Prostaglandin E$_2$ levels in gingival crevicular fluid during tooth- and bone-borne expansion

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SUMMARY The purpose of this study was to compare Prostaglandin E$_2$ (PGE$_2$) levels in gingival crevicular fluid (GCF) of young adults with maxillary constriction during tooth- and bone-borne expansion. Thirty patients, 15 females and 15 males, with a mean age of 17.3 ± 2.8 years were divided into three groups. Group I consisted of 10 patients, five females and five males, treated by transpalatal distraction (TPD) as a bone-borne device, group II 10 patients, five females and five males, with a Hyrax appliance as a tooth-borne device, and a control group of 10 patients, five females and five males, without any expansion appliances. GCF samples were collected with filter paper strips at six observation periods in order to evaluate the effect of heavy orthopaedic forces in both groups. In group II, the samples were additionally collected at two pre-treatment time points in order to evaluate the effect of the forces generated by the separators. An automated enzyme immunoassay was used to measure PGE$_2$ in the GCF. The differences within the groups were evaluated with a pairwise *t*-test and the differences between the groups were determined by the Mann–Whitney U-test.

The mean PGE$_2$ level was significantly elevated on day 4 after placement of the separators in group II ($P < 0.05$). The PGE$_2$ values in group II were significantly different to those in group I and the controls at all observation periods. Lower PGE$_2$ levels were observed in group I compared with group II and the controls. Expansion using the TPD method could potentially enhance the prognosis of the teeth by inducing more skeletal dental changes when compared with the Hyrax appliance.

Introduction

Bone remodelling is a complex process that is regulated by local factors such as cytokines, and growth and systemic factors such as hormones (Rossi *et al.*, 1996). An acute inflammatory response is initiated with orthodontic forces. Osteoblastic and osteoclastic activities occur as a result of the inflammatory response of the surrounding tissues (Proffit *et al.*, 1986; Grieve *et al.*, 1994; Sarı *et al.*, 2004). Prostaglandins, produced by deformed osteoblasts and gingival fibroblasts, have been implicated in the cytokines of this inflammatory reaction (Saito *et al.*, 1991) Among the subclasses of prostaglandins, Prostaglandin E$_2$ (PGE$_2$) is closely related to bone resorption (Norrdin *et al.*, 1990).

Maxillary transverse deficiencies can be corrected with slow or rapid palatal expansion (RPE), surgically assisted RPE (SARPE), or a two piece Le Fort I osteotomy (Mommaerts, 1999). Slow expansion is indicated for dental transverse discrepancies in young subjects, while RPE is indicated in adolescents with transverse discrepancies, whether skeletal and/or dental (Bishara and Staley, 1987). Although it may be possible to expand the maxilla in older patients, the results are neither as predictable nor as stable. In order to overcome this, RPE may be accompanied by corticotomies to release the areas of bony resistance. In SARPE, tooth-borne conventional devices are still the

preferred appliance type. However, they have the same disadvantages including periodontal ligament compression, buccal root resorption, dehiscences, and tooth tipping (Moss, 1968; Barber and Sims, 1981; Bishara and Staley, 1987; Mommaerts, 1999). Lanigan and Mintz (2002) reported temporary partial paralysis of the oculomotor nerve as another complication of SARPE.

Recently, bone-borne transpalatal distractors, such as the Rotterdam palatal distractor, have been developed in order to eliminate the undesired effects of RPE and SARPE (Koudstaal *et al.*, 2006). These devices are either screwed to the palatal vaults on each side of the palate or have pins that automatically stabilize the device without the need for screw fixation. Due to the necessity of palatal flap surgery, both techniques could be considered as invasive. Expansion of the posterior anchor teeth has been shown to result in more expansion of the anterior anchor teeth in both RPE (Adkins *et al.*, 1990) and SARPE (Bays and Greco, 1992) procedures. Pinto *et al.* (2001) reported that an increase in posterior expansion width during tooth-borne expansion reflects buccal tilting of the appliance carrying anchor teeth. They also reported that the expansion maintained by transpalatal distraction (TPD) is orthopaedic with minimal buccal tilting of the bony segments. Harzer *et al.* (2006) developed a procedure for bone-borne expansion using a Hyrax screw

fixed to both halves of the maxilla. They observed that bone-borne fixation induced greater bodily movement of the maxillary halves during expansion. Chung and Goldman (2003) evaluated the effect of dental tipping and dental rotation immediately after SARPE. They found that SARPE resulted in slight mesiobuccal rotation and significant buccal tipping of the first premolars and first molars.

Interleukin-1 beta (IL-1β) is known to be an inducer for Prostaglandin E$_2$ (PGE$_2$). Norrdin *et al.* (1990) and Sandy *et al.* (1993) reported that IL-1β synergistically up-regulates the formation of prostaglandins in periodontal cells under mechanical stress. Tzannetou *et al.* (1999) detected IL-1β and beta-glucuronidase in the gingival crevicular fluid (GCF) during RPE. They also found that orthodontic and orthopaedic forces evoked changes in the levels of the inflammatory mediators in the periodontal tissues, which might trigger biological processes associated with remodelling of the alveolar bone surrounding the roots.

The purpose of this study was to compare the PGE$_2$ levels in GCF, during maxillary expansion with bone-borne TPD and tooth-borne RPE devices.

Subjects and methods

A total of 30 adult orthodontic patients, 15 females and 15 males, mean age of 17.3 ± 2.8 years, with constricted maxillary arches who fulfilled the following criteria were included in the study:

1. All premolars present and fully erupted.
2. No history of systemic diseases.
3. Good periodontal health with no radiographic evidence of bone loss, i.e. periodontal probing depths equal to or less than 3 mm and no signs of gingival inflammation.
4. No history of antibiotic or anti-inflammatory drug use in the month preceding the study.
5. The female subjects were not pregnant.

Informed consent was obtained from all patients. The subjects were instructed to brush their teeth once in the morning after breakfast and once at night before bedtime for a minimum of 3 minutes in order to maintain periodontal prophylaxis and oral hygiene. Each patient was asked to use 0.5 ml of 0.2 per cent chlorhexidine gluconate mouth rinse following brushing.

The patients were divided into three groups. Group I included 10 patients, five females and five males, who received a TPD device. Distraction was delivered with the guidance of a TPD transporter as previously described by Sarı *et al.* (2007). Group II comprised 10 patients, five females and five males, who underwent SARPE. Care was taken to ensure that the arms of the Hyrax appliance were parallel to the palatal mucosa. The second premolars were not included in the appliance design. The control group included 10 patients, five females and five males, who did not receive any orthodontic treatment.

The patients in group II were instructed to turn the Hyrax appliances once in the morning and once at night for a total activation of 0.5 mm/day. Expansion of the TPD occurred at a rate of 0.33 mm/day, starting 1 week after surgery. Both Hyrax expansion and TPD were continued until the required expansion was achieved. Maxillary expansion was obtained in 2 weeks in both groups. At the end of that period, the screws were locked in place. The patients were observed every 7 days during the activation period of the appliance and for 28 days during passive wear.

Surgical procedure for groups I and II

All surgical procedures were carried out under general anaesthesia as described by Cureton (1998) and Atac e*t al.* (2006). The incisions were bilateral at the depth of the vestibule from the first molar area to the distal aspect of the lateral incisor. The mucoperiosteum was elevated, and the maxillary bone was exposed from the piriform aperture anteriorly to the pterygomaxillary fissure posteriorly. Osteotomy was performed horizontally above the apices of the teeth, including the release of the pterygoid junction. A thin osteotome was used to mallet between the central incisors just below the anterior nasal spine. Antibiotics, analgesia, and an oroantral regimen were prescribed for all patients.

GCF sample collection

GCF samples were obtained from the mesiobuccal and mesiopalatal gingival sulci of the maxillary permanent first molars, maxillary first premolars, and maxillary permanent central incisors at six observation periods, O1, O2, O3, O4, O5, and O6. Additionally, two samples, S1 and S2, were collected from group II in order to evaluate the effect of light forces generated by the separators prior to banding of the maxillary permanent first molars and first premolars. Note that in S1, GCF samples were collected from all participants prior to placement of the separators and the S2 samples were obtained at the fourth day after S1 before fitting the molar and premolar bands. This extra information was used to compare the changes in the prostaglandin levels within group II. The GCF samples obtained from groups I and II were used to evaluate the effects of heavy orthopaedic forces generated by the Hyrax and the TPD and to compare the differences between the groups. The sample collection was continued for a period of 28 days. The details of the observation periods are shown below.

O1: Initial samples were obtained prior to the start of expansion. In group I, TPDs were placed and expansion was initiated 1 week following surgery. GCF samples were obtained before the start of expansion in group I. In group II, expansion was initiated immediately after insertion of the Hyrax appliances.

O2 (24 hours): Activation of the screws in both groups measuring GCF at this time point.

O3: At day 7 following appliance activation.

O4: Following 14 days of active appliance wear. The screws of both groups were locked in place at this time point.

O5: After 7 days of retention (21 days).

O6: On day 28 of retention.

S1 (Baseline: 0): GCF samples were collected from all subjects in group II prior to placement of the separators. Loose 4.4 mm S2 modul separators (3M Unitek Ortodontic Products, Monrovia, California, USA) were placed between the mesial and distal interproximal areas of the maxillary permanent first molars and the maxillary first premolars.

S2 (4 days after S1): GCF samples were obtained from group II. Molar and premolar bands were inserted in order to fabricate the Hyrax appliances. Alginate impressions were taken, and separators were replaced. Following S2, all patients in group II underwent a Le Fort I osteotomy.

GCF sampling took place in a temperature-controlled area, maintained at 20°C and 40 per cent relative humidity between 09:00 and 10:00 a.m. This was done with six filter paper strips for GCF, which were housed in a single Eppendorf tube. All filter papers were autoclaved and weighed on a digital scale (Mettler AT-210; Mettler-Toledo Inc., Columbus, Ohio, USA) before use. The sites under investigation were isolated with cotton rolls. Supragingival plaque was removed, and the region was dried with an air syringe. Two filter papers for the mesiobuccal of the maxillary permanent first molars, two for the mesiobuccal of the first premolars, and two for the mesiobuccal of the maxillary permanent central incisors were inserted into the gingival crevice for 30 seconds. Samples containing blood were discarded. Acceptable filter papers were placed in the eppendorf tubes and weighed again to determine the volume of fluid collected.

A sterilized saline solution (250 μl) was added to the eppendorf tubes and the samples were centrifuged for 1 minute. All cytokines were recovered from the paper strips after 5 minutes of centrifugal elution. The papers were then removed and the solutions stored at −70°C until immunoassay.

GCF samples of the control group were also prepared following the same protocol.

PGE$_2$ assay

A commercial PGE$_2$ enzyme-linked immunosorbent assay kit (BioSource International, Camarilo, California, USA) was used to determine PGE$_2$. The standards for preparation of PGE$_2$ required eight eppendorf tubes that were numbered from one to eight. An aliquot of 900 μl automated enzyme immunosorbent (EIA) buffer was added to tube one. Tubes two to eight were filled with 500 μl EIA buffer. Then, 100 μl of the bulk standard was transferred to tube one and mixed thoroughly to make a 1 pg/ml standard. Then, 500 μl

of the standard solution from tube one was placed in tube two and mixed thoroughly. Next, 500 μl from tube two was placed in tube three and mixed thoroughly. This procedure was repeated for tubes three to eight. EIA 100 μl buffer was added to non-specific binding and 50 μl EIA buffer to maximum binding (N$_0$) wells. Fifty microlitres of each diluted standard solution and 50 μl of each sample was then transferred to the appropriate wells. Finally, PGE$_2$ acetylcholinesterase (AChE) conjugate (PGE$_2$ Tracer; 50 μl) and then PGE$_2$ monoclonal antibody (50 μl) was transferred to each well according to the instructions in the PGE$_2$ assay protocol (Cayman Chemical Company, Ann Arbor, Michigan, USA). The plate was then covered and incubated for 18 hours at 4°C. At the end of incubation, the wells were washed five times with Wash Buffer (i.e. ultra pure water-free organic contaminants). Ellman's Reagent (which contains the substrate to AchE; 200 μl) was added to each well followed by the addition of 5 μl of the tracer, Total Activity. The plate was covered with plastic film and shaken on a microtiter EIA shaker for 60 minutes in the dark. The plate was then read at 450 nm on an EIA assay reader (EL 312e Biotek Instruments, Winooski, Vermont, USA) within 2 hours.

Statistical analysis

The data were analysed using the Statistical Package for Social Sciences Version 13.0 (SPSS Inc., Chicago, Illinois, USA). Within-group differences of PGE$_2$ levels between O1 and O6 and between S1 and O2 were evaluated by the pairwise *t*-test. The differences between the PGE$_2$ levels of the groups at the beginning and at O2, O3, O4, O5, and O6 were determined by the Mann–Whitney U-test. Statistical significance was set at $P < 0.05$.

Results

PGE$_2$ levels in group II were significantly increased on day 4 following the insertion of separators when compared with S1 values ($P = 0.000$). However, no statistical differences were observed between S1 and O1 (7 days after the separators were removed; $P = 0.165$). PGE$_2$ levels in GCF were increased after 24 hours of activation (O2) with the Hyrax screw. This increase was found to be significantly different when compared with baseline values ($P = 0.000$) as well as with the values at S2 ($P = 0.002$; Table 1).

Following activation of the screws (O1), a significant increase in PGE$_2$ levels was observed in groups I and II ($P < 0.05$). Despite this significant increase, a decrease was observed during O5 and O6 in group I, which resulted in significantly different PGE$_2$ levels of GCF compared with O1 ($P = 0.231$). In group II, PGE$_2$ levels of GCF at O2, O3, O4, O5, and O6 were significantly greater than those observed at O1 while PGE$_2$ levels in group I at O2 were not statistically different compared with the levels at O5

($P = 0.024$). PGE$_2$ values in the control group did not show any significant increases during the study. The changes in the PGE$_2$ levels are shown in detail in Tables 2 and 3.

Group comparisons at O2 demonstrated a significant increase in PGE$_2$ levels following activation in groups I and II ($P = 0.000$) compared with those of the control group. In addition, the increase in PGE$_2$ in group II was found to be significantly different from group I at O2. In general, the mean PGE$_2$ levels in group II were significantly higher than in group I at both activation periods, O3 and O4, and both retention periods, O5 and O6 ($P = 0.000$). On the other hand, significant elevation in the PGE$_2$ levels was observed in group II for all observation periods ($P = 0.000$) compared with the control group. When the mean PGE$_2$ level in group

I was compared with that of the control group, significant differences were observed between activation of the screws, O2, and first week retention periods O5 ($P < 0.05$). However, no statistically significant differences were noted in the PGE$_2$ levels in GCF ($P = 0.445$) between group I and the control group at O6. The group comparisons are shown in Table 4 and Figure 1.

Discussion

Orthodontic forces induce inflammatory events in the periodontium that result in bone resorption and orthodontic tooth movement (Grieve *et al.*, 1994). At the bimolecular level, prostaglandins, growth factors, and cytokines are

Table 1 Evaluation of the effects of light and heavy orthopaedic forces on tooth movement in group II (surgically assisted rapid palatal expansions) at baseline (S1), 4 days after S1, initial expansion (O1), and following 24 hours of expansion (O2).

	S1	S2	*P* S1–S2	O1	*P* S1–O1	*P* S2–O1	O2	*P* S1–O2	*P* S2–O2
Group II ($n = 10$)	40.56 ± 2.92	59.11 ± 4.76	0.000	39.11 ± 1.27	0.165	0.000*	67.67 ± 4.74	0.000*	0.002*

Significance level $\alpha = 0.05$. Values are mean $\pm$ standard deviation.
*$P < 0.05$.

Table 2 Comparison of Prostaglandin E$_2$ levels (picogram/microlitre) at 24 hours (O2), 7 days (O3), 14 days (O4), 21 days (O5), and 28 days (O6) with O1 (initial samples).

Groups	O1	O2	*P* O1–O2	O3	*P* O1–O3	O4	*P* O1–O4	O5	*P* O1–O5	O6	*P* O1–O6
Group I ($n = 10$)	38.22 ± 2.54	45.89 ± 2.32	0.000*	47.89 ± 1.69	0.000*	50.2 ± 2.59	0.000*	44.22 ± 2.54	0.000*	39.56 ± 1.51	0.231
Control ($n = 10$)	37.67 ± 2.24	37.89 ± 2.32	0.594	37.78 ± 2.49	0.865	38.56 ± 3.09	0.086	38.00 ± 3.16	0.500	38.56 ± 2.30	0.069
Group II ($n = 10$)	39.78 ± 1.22	67.67 ± 1.72	0.000*	80.56 ± 4.22	0.000*	90.00 ± 3.77	0.000*	78.67 ± 6.40	0.000*	93.11 ± 3.86	0.000*

Significance level $\alpha = 0.05$. Values are the mean $\pm$ standard deviation.
*$P < 0.05$.

Table 3 Statistical evaluation of Prostaglandin E$_2$ (picogram/microlitre) levels between the transpalatal distraction (group I), surgically assisted rapid palatal expansion (group II), and controls at 24 hours (O2), 7 days (O3), 14 days (O4), 21 days (O5), and 28 days (O6).

Groups	*P* O2–O3	*P* O2–O4	*P* O2–O5	*P* O2–O6	*P* O3–O4	*P* O3–O5	*P* O3–O6	*P* O4–O5	*P* O4–O6	*P* O5–O6
Group I ($n = 10$)	0.002*	0.000*	0.024	0.000*	0.006*	0.000*	0.000*	0.000*	0.000*	0.000*
Control ($n = 10$)	0.886	0.347	0.834	0.111	0.452	0.791	0.288	0.366	1.	0.302
Group II ($n = 10$)	0.000*	0.000*	0.000*	0.000*	0.000*	0.239*	0.000*	0.000*	0.012*	0.000*

Significance level $\alpha = 0.05$. Values are the mean $\pm$ standard deviation.
*$P < 0.05$.

Table 4 Intergroup comparisons of Prostaglandin E_2 (picogram/microlitre) levels at the different time points for the transpalatol distraction (group I), surgically assisted rapid palatal expansion (group II), and the controls at initial expansion (O1) and at 24 hours (O2), 7 days (O3), 14 days (O4), 21 days (O5), and 28 days (O6) after expansion.

Time	P	P	P
	Group I–control ($n = 10$)	Group I–group II ($n = 10$)	Group II–control ($n = 10$)
O1	0.754	0.117	0.057
O2	0.000*	0.000*	0.000*
O3	0.000*	0.000*	0.000*
O4	0.000*	0.001*	0.000*
O5	0.001*	0.000*	0.000*
O6	0.445	0.000*	0.000*

Significance level $\alpha = 0.05$. Values are the mean ± standard deviation
*$P < 0.05$.
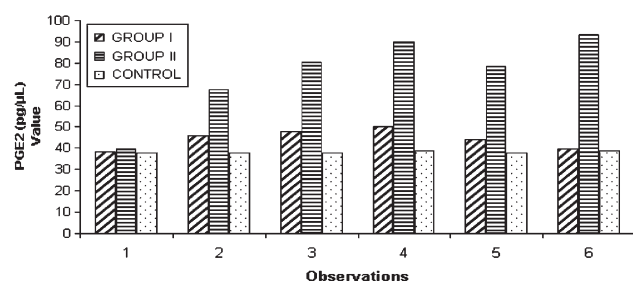
Figure 1 Prostaglandin E_2 (PGE$_2$; picogram/microlitre) levels in group I (transpalatal distraction), group II (surgically assisted rapid palatal expansion), and the controls at the different observation periods.

released from periodontal ligament cells (Sandy *et al.*, 1993). Previous studies have shown that when an orthodontic force is applied to periodontal tissues, inflammatory cytokines and prostaglandins are expressed (Saito *et al.*, 1991; Grieve *et al.*, 1994; Sarı *et al.*, 2004). In this study, PGE_2 levels in GCF showed changes dependent on the activation periods in both groups.

Maxillary expansion was performed using orthopaedic forces in both groups in the study. It was observed that PGE_2 levels in GCF collected from the first molars of healthy adolescents increased after separator placement (S2) and 24 hours following activation of the Hyrax appliance (O2). These results indicate that either light or heavy forces can induce a biochemical response in the periodontium. The intragroup findings of the present study were similar to those of Tzannetou *et al.* (1999) who evaluated the IL-1β (synergistic with PGE_2) and beta-glucuronidase in GCF around molars during RPE.

Variations in PGE_2 levels in GCF in both study groups were observed. After the initial peaks of PGE_2 at 24 hours, PGE_2 levels were higher compared with baseline values

during the following 2 weeks in both groups. PGE_2 levels decreased at the end of the expansion periods. However, the differences between the PGE_2 levels at O2 (24 hours of activation) and O5 (1 week retention) were not significantly different, whereas the differences in the levels of PGE_2 at O6 (2 weeks of retention) and O5 were statistically significant from the PGE_2 levels at O4, in group II. Although a significant decrease in PGE_2 values at O5 and O6 was observed compared with those at O4, PGE_2 levels at O3 and at O4 were maintained at significantly higher levels than those at O2 in group I. Additionally, the PGE_2 values at O6 were not significantly different from the baseline values in group I. The dissipation of fibroblast activation and orthodontic force decay were most likely responsible for this change in PGE_2 in both groups.

The stability of SARPE has been examined in previous studies (Bays and Greco, 1992; Pogrel *et al.*, 1992). Those investigators evaluated the relapse rate of palatal expansion after SARPE and found a mean relapse rate of 8.8 mm at the canines and 7.7 mm at the molars. However, Phillips *et al.* (1992) found that relapse in the second molar region was higher than in the first premolar region. For prevention of relapse, overexpansion in SARPE cases has been recommended (Moss 1968; Atac *et al.*, 2006; Tausche *et al.*, 2007). In the present study, the high values of PGE_2 at O5 and O6 in group II could be attributed to the relapse tendency of the maxillary segments due to continuous fibroblast activation. Although PGE_2 levels at O6 were nearly the same as baseline values in group I, the relapse could be due to tension of the palatal tissues. Contrary to tooth-borne expansion, Kraut (1984) reported that distraction devices can be used with an overcorrection of as little as 0.5–1.5 mm.

Dental tipping with surgically assisted tooth-borne appliances has been shown to be greater than that with bone-borne appliances. Tausche *et al.* (2007) evaluated three-dimensional changes with the Dresden distractor on dental, skeletal, and alveolar structures and found that bone-borne expansion appliances protect teeth by inducing more skeletal and less dental change. With conventional tooth-borne appliances such as the Hyrax that was used in the present study, expansion force was transmitted via anchor teeth to the alveolar bone and thus dental tipping was always greater, or at least equal to, alveolar ridge tipping. On the other hand, skeletal tipping during bone-borne expansion is more than dental tipping as a result of the forces transferred directly to the bone. The higher levels of PGE_2 recorded in group II coincide with the results of Tausche *et al.* (2007). However, following activation of the screws in group I, PGE_2 levels at O2, O3, O4, and O5 were found to be significantly higher than those in the control group. This could be explained by adaptive orthodontic tooth movement during orthopaedic palatal expansion in group I.

When post-expansion PGE_2 level changes were evaluated, group II showed higher PGE_2 levels than group I. This could

be explained by the ongoing bone remodelling with fibroblast activation around the anchor teeth during the 2 week retention phase. This result indicates that both maxillary segments need to be retained to avoid the relapse tendency in SARPE cases.

Conclusion

This study investigated PGE$_2$ in GCF. Increases in PGE$_2$ levels were observed in both experimental groups. Both light orthodontic and heavy orthopaedic forces resulted in an increase in PGE$_2$ levels. This was found to be higher in the SARPE cases than in the TPD cases following activation of the screws and may be due to greater dental effects with the SARPE procedure. The low PGE$_2$ levels in group I could indicate that using TPD might have prevented unfavourable sequela, such as root resorption, bony dehiscences, and buccal tipping of the anchor teeth.

Further studies, investigating different factors present in GCF, are recommended for a thorough clinical comparison of tooth- and bone-borne expansion appliances.

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References

Adkins M D, Nanda R S, Currier F G 1990 Arch perimeter changes on rapid palatal expansion. American Journal of Orthodontics and Dentofacial Orthopedics 97: 194–199

Atac A A T, Karasu H A, Aytac D 2006 Surgically assisted rapid maxillary expansion compared with orthopedic rapid maxillary expansion. Angle Orthodontist 76: 353–359

Barber A F, Sims M R 1981 Rapid maxillary expansion and external root resorption in man: a scanning electron microscope study. American Journal of Orthodontics 79: 630–652

Bays R A, Greco J M 1992 Surgically assisted rapid palatal expansion: an outpatient technique with long-term stability. Journal of Oral and Maxillofacial Surgery 50: 110–113

Bishara S E, Staley R N 1987 Maxillary expansion: clinical implications. American Journal of Orthodontics and Dentofacial Orthopedics 91: 3–14

Chung C H, Goldman A M 2003 Dental tipping and rotation immediately after surgically assisted rapid palatal expansion. European Journal of Orthodontics 25: 353–358

Cureton S L 1998 A significant transverse discrepancy: a case with a high mandibular plane angle, a severe maxillary arch length deficiency, and significant transverse discrepancy,. American Journal of Orthodontics and Dentofacial Orthopedics 114: 307–310

Grieve W G, Johnson G K, Moore R N, Reinhardt R A 1994 Prostaglandin E (PGE) and interleukin-1β (IL-1β) levels in gingival cervicular fluid during human orthodontic tooth movement. American Journal of Orthodontics and Dentofacial Orthopedics 105: 369–374

Harzer W, Schneider M, Gedrange T, Tausche E 2006 Direct bone placement of the Hyrax fixation screw for surgically assisted rapid palatal expansion (SARPE). Journal of Oral and Maxillofacial Surgery 64: 1313–1317

Koudstaal M J, van der Wal K G, Wolvius E B, Schulten A J 2006 The Rotterdam palatal distractor: introduction of the new bone-borne device and report of the pilot study. International Journal of Oral and Maxillofacial Surgery 35: 31–35

Kraut R A 1984 Surgically assisted rapid maxillary expansion by opening the midpalatal suture. Journal of Oral and Maxillofacial Surgery 42: 651–655

Lanigan D, Mintz M S 2002 Complications of surgically assisted rapid palatal expansion: review of the literature and report of a case. Journal of Oral and Maxillofacial Surgery 60: 104–110

Mommaerts M Y 1999 Transpalatal distraction as a method of maxillary expansion. British Journal of Oral and Maxillofacial Surgery 37: 268–272

Moss J P 1968 Rapid expansion of the maxillary arch. II. Indications for rapid expansion. The Journal of Practical Orthodontics 2: 215–223

Norrdin R W, Jee W S S, High W B 1990 The role of prostaglandins in bone in vivo. Prostaglandins, Leukotrienes, and Essential Fatty Acids 41: 139–149

Phillips C, Medland W H, Fields Jr H W, Proffit W R, White Jr R P 1992 Stability of surgical maxillary expansion. International Journal of Adult Orthodontics and Orthognathic Surgery 7: 139–146

Pinto P, Mommaerts M, Wreakes G, Jacobs W 2001 Immediate post expansion changes following the use of the transpalatal distractor. Journal of Oral and Maxillofacial Surgery 59: 994–1000

Pogrel M A, Kaban B, Vargervik K, Baumrind S 1992 Surgically assisted rapid maxillary expansion in adults. International Journal of Adult Orthodontics and Orthognathic Surgery 7: 37–41

Proffit W, Fields H W, Ackerman J, Thomas P, Tulloch J F 1986 The biological basis of orthodontic therapy. In: Rudolph P (ed.). Contemporary orthodontics, 2nd edn. Mosby, St Louis, pp. 296–325

Rossi M, Whitcomb S, Lindemann R 1996 Interleukin-1β and tumor necrosis factor- α production by human monocytes cultured with L-thyroxine and thyrocalcitonin: relation to severe root shortening. American Journal of Orthodontics and Dentofacial Orthopedics 110: 399–404

Saito M, Saito S, Ngan P W, Shanfeld J, Davidovitch Z 1991 Interleukin 1 beta and prostaglandin E are involved in the response of periodontal cells to mechanical stress in vivo and in vitro. American Journal of Orthodontics and Dentofacial Orthopedics 99: 226–240

Sandy J R, Farndale R W, Meikle M C 1993 Recent advances in understanding mechanically induced bone remodeling and their relevance to orthodontic theory and practice. American Journal of Orthodontics and Dentofacial Orthopedics 103: 212–222

Sarı E, Olmez H, Gürton Ü 2004 Comparison of some effects of acetylsalicylic acid and rofecoxib during orthodontic tooth movement. American Journal of Orthodontics and Dentofacial Orthopedics 125: 310–315

Sarı E, Uçar C, Ceylanoglu C 2007 Transpalatal distraction in a patient with a narrow maxilla. Angle Orthodontist 77: 1126–1131

Tausche E, Hansen L, Hietschold V, Lagravère M O, Harzer W 2007 Three-dimensional evaluation of surgically assisted implant bone-borne rapid maxillary expansion: a pilot study. American Journal of Orthodontics and Dentofacial Orthopedics 131: 92–99

Tzannetou S, Efstratiadis S, Nicolay O, Grbic J, Lamster I 1999 Interleukin-1 beta and beta-glucuronidase in gingival crevicular fluid from molars during rapid palatal expansion. American Journal of Orthodontics and Dentofacial Orthopedics 115: 686–696