a greater increase in ANB than the early mixed dentition group (MD = 1.80, 95% Cl = 0.39 - 3.20, P = 0.01). 4: SN/GoGn angle. The primary dentition group presented a greater increase in SN/GoGn angle than the early mixed dentition group (MD = 0.82, 95% Cl = 0.29 - 1.34, P = 0.002). 5: ANS-the length. The primary dentition group showed a greater increase in ANS-the length than the early mixed dentition group (MD = 1.57 mm, 95% Cl = 0.65 - 2.49, P < 0.001).



Figure 3. Meta-analysis between early mixed dentition and late mixed dentition.

The efficacy assessment of the early mixed dentition group for Class III malocclusion versus the late mixed dentition group. The comparison was performed using six indices. 1: Angle SNA. There were no significant differences in SNA between the two groups (MD = -0.39, 95% Cl = -0.82 - 0.05, P = 0.08). 2: Angle SNB. The early mixed dentition group presented a greater decrease in SNB than the late mixed dentition group (MD = -0.45, 95% Cl = -0.45, 95% Cl = -0.47 - 0.48, P = 0.08). 4: SN/GoGn angle. There were no significant differences in SN/GoGn angle between the two groups (MD = -0.21, 95% Cl = -0.42 - 0.00, P = 0.05). 5: ANS-Me length. The late mixed dentition group presented a greater increase in ANS-Me length than the early mixed dentition group (MD = -1.13, 95% Cl = -1.45 - -0.80, P < 0.001). 6: overjet. The late mixed dentition group presented a greater increase in overjet than the early mixed dentition group (MD = -0.74, 95% Cl = -0.98 - -0.50, P < 0.001).

III relationship. However, treatment duration and patient co-operation should not be overlooked when considering early treatment. In addition, although the variations in effectiveness between the various dental stage groups were generally statistically significant, most variations were small. This may affect clinical significance as standard deviations of 2 mm and 2 degrees have been considered as the threshold for clinically meaningful differences.²⁸ It has been found that an extra-oral protrusive force could cause remodelling of the circummaxillary sutures and maxillary tuberosity, as well as produce forward movement and anterior displacement of the maxilla.⁶ Histological studies have shown that maxillary growth is dependent on the sutural activity located at the anterior border of the pterygoid process. The pterygopalatine and zygomaticomaxillary sutures require reaction in craniofacial complex



Figure 4. Meta-analysis between late mixed dentition and early permanent dentition.

The efficacy assessment of the late mixed dentition group for Class III malocclusion versus the early permanent dentition group. The comparison was performed using six indices. 1: Angle SNA. There were no significant differences in SNA between the two groups (MD = 0.61, 95% Cl = -0.16 - 1.38, P = 0.12). 2: Angle SNB. There were no significant differences in SNB between the two groups (MD = -0.10, 95% Cl = -0.79 - 0.59, P = 0.78). 3: Angle ANB. There were no significant differences in ANB between the two groups (MD = -0.10, 95% Cl = -0.28 - 1.99, P = 0.23). 4: SN/GoGn angle. There were no significant differences in SN/GoGn angle between the two groups (MD = -0.67, 95% Cl = -0.83 - 2.18, P = 0.38). 5: overjet. There were no significant differences in overjet between the two groups (MD = -0.38, 95% Cl = -0.45 - 1.22, P = 0.37). 6: Wits. There were no significant differences in Wits between the two groups (MD = -0.37, 95% Cl = -2.07 - 1.32, P = 0.67).



Figure 5. Meta-analysis between early mixed dentition and early permanent dentition.

The efficacy assessment of the early mixed dentition group for Class III malocclusion versus the early permanent dentition group. The comparison was performed using three indices. 1: Angle SNA. The early mixed dentition group presented a greater increase in SNA than the early permanent dentition group (MD = 1.02, 95% Cl = 0.05 - 2.0, P = 0.04). 2: Angle SNB. There were no significant differences in SNB between the two groups (MD = -0.69, 95% Cl = -2.08 - 0.70, P = 0.33). 3: Angle ANB. The early mixed dentition group presented a greater increase in ANB than the early permanent dentition group (MD = 1.89, 95% Cl = 1.27 - 2.50, P < 0.001).

remodelling during the treatment of skeletal Class III malocclusion.²⁹ Although clinical observations have suggested that the pterygopalatomaxillary suture may still be patent during adolescence and may keep playing a role in facial growth, there are few studies that show an accurate fusion time of these sutures prior to puberty.

In addition to chronological age, physiological age associated with dental age has been found to be clinically useful as a maturity indicator determining the pubertal growth period.³⁰ It has been commonly applied in clinical trials when assessing and grouping a patient's growth stage. Previous studies have mostly focused on the mixed dentition and pubertal spurt, and a number of studies have also looked into relatively younger patients in the primary dentition as well as older patients in the early permanent dentition, with encouraging treatment results. Therefore, the present review included a wide range of dental stages; i.e., primary dentition, early mixed dentition, late mixed dentition, and the early permanent dentition.

In the current study, the maxillary protraction carried out during the primary dentition showed greater sagittal improvements than outcomes generated in the early and late mixed dentitions. These findings are in agreement with previous studies,^{3,13,21} which have suggested that early treatment may be worthy of consideration for the management of a skeletal Class III malocclusion once a clear diagnosis is made and helpful patient co-operation occurs. Although the SNB angle decreased significantly more in the early mixed dentition compared with the late mixed dentition, the difference in treatment outcome between the early mixed dentition and late mixed dentition was not clearly evident based on the current meta-analysis. The change in SNB could also be due to the natural growth of the mandible, which resulted in the forward movement of point B leading to a natural change, particularly when patients grow relatively faster during the late mixed dentition than in the early mixed dentition. The improvement in overjet was a result of a skeletal effect (SNA, SN/GoGn and ANS/Me) and a dental effect (inclination of the mandibular incisors).⁶ The maxillary protraction carried out during the late mixed dentition showed similar sagittal improvements as treatment performed during the early permanent dentition, which is consistent with the previous studies.^{4,12} No difference has been found in the effect of maxillary advancement after maxillary protraction between the pre-pubertal and pubertal growth peak groups, but there was less maxillary skeletal advancement in the post-pubertal growth peak group.23

SINA	Primary d	entition g	roup	Late mixed	l dentition g	roup		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Kapust 1998	3.71	1.36	15	1.89	1.4	16	37.2%	1.82 [0.85, 2.79]	
Saadia 2000	1.41	1.66	38	1.5	1.18	19	62.8%	-0.09 [-0.84, 0.66]	
Fotal (95% CI)			53			35	100.0%	0.62 [0.03, 1.21]	◆
Heterogeneity: Chi ² =	9.32, df = 1	P = 0.002	2); l² = 899	%					
Test for overall effect:	Z = 2.05 (P =	= 0.04)							Favours Late mixed dentition group Favours Primary dentition group
SNB	Drimonyd	ontition d		Lato miyor	I dontition a			Maan Difforence	Maan Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Direrence	N Eived 95% Cl
Kanust 1998	-1 19	0.89	15	-1 15	0.92	16	55.7%	-0.04 [-0.68 0.60]	
Saadia 2000	-0.88	1.49	38	0.06	1.19	19	44.3%	-0.94 [-1.65, -0.23]	
Total (95% CI)			53			35	100.0%	-0.44 [-0.91, 0.04]	◆
Heterogeneity: Chi ² =	3.39, df = 1 (P = 0.07)	l² = 71%						
Test for overall effect:	Z=1.81 (P=	0.07)							Favours Primary dentition group Favours Late mixed dentition group
ANB									
Study or Subgroup	Moan	enution (roup Total	Late mixe	a denuition g	Total	Mojaht	Mean Difference	Mean Difference
Kanust 1998	4 9	1.55	15	3.04	1.6	16	40.5%	1 86 0 75 2 971	
Saadia 2000	2.16	1.68	38	1.39	1.65	19	59.5%	0.77 [-0.14, 1.68]	+=-
Total (95% CI)			53			35	100.0%	1.21 [0.51, 1.92]	◆
Hotorogonoity: Chiž -	2.21. df = 1	(P = 0.14)	: l ² = 55%			55			+ <u>+</u> + <u>+</u> + <u>+</u> +
<u> </u>									

Figure 6. Meta-analysis between primary dentition and late mixed dentition.

The efficacy assessment of the primary dentition group for Class III malocclusion versus the late mixed dentition group. The comparison was performed using three indices. 1: Angle SNA. The primary dentition group presented a greater increase in SNA than the late mixed dentition group (MD = 0.62, 95% Cl = 0.03 - 1.21, P = 0.04). 2: Angle SNB. There were no significant differences in SNB between the two groups (MD = -0.44, 95% Cl = -0.91 - 0.70, P = 0.04). 3: Angle ANB. The primary dentition group presented a greater increase in ANB than the late mixed dentition group (MD = 1.21, 95% Cl = 0.51 - 1.92, P < 0.001).

Previous studies have also reported no difference between an early treatment group (7-10 years old) and a late treatment group (11-14 years old),³¹ but the present study applied chronological age, rather than dental age, to group participants. In addition, there was great variation between the included studies regarding the type of appliances, the wear time per day, the force strength applied, and the possible combination with RME (rapid maxillary expansion), which could potentially contribute to the clinical heterogeneity of the studies included in the systematic review. As an example in the quantitative analysis of the study, nine studies used facemask in combination with RME, 2,8,11,13,14,20-23 while seven studies used facemask alone.^{3,4,7,24-27} It was noted that a number of studies reported that there was no significant difference in the treatment outcomes of maxillary protraction with or without RME, except for reduced upper incisor angulation when the RME was performed.^{10,32,33} The follow-up period of the included studies was relatively short, and ranged from six months to two years. The long-term effect of maxillary protraction therapy still requires more well-designed, controlled trials.

Conclusion

The dental stage affected the treatment outcome of protraction in hypoplastic maxillary Class III children.

The treatment effect at an early dental stage may be more effective than that at a later stage in improving the skeletal Class III relationship. However, treatment duration and patient co-operation should not be neglected when considering early treatment. The long-term effect of maxillary protraction therapy still requires more well-designed, controlled trials.

Conflict of interest

The authors declare that they have no conflict of interest.

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