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Review Article

Transverse Skeletal Effects of Rapid Maxillary Expansion in Pre and Post Pubertal Subjects: A Systematic Review

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Keywords: Rapid maxillary expansion; Rapid palatal expansion; Pre-pubertal, Post-pubertal; Skeletal effects

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Abstract

OBJECTIVE: The aim of this systematic review was to assess the transverse skeletal effects of rapid maxillary expansion (RME) in pre and post-pubertal subjects.

MATERIAL AND METHODS: Five databases were searched till May 2018; Pubmed, Cochrane, Scopus, Lilacs and Web of science in addition to the manual search of other sources. There were no language restrictions. Methodological Index for Non-Randomized Studies MINORS was used to assess the quality and risk of bias of the trials included.

RESULTS: Six studies were finally included in the qualitative analysis. A meta-analysis wasn't performed due to the heterogeneity of methodologies and outcomes. All of the included studies showed drawbacks in their structure yielding weak evidence. On the short term, RME caused an increase in the maxillary and lateral-nasal widths in pre-pubertal subjects by 3.4 mm and 3.3 mm, and by 2.8 and 2.2 mm respectively in post-pubertal subjects. Although statistically insignificant, the maxillary width increase was more than that of the post-pubertal subjects by 0.6 mm. Over the long term, expansion produced permanent increases in the transverse dimensions of both the dento-alveolar and skeletal components of the maxilla and circum-maxillary structures in pre-pubertal subjects. The post-pubertal subjects presented with a statistically significant increase only in the later-nasal width by 1.3 mm than the untreated controls with no permanent increase in the skeletal maxillary width.

CONCLUSION: The literature is very deficient regarding the use of skeletal age as a reference in the treatment of skeletal crossbites using RME. Only weak evidence exists supporting the increased maxillary and lateral-nasal widths after tooth-tissue borne RME in pre-pubertal subjects, with these effects being less in the post-pubertal ones.

Introduction

Transverse maxillary deficiency is a common finding among populations, mostly presented with a unilateral or bilateral posterior crossbite. The posterior crossbite is reported to be the most prevalent type of malocclusion occurring between 8% and 22% [1]. Whether skeletal or dental, crossbites should be treated once diagnosed, as it is believed that skeletal crossbites affect TMJ functions, chewing patterns, breathing habits and tongue posture. The main goal of skeletal crossbite correction resulting from a maxillary deficiency is achieving transverse skeletal expansion of the maxilla with the least dental effects allowing optimum coordination of the maxillary and mandibular dental arches.

In 1975, Melsen [2] divided the morphological development of the median palatine suture (MPS) into 3 stages, proposing that opening of the suture through maxillary expansion is best done before the age of 15 years as, after that age, the growth of the suture was observed to be ceased. This conclusion was also highlighted in 1977 when Person and Thilander [3] demonstrated in a histological study that the degree of suture obliteration increases from the juvenile period to adulthood, yet complete suture closure was rarely found until the third decade of life. Accordingly, practitioners for decades have been using the chronological age to decide the treatment of choice for the transverse maxillary skeletal deficiency: slow or rapid maxillary expansion (SME/RME) for that who are under 15 years of age and surgically assisted rapid palatal expansion (SARPE) for those who are above that age [4].

Since categorising subjects by chronological age has many limitations compared to measuring the developmental status of individuals about specific stages of skeletal maturation, Fishman [5] in 1994 correlated between his famous eleven skeletal maturational stages and the percentage of the MPS closure using occlusal radiographs. Surprisingly, the study found that at the maturational age of skeletal maturational index (SMI) 11, only 50% of the MPS was approximated. Since then, authors [6], [7], [8], [9], [10] started to investigate the validity of the chronological age in decision making when it comes to expansion, and a paradigm shift has occurred with an ample of researches [11], [12], [13], [14], [15], [16], [17], [18] aiming at suture separation in young adults through non-surgical RME. These studies tried to make use of the partially fused MPS and performed non-surgical RME in postpubertal subjects. A debate has aroused since then around the success of non-surgical RME in adults when compared to RME in pre-pubertal subjects.

To our knowledge, a well-designed systematic review evaluating the effects of RME in pre- and post-pubertal subjects; according to the skeletal age, hasn’t been conducted yet. Such review would help to deliver the status of evidence to solve this debate and provide a guide to future clinical practice, aiming for the optimum treatment option customised to each patient according to his/her skeletal age.

Hence, the aim of the current systematic review was to provide the answer to the following question: in Pre- and Postpubertal subjects with skeletal maxillary constriction, does rapid maxillary expansion (RME) cause widening in the mid-palatal suture (MPS) and/or an increase/change in any skeletal transverse maxillary measurement?

Material and Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Cochrane handbook for systematic reviews of intervention [19]. The protocol was registered at the Evidence-Based Center, Faculty of Dentistry, Cairo University (online registration was not performed).

Information sources, search strategy, and study selection Pubmed, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library), Lilacs, Web of Science and Scopus were electronically searched till May 2018 with no language restrictions. Details of the PubMed search are shown in table [1]. Manual Search was performed in the following journals *American Journal of Orthodontics & Dentofacial Orthopedics, The Angle Orthodontist, European Journal of Orthodontics, Progress in Orthodontics, Orthodontics & Craniofacial Research* and *Seminars in* Orthodontics (Figure 1).

Table 1: PubMed search strategy

#1	Crossbite OR crossbite OR skeletal crossbite OR skeletal cross bite OR posterior crossbite OR posterior crossbite OR bilateral crossbite OR unilateral crossbite OR constrict* maxilla OR narrow maxilla
#2	Rapid palatal expat* OR rapid maxillary expan* OR palatal expan* OR maxillary expan* OR bone borne maxillary expan* OR tooth borne maxillary expan* OR miniscrews assisted rapid maxillary expan* OR miniscrews assisted rapid palatal expan* OR maxilla* wide* OR Haas OR hyrax
#3 (#1 AND #2)	Cross bite OR crossbite OR skeletal crossbite OR skeletal cross bite OR posterior crossbite OR posterior cross bite OR bilateral crossbite OR unilateral crossbite OR constrict* maxilla OR narrow maxilla AND Rapid palatal expan* OR rapid maxillary expan* OR palatal expan* OR maxillary expan* OR bone borne maxillary expan* OR tooth borne maxillary expan* OR miniscrews assisted rapid maxillary expan* OR miniscrews assisted rapid palatal expan* OR maxilla* wide* OR Haas OR hyrax

At the same time, grey literature and unpublished data were electronically searched at the *Central Library of Cairo University, Egyptian Universities Libraries, Clinical Trials.gov* and *Edinbrugh Research Archive* using the following keywords: “posterior crossbite”, “hyrax”, “rapid maxillary expansion”, “rapid palatal expansion” an “maxillary transverse deficiency”.

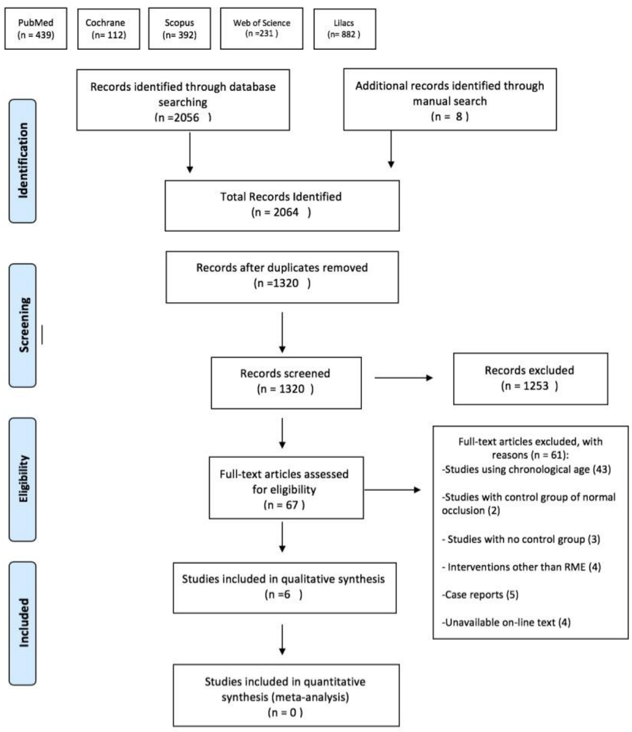

Figure 1: PRISMA diagram of article retrieval

Two investigators (N.S) and (S.K) independently performed the search and any points of disagreements or conflicts were finalized through discussion with the third author (M.F), and the final inclusion of the study was after the agreement.

Eligibility Criteria

The search was conducted upon certain inclusion and exclusion criteria shown in Table 2. An article was considered eligible if it included at least two treatment groups; a study group with rapid palatal expander and an untreated control group. After removal of the internal and external duplicates, the articles obtained from all the databases and manual search were screened by title, abstract and full texts. The full text was obtained when titles and abstracts were insufficient to decide.

Data Items and Collection

The investigators used the identified articles to develop data extraction sheets to, and data were extracted by each investigator independently. The following data were collected: study design, demographic data including participants' maturational status, number, gender and number of groups, an appliance for RME, its anchorage and design, the frequency of activation, retention protocol and timing and method of records collection.

Quality Assessment of Individual Studies

Evaluation of the methodological quality was intended to be performed using the Cochrane Risk of Bias Tool [19] to analyse the risk of bias in RCT's. An overall assessment of the risk of bias (high, unclear, low) was made according to seven criteria for assessment: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of assessors, incomplete outcome data, selective reporting of outcomes, and other potential sources of bias.

MINORS [20] (Methodological Index for Non-Randomized Studies) was the tool of choice for non-randomized controlled and retrospective studies due to its simplicity and reliability. For each article, 12 points were to be assessed: a clearly stated aim, inclusion of consecutive patients, prospective collection of data, endpoints appropriate to the aim of the study, unbiased assessment of the study endpoints, follow up period appropriate to the aim of the study, loss to follow up less than 5%, prospective calculation of the study size, adequate control group, contemporary groups, baseline equivalence of groups and adequate statistical analyses.

The items are scored 0 if not reported, 1 if reported but inadequate or 2 if reported and adequate. The global ideal score is 16 for non-comparative studies and 24 for comparative studies.

Table 2: Inclusion and exclusion criteria of the studies

	Inclusion Criteria	Exclusion Criteria
1. Population	- Any age group concerning the maturational status. - Both sexes - Transverse Skeletal maxillary constriction	- Not referring to the maturational status index - Dental & functional cross bites - Skeletal mandibular asymmetry - Cleft lip and palate - Syndromic patients
2. Intervention	Any rapid palatal expander (tooth-borne or bone-borne)	- SARPE - Corticotomy or any other surgical intervention/ Distractors - Receiving fixed orthodontic treatment or any conjunctive treatment as headgear, face mask, chin cup…etc
3. Comparator	Presence of untreated control groups	If a control group is absent/ with normal occlusion/ receiving any orthodontic treatment
4. Outcomes	The primary outcome of the search was to detect any change in maxillary transverse skeletal measurements following RME. Secondary outcomes included detecting changes in: 1. Nasal airway 2. Maxillary and mandibular dental arches 3. Facial and nasal soft tissues.	Any irrelevant outcome
5. Study Design	1. Randomised clinical trials (RCT's) 2. Quasi-randomised clinical trials. 3. Prospective controlled clinical trials (CCT's) 4. Retrospective controlled trials.	- Abstracts - Comments - Case Reports - Narrative Reviews - Case series - Expert opinion - Systematic reviews and meta-analyses - In vitro studies.

Summary Measures and Approach to Synthesis

The final studies included in this review measured different aspects of the effects RME that made the collected data not combinable. Thus, a meta-analysis was not performed due to the great clinical heterogeneity and variation among the measured outcomes, and only a qualitative analysis was performed.

Results

Study Selection and Characteristics: Two thousand and sixty-four articles were obtained from the electronic search of the five databases and eight articles obtained from the manual search. By applying the inclusion and exclusion criteria, 67 articles were found to be eligible and were read as full text.

Most of the excluded studies [11], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40], [41], [42], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63] divided the samples into treated and untreated control groups according to their chronological age and not according to their skeletal age. Seventeen studies [11], [21], [22], [26], [27], [36], [37], [38], [45], [46], [47], [51], [52], [54], [60], [63], [64], [65] had an untreated control group with normal occlusion or with other types of malocclusions other than posterior crossbites. Other reasons for exclusion included, subjecting the control groups to treatment [11], [32], [44], case reports [66], [67], [68], [69], using interventions other than RME [50], [51], [53], [54], [56], [64], [65], [70] or absence of a control group [31], [71], [72]. Articles which couldn't be retrieved also were excluded [73], [74], [75], [76], [77], [78]. Finally, six trials [12], [79], [80], [81], [82], [83] were included in the qualitative analysis; four prospective controlled studies [79], [80], [82], [83], one retrospective study(12) and one prospective with a retrospective control group [81] that evaluated the long term changes of RME. Two researchers studied the effect of RME in pre and post pubertal subjects [12], [79] while the remaining four articles evaluated the effects in pre-pubertal subjects only [80], [81], [82], [83].

Description of intervention

In the previously mentioned studies, bonded acrylic splints, banded Haas, bonded and banded hyrax was used for expansion without using any bone borne appliances. The studies reported that expansion was found sufficient when observing the palatal cusps of the upper molars occluding with the buccal cusps of the lower ones [79], [80], [81], [83] or when the amount of screw expansion reached 10.5mm [12]. One study(82) didn't mention the reference for stopping the activation. Retention protocol varied among the six studies from leaving the appliance in situ for an average of 5 months [81], [83], 65 days [12] and one week then replacement by a removable appliance [79]. The method of retention wasn't mentioned in two studies [80], [82] and only the immediate RME effects were evaluated. The characteristics of the included studies are shown in Table 3.

Risk of Bias within the Studies

As mentioned previously, no RCTs were included in the qualitative assessment, and so the MINORS tool was used for quality assessment. Upon applying the Minors methodological index for grading of the 6 included articles, the resulting scores were found to be below the ideal global score 24 [20]. The highest score recorded was 21[83], and the last one was 13 [79]. All the studies had lack of blinding in measurements. The studies didn't report any dropouts or change in follow up sample ratio and lacked proper sample size calculations Table 4.

Results of Individual Studies

Treatment effects of the RME were analyzed according to each study's main outcome: postero-anterior radiographs [12], digital dental casts [81], [83], acoustic Rhinometry [79], 3 dimensional stereo-photogrammetry [80] and direct measurements of the nasal soft tissues were used [82] and shown in Table 5.

Table 3: Design, patients' demographic characteristics, treatment duration and retention, interventions, and outcomes of studies included in the qualitative synthesis.

	Study Design	Eligibility Criteria Inclusion Criteria	Exclusion Criteria	Total Sample *n*=	Grouping	Appliance Used / Anchorage	Average Tx Time	Retention Protocol	Records Taken, Timing	Reference of Maturation	Outcomes
Baccetti et al (2001) [13]	Retrospective Controlled Trial	NA	NA	42	ETG= 29 LTG=13 ECG=11 LCG=9	Haas -2 turns/day till the expansion screw reaches 10.25mm	About 21 days	Haas kept in place for an average of 65 days (42-75 days)	Postero-anterior X-rays T0,T1, T6	CVM ETG:CVS1-3 LTG: CVS 4-6 ECG:CVS 1-3 LCG:CVS4-6	-Transverse skeletal measurements. -Dental measurements.
Bicakci et al. (2005) [16]	Prospective Controlled Trial	-Transverse maxillary deficiency -Bilateral CB -No history of nasal disease -Presence of adequate nasal cavity space.	NA	58	ETG=16 LTG=13 ECG= 16 LCG= 13	Hyrax (fully tooth& tissue borne) -2turns/ day	23-27 days	Hyrax kept in place for 1w, then a new removable app used for retention for 3m	Acoustic Rhinometry At T0, T1, T2 (T0 &T3 only for controls)	CVM ETG: CVS1-3 LTG: CVS4-6 ETC: CVS-3 LTC: CVS4-6	Minimal cross-sectional area (MCA) of the nasal cavity.
Dindaroglu et al. (2016) [17]	Prospective Controlled Trial	-Skeletal Maxillary Transverse Deficiency -Skeletal development not exceeding MP3 cap stage -No history of orthodontic treatment.	NA	50	S.G= 25 C.G= 25	Bonded type expansion appliance (Extended onto occlusal surface of post teeth) -2turns/ day	14-19 days	NA	3D Stereo-photogrammtric images in NHP (natural head position) At T0,T1	MP3 cap stage	Facial soft tissue changes
Geran,et al (2006) [18]	Prospective Controlled Trial with a retrospective control	-Crowding -Lingual CB -Esthetics -The tendency towards a CI.II malocclusion	NA	77	S.G=51 C.G= 26	Bonded acrylic splint appliances (Bonded acrylic splints covered upper D, E,6) -1turn/day	NA	Appliance left in place for 5m, then stabilisation with a palatal plate full time for 12m	Digital dental casts T0, T6 (after completion of phase II treatment), T7	CVM (CVS 1-3)	Transverse dental changes, molar angulation
Santariello et al. (2014) [19]	Prospective Controlled Clinical Trial	NA	NA	102	S.G= 61 C.G= 41	Banded Hyrax on upper 6 -Protocol of activation NA	NA	NA	Nasal Soft Tissue Width Measurement. T0, T1, T3	CVM (CVS 1-3)	Changes in nasal soft tissue dimensions
Ugolini et al. (2016) [20]	Prospective Controlled Clinical Trial	-Unilateral posterior CB -Early or mid-mixed dentition stage -Angle Cl.I or Cl.II - CVS 1-3 -No orthodontic treatment in maxilla or mandible	-Angle CI.III -Previous orthodontic treatment. -Hormonal imbalances -TMD, Arthritis -Craniofacial Abnormalities	48	S.G= 33 C.G= 15	-Banded Haas, tooth tissue supported -2turns/ day	3w	Haas was left in situ 5-9 m	Digital dental casts At T0, T4	CVM (CVS 1-3)	Transverse mandibular dental changes.

CB; crossbite, CVS; cervical vertebral stage, ETG; early treated group, ETC: early treated control, LTG; late treated group, LTC; late treated control, SG; study group, CG; control group, T0; pre-expansion, T1; immediate post-expansion, T2; 3 months post-expansion, T3; 6 months post expansion, T4; 1 year post- expansion, T5; 3 years post- expansion, T6; 5 years post-expansion, T7: 10 years post expansion.

Bacetti et al., [12], assessed the short and long term skeletal and dental effects of RME in both pre and post-pubertal subjects. On the short term, RME was found to cause more skeletal effects in the pre-pubertal than the post pubertal subjects, causing a statistically significant increase in the latero-nasal width (1.1 mm more than the post-pubertal group) and a statistically insignificant increase in maxillary width (0.6 mm more than the post-pubertal subjects). In both groups, increments for maxillary intermolar width were about 9 mm. Regarding the long-term effects, in the pre and post-pubertal groups, RME therapy produced a significant net gain over the controls of 2.7 mm and 3.5 mm in maxillary intermolar width, respectively. This increase was associated with a significant skeletal maxillary widening and an increase in the laternonasal width only in the early-treated group by 3mm and 2.3 mm respectively. Bicakci et al., [79] evaluated the overall changes produced by RME in both pre and post-pubertal subjects.

Table 4: Applying the MINORS tool on the 6 included studies

	Accetti et al (2001) [13]	Icakci et al (2005) [16]	Indaroglu et al (2016) [17]	Eran et al (2006) [18]	Antariello et al (2014) [19]	Golini et al (2016) [20]
Clearly stated aim	2	2	2	1	2	2
Inclusion of consecutive patients	1	2	2	2	2	2
Prospective Collection of Data	0	1	2	1	2	2
Endpoints appropriate to the aim of the Study	2	2	2	1	2	1
Unbiased assessment of study endpoint	0	0	0	0	0	0
Follow up period appropriate to the aim of Study	2	2	2	2	2	2
Loss to follow up less than 5%	2	0	0	2	0	2
Prospective calculation of the study size	0	0	2	0	0	2
Adequate control group	2	2	1	2	1	2
Contemporary Groups	0	0	2	0	2	2
Baseline Equivalence of Groups	1	0	1	2	1	2
Adequate Statistical Analyses	2	2	2	2	2	2
TOTAL SCORE	**4**	**3**	**8**	**5**	**5**	**1**

They revealed that there was a statistically significant increase in the nasal minimum cross-sectional area (MCA) by 0.34 cm^2 and 0.19 cm^2, and a significant gain over the controls of 0.26 cm^2 and 0.17 cm^2, in both groups respectively. Although the increase in MCA was greater in the pre-pubertal group, the difference was not statistically significantly greater than the post-pubertal group.

Table 5: Main outcomes of the studies included in the search.

Skeletal Measurements (median)

Study		T1-T0 ETG	T1-T0 LTG	T6-T0 ETG	T6-T0 ETC	T6-T0 LTG	T6-T0 LTC
Baccetti et al (2001) [13]	Bizygomatic width	0.4	0.3	10.2	11.6	3.2	2.2
	Maxillary Width	3.4	2.8	4.3	1.3	1.8	0.9
	Lateronasal width	3.3	2.2	4.5	2.2	2.2	0.7

Nasal Measurements — MCA (T2-T0)

Study	ETG	ETC	LTG	LTC
Bicakci et al. (2005 [16]	0.34± 0.26	0.08± 0.10	0.19±0.16	0.02± 0.03

Nasal Measurements — Nasal Soft Tissue Width

Study		SG T1-T0	SG T3-T0	SG T3-T1	CG T3-T0
Santariello et al. (2014) [17]	AB	0.42	0.36	-0.06	-0.09
	GAC	0.88	0.79	-0.09	-0.14

Facial Soft tissue — T1-T0

Study		U Face	L Face	U Lip	L Lip	Nose
Dindaroglu et al. (2016) [18]	SG	0.42 ± 0.17	0.69 ± 0.30	0.62 ± 0.28	0.60 ± 0.34	0.41 ± 0.21
	CG	0.16± 0.08	0.18 ± 0.07	0.13 ± 0.09	0.17 ± 0.11	0.12 ± 0.07

Dental Measurements — T1-T0 (median) / T6-0

Study		T1-T0 ETG	T1-T0 LTG	T6-0 ETG	T6-0 ETC	T6-0 LTG	T6-0 LTC
Baccetti et al (2001) [13]	U6 width	9.3	8.1	3.2	0.5	3.5	0.0
	L6 width	0.7	0.2	0.7	0.4	1.4	-0.9

Dental Measurements — T6-T0

Study			SG	CG
Geran et al. (2006) [19]	IMW	U	4.3 ± 2.0	0.9 ±1.1
		L	1.7 ± 1.5	1.9±1.8
	IPW 2nd	U	5.3 ± 2.0	1.5 ± 1.4
		L	3.2 ± 1.5	2.5±1,8
	IPW 1st	U	5.3 ±2.0	1.6 ±1.3
		L	4.1 ±1.8	3.4± 2.2
	ICW	U	4 ± 1.6	1.4 ±1.5
		L	1.5±1.6	1.0±1.7
	Arch Perimeter	U	0.9 ± 3.2	-1.8 ±2.3
		L	-2.4 ±3.4	-4.4 ±2.5
	Molar angulation	U	6.2 ±5.6	3.2 ±4.1
		L	-5.4 ±6.7	-3.3 ±5.7

Dental Measurements — T4-T0

Study		SG	CG
Ugolini et al. (2016) [20]	L IMW	1.1 ± 1.5	-0.8 ± 0.8
	L ICW	0.4 ± 1.6	-0.6 ±0.8
	Molar angulation	5.2 ±6.3	-3.5 ±5.5
	Canine angulation	0.7 ±6.4	-4.4 ±5.8
	Incisor angulation	1.9 ±3.6	-2.4 ±3.7

AB; distance bet the widest points of the nose insertion into the soft tissues of the face, GAC; distance bet right and left alae, IMW; intermolar width, IPW 2ND: interpremolar width at 2nd premolar, IPW 1st; interpremolar width at 1st premolar, ICW; intercanine width, U; upper, L; lower, ETG; early treated group, ETC: early treated control, LTG; late treated group, LTC; late treated control, SG; study group, CG; control group, T0; pre-expansion, T1; immediate post-expansion, T2; 3 months post- expansion, T3; 6 months post expansion, T4; 1 year post-expansion, T5; 3 years post- expansion, T6; 5 years post- expansion, T7: 10 years post expansion.

Long term treatment changes with RME followed by fixed appliances were assessed by Geran et al., [81] in pre-pubertal subjects.

Their results showed that RME produced greater increments in all variables for maxillary and mandibular arch widths when compared with the controls. Maxillary arch perimeter increased in the study group by (0.9 mm) and decreased in the control group by (1.8 mm). On the other hand, the mandibular arch perimeter decreased less in the study group by (–2.4 mm) versus (– 4.4 mm) in the control group. Long term treatment changes with RME followed by fixed appliances were assessed by Geran et al., [81] in pre-pubertal subjects. Their results showed that RME produced greater increments in all variables for maxillary and mandibular arch widths when compared with the controls. Maxillary arch perimeter increased in the study group by (0.9 mm) and decreased in the control group by (1.8 mm). On the other hand, the mandibular arch perimeter decreased less in the study group by (–2.4 mm) versus (– 4.4 mm) in the control group.

Regarding the effect of RME on soft tissue nasal width in pre-pubertal subjects, Santariello et al., [82] reported an increase in the distance between the widest points of the right and left alae of (0.8 ± 0.2 mm) in the study group with insignificant changes in the distance between the widest points of the insertion of the nose into the soft tissues of the face. When compared to the control group after a retention period of 6 months, a statistically significant increase of only the GAC width was found in the study group.

Spontaneous mandibular response to RME in pre-pubertal subjects was assessed by Ugolini et al., [83] 15 months post-expansion. The study reported a significant increase in the mandibular intermolar width by 1.9 mm. Control subjects showed a tendency towards contraction of the transverse dimensions and a decrease in a molar, canine, and inferior incisor angulation values.

Discussion

Summary of Evidence

Since the debate is still ongoing, and there is no exact recommendation of the best timing or age to perform a successful RME, hence the aim of the present review had emerged. The objective of this systematic review was to search the literature for any valid evidence supporting the effects of RME in pre and post-pubertal subjects.

RME has many effects on the nasomaxillary complex other than transverse maxillary expansion and correction of crossbites. Effects of RME were studied on skeletal transverse, vertical and anteroposterior position of the nasomaxillary structures [84], [85], maxillary and mandibular transverse arch dimensions [86], [87], upper airway dimensions [88], [89], bite force, changes in the masticatory cycle and occlusal force distribution [90], swallowing [25] and condylar response [91], [92], [93], changes in head posture and scapular position, natural head position [94], enamel demineralization and white spot lesion formation [23], [57], hearing loss [95], [96], nocturnal enuresis [21], [97], [98], eruption of 3rd molars [55], Class II div1 [99], speech and voice function [58], [100], [101], obstructive sleep apnea(102), tongue posture [103] and Holdaway soft tissue analysis [104]. Effects of RME have also been studied on basal bone changes even in the absence of crossbites [105].

For almost four decades, since Melsen [2] revealed the three maturational stages of the MPS, concepts surrounding RME had greatly changed. Great variability of suture fusion among different age groups had been shown [5], [8], [106] Trials that correlate the MPS maturation with different skeletal maturity methods are increasingly aiming to find the eldest adolescent or youngest adult that could benefit from RME treatment [7], [10], [11], [13], [18], [107]. Hence, the time to shift to using the individual’s skeletal age rather than the chronological age to gain the maximum effects out of non-surgical RME. Thus, one of the most important inclusion criteria of the studies in this review was dividing the sample according to their skeletal age. Moreover, including studies with untreated control groups was also important to overcome the confounding effect of the craniofacial growth during the study period [35], [43]. The control group had to have a transverse skeletal deficiency as well because various malocclusions are associated with a distinctive craniofacial pattern [108], so it would make more sense to compare subjects with the same malocclusion.

Upon searching the literature, this systematic review included both prospective and retrospective controlled studies that classify their samples according to their skeletal age. Sixty-seven articles were read by full text, and only 6 articles were finally included, four of which were prospective controlled trials, one was a prospective trial with a retrospective control and the final study was a retrospective trial. No well-designed RCTs were found to be eligible for this search, and most of the trials included in this search had methodological problems. None of the studies included assessed the effects of bone- borne RME and instead, tissue and tooth borne RME were studied. Bone borne RME might have yielded different results in this case. The outcomes of the six studies were quite variable as shown in Table 3. Two trials studied the effects of RME on the dental arches: Geran et al., [81] measured the change in both the upper and lower intermolar width, interpremolar width, intercanine width and molar angulation after 5 years of expansion in pre-pubertal patients.

On the other hand, Ugolini et al., [83] measured the changes mentioned above only in the lower arch 15 months following RME, and so the pooling of the results into a quantitative search was impossible as the study endpoints were extremely different. Hence, a meta-analysis wasn't performed. Although non-comparable to one another, the conclusions of Geran et al., [81] resembled that of an earlier systematic review [109] evaluating the long-term dental changes following RME. Two studies [11], [45] included in the mentioned review evaluated the long-term changes on dental casts showing an increase in both the maxillary and mandibular intermolar width with the increase being greater in the maxillary arch.

Since the demand for perfect esthetics is becoming as important as obtaining comfortable, healthy and stable results after orthodontic treatment, the effect of RME on facial soft tissues was considered as an important secondary outcome in this review. These changes were measured by Dindaroglu et al., [80] using 3 D stereophotogrammetric photographs immediately following RME via 3D deviation analyses on 3D stereophotogrammetric images. Being in close relation to the nasomaxillary complex, the nose changes was of great importance and showed a mean maximum deviation limit of 0.77 ± 0.34mm and -0.94 ± 0.41 mm. On the other hand, Santariello et al., [82] targeted the changes in nasal soft tissue widths following RME in pre-pubertal subjects only. Although statistically significant, the increase in the width of the base of the nose was considered clinically insignificant. Nasal measurements were also the primary outcome of interest of Bicakci et al., [79]; the trial measured the change in the MCA of the nasal cavity using acoustic Rhinometry following RME in pre and post-pubertal subjects. It concluded that RME not only expanded the maxilla but decreased the nasal resistance through effectively increasing the nasal MCA, being more effective in pre-pubertal than post-pubertal patients. This finding is emphasised by a recent trial [110] that assessed the short-term nasal changes following RME in mouth breathers using cone beam computed tomography. The study concluded that not only does RME increases the nasal airway volume, but is also capable of changing the nasal form and function, increasing a mouth breather chances to gradually attain normal nasal breathing. In 2016, a systematic review of systematic reviews and meta-analyses [111] was conducted to assess the dental and skeletal effects of palatal expansion techniques among different chronological age groups. It reported that significantly more favourable immediate skeletal changes occurred when RME was performed before the pubertal growth peak, based on low evidence [112], [113]. This systematic review, however, didn't strictly select the articles that used the skeletal age indices in their subject recruitment strategy. Conclusions of that review were mainly based on the study by Bacetti et al., [12] that assessed the transverse skeletal and dental effects of RME in pre and post-pubertal subjects and reported that maxillary adaptations to RME are more likely to be of a dento-alveolar origin rather than a skeletal one when expansion was performed in post-pubertal subjects. Although being the first study to assess the impact of skeletal age on the results of RME, the trail had many limitations. In addition to being a retrospective study, the inclusion and exclusion criteria of the recruited sample were questionable. It wasn't clear if RME was the sole treatment received by the study group or if expansion was performed in conjunction with other treatment modalities as part of a comprehensive orthodontic treatment. Multiple confounders could have been present at baseline, were the only reported baseline similarity between the study and control groups was the skeletal maturational stage without referring to the type of malocclusion of the control group. Comparing changes following RME in transverse skeletal deficiencies to normal skeletal relationships might be misleading. Also, a great variation among the group sizes was observed where 29 subjects were in the early treated group versus 11 controls, and 13 subjects were in the late treated group versus 9 controls. The study had a high detection bias due to the absence of blinding of outcome assessment. Definitive conclusions can't be withdrawn from such a trial owing to the mentioned methodological limitations Correctly choosing the most applicable tool for quality assessment of the non-randomized studies included in the review was of great importance. An ideal index should be simple, yet highly sensitive and reliable, and hence MINORS was used [20], [114]. Since the global ideal score is 24 for comparative studies [20], any article scoring less than 24 points will be considered as of 'poor quality'. In our search, the included articles scored 14 [12], 13 [79], 18 [80], 15 [81], 15 [82] and 21[83] points in the MINORS scale and hence, all studies give poor-quality evidence supporting their outcome. A definitive conclusion cannot, therefore, be drawn neither upon the short- or long-term skeletal effects of RME nor upon its effects on the nasal airway, maxillary and mandibular dental arches, facial and nasal soft tissues in pre and post-pubertal subjects.

Strengths and Limitations: The current review search strategy had strict inclusion and exclusion criteria, had no language restrictions, included multiple electronic database searches and involved a detailed manual searching process. The evidence retrieved from this systematic review has to be interpreted with caution as retrospective studies were included.

Conclusions

According to the existing evidence from this review, the following conclusions could be stated regarding the transverse skeletal effects of RME in pre and post-pubertal subjects:

1. The quality level of the studies included in this review was not sufficient to draw conclusive evidence regarding the transverse skeletal effects of RME in pre and post-pubertal subjects.

2. Studies considering the skeletal age for a successful RME treatment are very scarce in the literature. The only available weak evidence suggests that patients treated by tooth-tissue borne RME before the pubertal peak exhibit more increase in the skeletal transverse dimension than do post-pubertal ones, with the pre-pubertal sample being more stable in their long-term treatment results than the post-pubertal.

3. Regarding the transverse skeletal effects of RME, as well as its effect on maxillary and mandibular dental arches, nasal airway, facial and nasal soft tissues, weak evidence supports positive changes in those outcomes in pre-pubertal subjects.

4. For post-pubertal subjects, the only available low-quality evidence suggests an increase in the nasal cross-sectional area immediately following RME.

Implications for Research: Carrying out a well-designed randomised controlled clinical trial is strongly recommended to assess the various effects of RME in pre and post-pubertal subjects. Future research should recruit the samples according to their skeletal age and should ensure the presence of a true skeletal maxillary constriction in both the study and control groups.

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