Efficacy of Using PDGF and Xenograft With or Without Collagen Membrane for Bone Regeneration Around Immediate Implants With Induced Dehiscence-Type Defects: A Microcomputed Tomographic Study in Dogs

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Background: Use of collagen membrane (CM) with xenograft and recombinant human platelet-derived growth factor (rhPDGF) in guided bone regeneration (GBR) is debatable. The aim of this microcomputed tomographic experiment was to assess the efficacy of using PDGF and xenograft (with or without CM) for GBR around immediate implants with dehiscence defects.

Methods: Ten beagle dogs underwent atraumatic bilateral second and fourth premolar extractions from both arches. A standardized dehiscence defect (6 × 3 mm) was created on the buccal bone and immediate implants were placed in distal sockets in each site. Animals were randomly divided into three groups: 1) group 1, xenograft with rhPDGF was placed and covered with CM; 2) group 2, xenograft with rhPDGF was placed over the defects; and 3) group 3, four immediate implants were associated with dehiscence (controls). After 16 weeks, animals were sacrificed and jaw segments were assessed for buccal bone thickness (BBT), buccal bone volume (BBV), vertical bone height (VBH), and bone-to-implant contact (BIC) using microcomputed tomography.

Results: BBT was higher in group 2 (1.533 ± 0.89 mm) than group 1 (0.745 ± 0.322 mm) (P <0.001) and group 3 (0.257 ± 0.232 mm) (P <0.05). BBV was higher in group 2 (67.87 ± 19.83 mm^3) than group 1 (42.47 ± 6.78 mm^3) (P <0.05) and group 3 (19.12 ± 4.06 mm^3) (P <0.001). VBH was higher in group 2 (6.36 ± 1.37 mm) than group 3 (0.00 ± 0.00 mm) (P <0.001). VBH was higher in group 1 (3.91 ± 2.68 mm) than group 3 (0.00 ± 0.00 mm) (P <0.05). BIC was higher in group 2 (67.25% ± 13.42%) than group 1 (36.25% ± 12.78%) (P <0.05) and group 3 (30.25% ± 7.27%) (P <0.01).

Conclusion: GBR around immediate implants with dehiscence defects using PDGF and xenograft alone resulted in higher BBT, BBV, VBH, and BIC than when performed in combination with CM. *J Periodontol 2013;84:371-378.*

KEY WORDS

Bone regeneration; dental implants; membranes; platelet-derived growth factor; x-ray microtomography.

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It is well acknowledged that the buccal process of alveolar bone is entirely composed of bundle bone and is therefore more susceptible to undergo resorption after tooth extraction compared to the lingual/palatal process.[1-8] Nevins et al.[9] reported that ≥20% of the buccal process of alveolar bone undergoes resorption within the first 12 weeks of tooth loss, whereas studies by Schropp et al.[7,8] reported that nearly 66% of the alveolar bone undergoes resorption within the first 3 months of tooth extraction. Results from a recent histologic study[4] on baboons emphasized that the buccal bone receives an essential share of its vascular supply from the adjacent interdental bone and not merely from the socket side of the alveolus. This study[4] also showed that extraction of multiple contiguous teeth is associated with a more intense alveolar bone remodeling around extraction sites because the interdental vascular supply is compromised to a much larger extent compared to when a single tooth is extracted. It has been reported that immediate implant placement in fresh extraction sites may prevent alveolar bone remodeling in the short term;[10,11] however, localized osseous defects around immediate implants placed in fresh extraction sites may present a challenge to the clinician.[12]

Guided bone regeneration (GBR) using barrier membranes has been applied in implant dentistry for increasing the width and height of the alveolar ridge in areas with insufficient bone.[9-13] Various combinations of resorbable membranes and bone grafts, such as collagen membranes (CMs) with demineralized freeze-dried bone allograft, CMs with deproteinized bovine bone, and dermal matrix membranes with bioactive glass have been used in GBR.[14,15] Although studies[16,17] have reported that placement of a barrier membrane over the bone grafts during GBR favors new bone formation around immediate implants, the contribution of resorbable membranes during GBR using xenografts and growth factors is unclear.

Growth factors are polypeptide hormones that regulate the cellular events associated with tissue regeneration and repair.[18-20] The platelet-derived growth factor (PDGF) has been comprehensively assessed with reference to periodontal regeneration.[19-24] Studies[19-24] have demonstrated that PDGF endorses formation of new bone tissues around immediate implants with periodontal bony defects in the presence, as well as absence, of barrier membranes. The present study is based on the null hypothesis that use of a resorbable barrier membrane during GBR with PDGF and xenograft does not enhance the buccal bone thickness (BBT), buccal bone volume (BBV), vertical bone height (VBH), and bone-to-implant contact (BIC) around immediate implants with buccal dehiscence-type defects.

The present microcomputed tomographic analysis aims to assess the efficacy of using PDGF and xenograft (either with or without a CM) on GBR around immediate implants with dehiscence-type defects in a canine model.

MATERIALS AND METHODS

Ethical Considerations

The study was approved by the ethical committee at the Engineer Abdullah Bugshan Research Chair for Growth Factors and Bone Regeneration (GFBR), King Saud University, Riyadh, Saudi Arabia. Preoperative animal care, all surgical procedures, and postoperative management of the animals were performed in accordance with the Animal Care Guidelines of GFBR.

Study Animals

Ten female beagle dogs with a mean age and weight of 19 ± 1 months and 13.8 ± 1.00 kg, respectively, were used. The animals were kept in individual cages and vaccinated against rabies and infectious hepatitis.

The non-surgical and surgical procedures were performed under general anesthesia[§] (10 mg/kg body weight).

Preoperative Management

During the housing period, the dogs underwent supragingival scaling twice a week for 3 weeks using an ultrasonic scaler.[‖] Intramuscular amoxicillin[¶] (25 mg/kg body weight) was administered 1 day before surgery, followed by a second dose of the same antibiotic[#] at the time of surgery.

Animal Grouping and Treatment of Dehiscence Defects

The animals were randomly divided into three groups (by picking a paper marked "group 1," "group 2," or "group 3" from a brown bag). Animal grouping was based on the methodology adopted for the treatment of dehiscence defects: 1) group 1 (18 defects), in which xenograft[**] soaked in recombinant human (rh) PDGF-BB[††] was placed over the defects and covered with a CM;[‡‡] 2) group 2 (18 defects), in which xenograft[§§] was soaked in rhPDGF-BB[‖‖] and placed over the defects; and 3) group 3 (four defects), in which four immediate implants[¶¶] were associated with dehiscence (controls, no treatment). In group 1 and group 2, 0.5 mL of 0.3

§ Pfizer, New York, NY.
‖ NSK, Westborough, MA.
¶ Betamox LA, Norbrook Laboratory, Newry, County Down, Ireland.
# Betamox LA, Norbrook Laboratory.
** Laddec, OST Development, Clermont-Ferrand, France.
†† GEM 21S, Osteohealth, Shirley, NY.
‡‡ Mem-Lok, BioHorizons, Birmingham, AL.
§§ Laddec, OST Development.
‖‖ GEM 21S, Osteohealth.
¶¶ Laser-Lok microchannels, BioHorizons, Birmingham, AL.

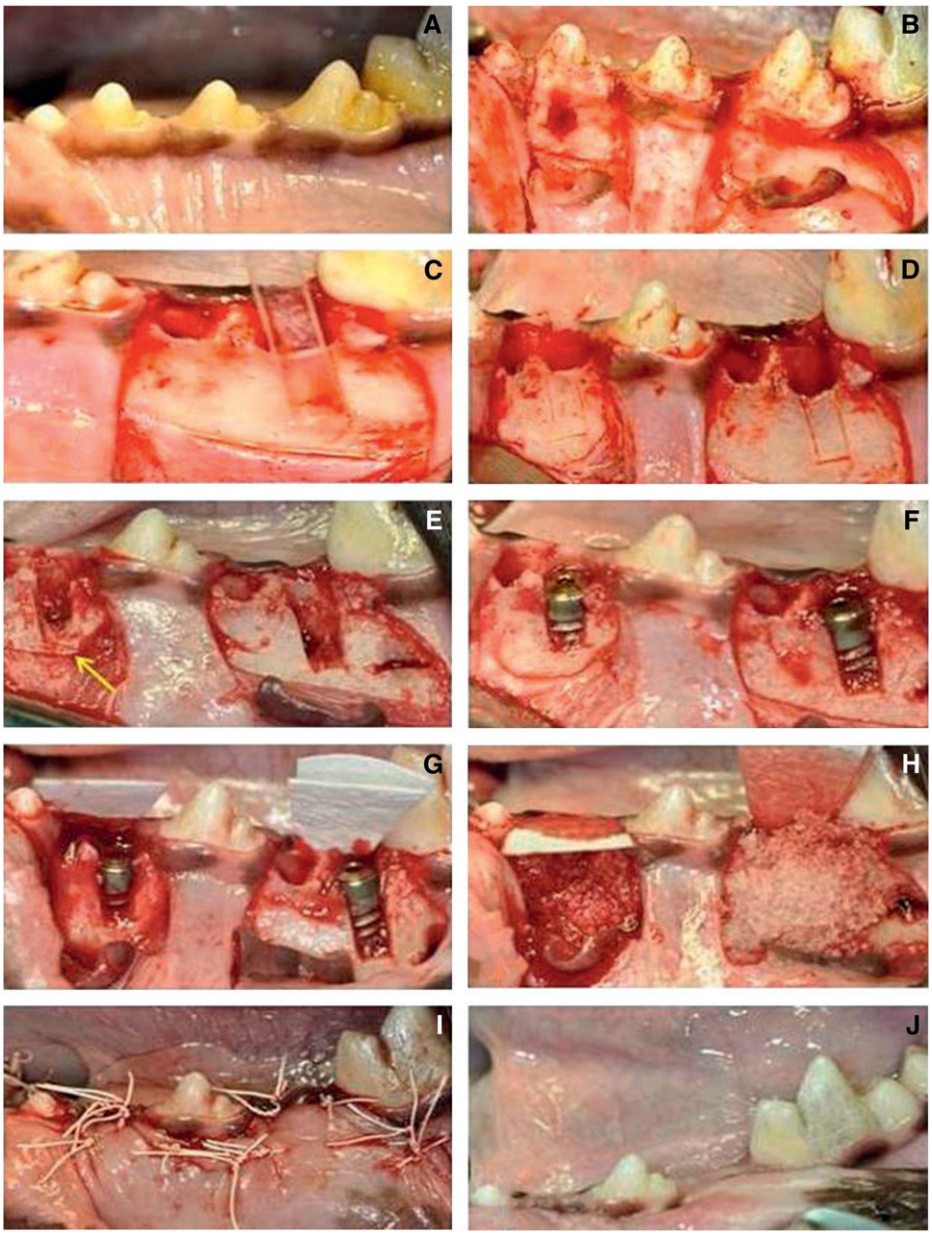

Figure 1.
A) *Preoperative photograph;* ***B)*** *elevation of full-thickness mucoperiosteal flaps;* ***C)*** *placement of stent on the buccal wall for creation of critical size defect;* ***D)*** *critical size defect (3 × 6 mm);* ***E)*** *placement of notch (yellow arrow);* ***F)*** *immediate implant placement;* ***G)*** *adaptation of CM;* ***H)*** *placement of xenograft;* ***I)*** *suturing; and* ***J)*** *1-month follow-up photograph.*

mg/mL rhPDGF was delivered using the particulate xenograft.[##22]

Surgical Protocol

After general anesthesia (as described above), animals were draped, and the surgical sites were swabbed with an antiseptic solution.*** Local anesthesia††† was administered in the bilateral premolar regions of both arches. Teeth (second premolar [P2] and fourth premolar [P4]) were atraumatically extracted using piezosurgery.‡‡‡ All buccal and lingual/palatal bone was sound with no dehiscence. Using a sulcular incision (with a no. 15 blade), full-thickness buccal and lingual/palatal flaps were raised to the mucogingival junction, after which a partial-thickness flap was raised to allow passive closure. Two vertical incisions (one mesial and one distal) were made. In each quadrant, P2 and P4 were extracted. A standardized hard acrylic stent§§§ was used to create a dehiscence bony defect (3 × 6 mm) on the buccal surface of the extraction socket (Fig. 1). This was followed by immediate implant‖‖‖ (3.8 × 10.5 mm) placement in the distal extraction sockets (Fig. 1) and assignment of this site to one of the three groups. The surgical wounds were sutured¶¶¶ to achieve primary closure.

Postoperative Management and Euthanasia

All animals received intramuscular (IM) injections of amoxicillin### (25 mg/kg body weight) every 8 hours for 5 days. Analgesics**** (0.01 to 0.02 mg/kg, IM) were administered immediately after surgery and every 8 hours for the first 2 days after surgery and then whenever needed depending on the presence of signs of pain by the animal (such as restlessness, unusual calmness, or refusal to eat). Plaque control procedures, using topical application of a 0.2% chlorhexidine digluconate solution,†††† were

Laddec, OST Development.
*** Purdue Fredrick Company, Stamford, CT.
††† Astra, Westborough, MA.
‡‡‡ Mectron, Piezosurgery, Columbus, OH.
§§§ Ellman International, Oceanside, NY.
‖‖‖ Laser-Lok microchannels, BioHorizons.
¶¶¶ Gore-Tex, W.L. Gore & Associates, Flagstaff, AZ.
Buprenorphine, SR Veterinary Technologies, Windsor, CO.
**** GUM, Sunstar GUM, Chicago, IL.
†††† Gore-Tex, W.L. Gore & Associates.

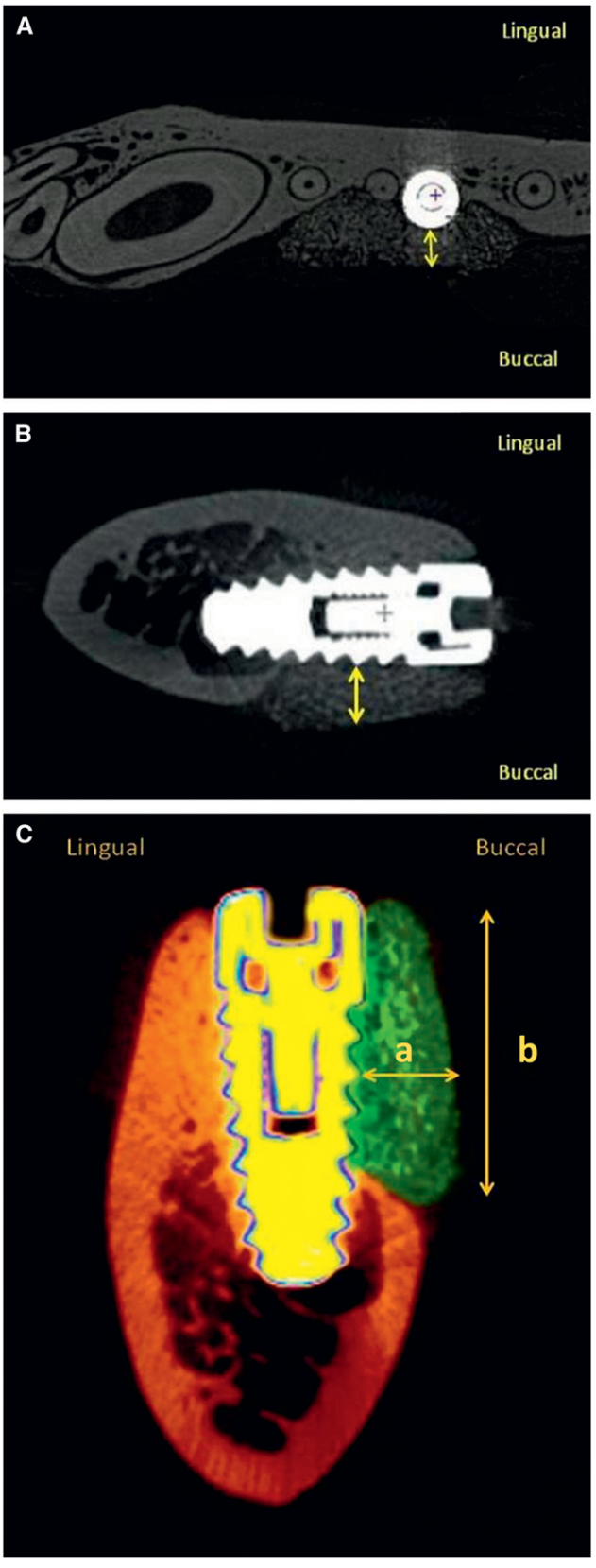

Figure 2.
Measurement of BBT (yellow arrows) around immediate implants: ***A)*** *axial view and* ***B)*** *sagittal view.* ***C)*** *Measurement of BBT (a) and VBH (b).*

performed twice weekly for 4 months after surgery. Sutures‡‡‡‡ were removed after 10 days of surgery, and the animals were kept on a soft diet throughout the study period.

After 4 months, the animals were sacrificed with an intravenous overdose of 3% sodium pentobarbital.§§§§

Hard-Tissue Sectioning and Microcomputed Tomography

The jaw segments containing the dental implants and associated mesial and distal tooth structures were removed en bloc using an electric saw‖‖‖‖ and fixed in 10% neutral formalin solution.

A microcomputed tomography (microCT) scanner¶¶¶¶ was used to evaluate the BBT, BBV, VBH, and BIC around immediate implants. The x-ray generator of the microCT was operated at an accelerated potential of 101 kV with a beam current of 96 μA using an aluminum filter with a resolution of 37.41-μm pixels. The BBT was measured at every 1-mm level starting from the alveolar crest to the base of the defect (Figs. 2A and 2B). The BBV was measured as described in a recent study.[25] In the adjacent teeth, VBH was measured via linear measurements (in millimeters) that extended from the crest of the implant to the apical notch (Fig. 2C). For BIC measurement, the total surface area of the region of interest (ROI) and the subset of the ROI surface that was intersected by binarized bone objects was measured via an analysis software.[3,26] The parameter thus measured was called ''intersection surface'' that corresponded to BIC. The BIC was calculated (at ×100 magnification) as the percentage of implant surface in contact with the bone through the whole perimeter of the implant.[3,26]

Statistical Analyses

Statistical analyses were performed using a statistical software.#### The power of the present study was 95% (common standard deviation of 1 mm and $\alpha = 0.05$). One-way analysis of variance was used to determine the differences in means of the BBT, BBV, VBH, and BIC among the groups. *P* values 0.05 were considered to be statistically significant. The data were normally distributed.

RESULTS

BBT

The mean BBT was significantly higher around dehiscence defects in group 2 (1.533 ± 0.89 mm) compared to that in group 1 (0.745 ± 0.322 mm) ($P<0.01$) and group 3 (0.257 ± 0.232 mm) ($P<0.05$). There was no significant difference in the BBT

‡‡‡‡ W.A. Butler Company, Dublin, OH.
§§§§ SP 1600, Leica, Bannockburn, IL.
‖‖‖‖ SkyScan 1172, CT-Analyser v.1.11.4.2+, Skyscan, Kontich, Belgium.
¶¶¶¶ nQuery Advisor v.7.0, Statistical Solutions, Saugus, MA.

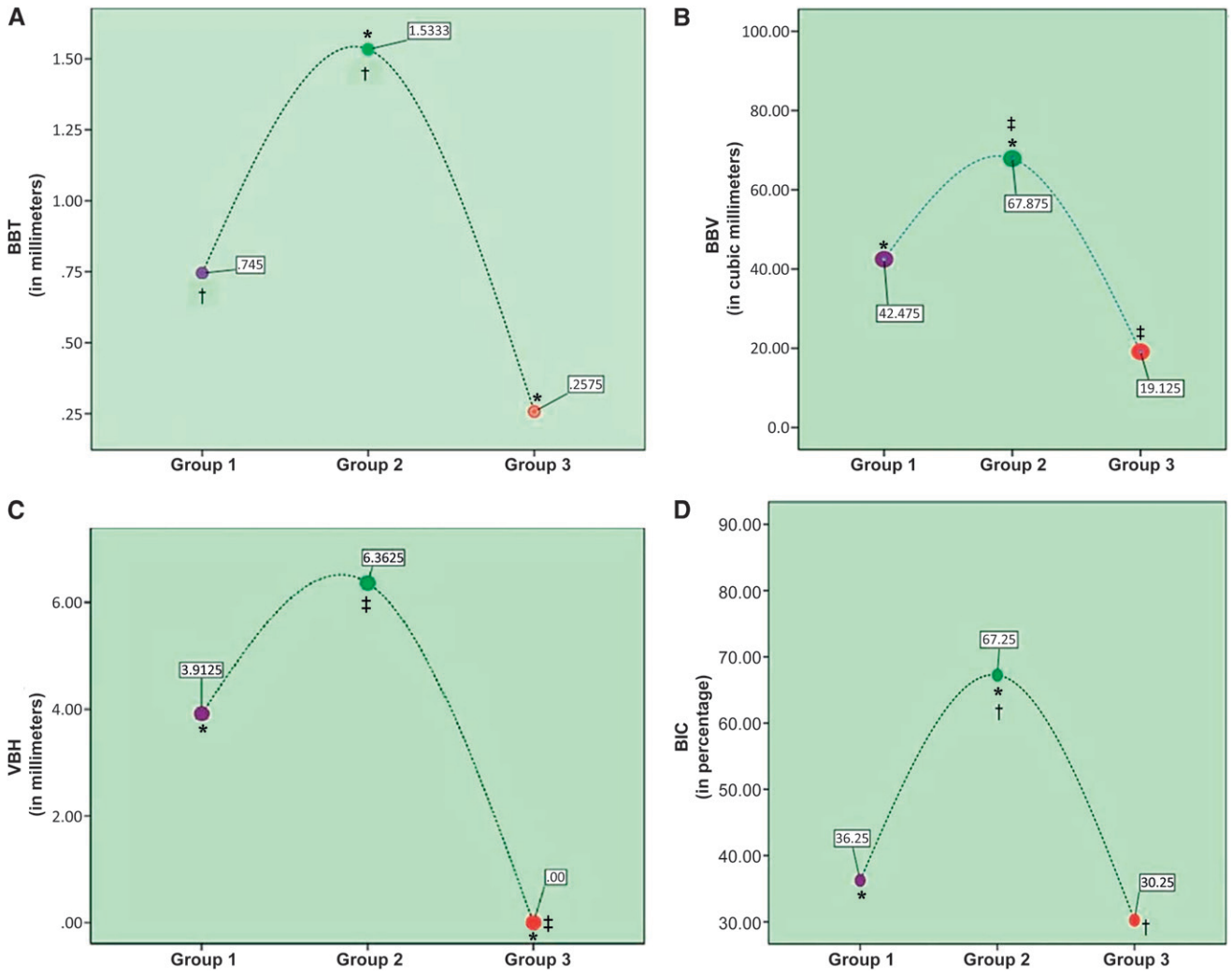

Figure 3.

A) *A graphic representation of the BBT around immediate implants with dehiscence in sites in group 1 (purple circle: PDGF + xenograft + CM), group 2 (green circle: PDGF + xenograft), and group 3 (orange circle: control/no treatment). BBT was significantly higher among sites in group 2 compared to sites in group 1 (P <0.01) and group 3 (P <0.05).* *P <0.05; †P <0.01. ***B)*** *A graphic representation of the BBV around immediate implants with dehiscence among sites in group 1 (purple circle: PDGF + xenograft + CM), group 2 (green circle: PDGF + xenograft) and group 3 (orange circle: control/no treatment). BBV was significantly higher among sites in group 2 compared to those in group 1 (P <0.05) and group 3 (P <0.001).* *P <0.05; ‡P <0.001. ***C)*** *A graphic representation of the VBH around immediate implants with dehiscence among sites in group 1 (purple circle: PDGF + xenograft + CM), group 2 (green circle: PDGF + xenograft), and group 3 (orange circle: control/no treatment). VBH was significantly higher among sites in group 2 compared to those in group 1 (P <0.05) and group 3 (P <0.001).* *P <0.05; ‡P <0.001. ***D)*** *A graphic representation of the BIC around immediate implants with dehiscence among sites in group 1 (purple circle: PDGF + xenograft + CM), group 2 (green circle: PDGF + xenograft), and group 3 (orange circle: control/no treatment). BIC was significantly higher among sites in group 2 compared to those in group 1 (P <0.05) and group 3 (P <0.01).* *P <0.05; †P <0.01.

between sites in group 1 (0.257 ± 0.232 mm) compared to group 3 (control group) (Figs. 3A, 4, and 5).

BBV

The mean BBV was significantly higher around dehiscence defects in group 2 (67.87 ± 19.83 mm^3) compared to group 1 (42.47 ± 6.78 mm^3) (P <0.05) and group 3 (19.12 ± 4.06 mm^3) (P <0.001). There was no significant difference in the mean BBV between group 1 (42.47 ± 6.78 mm^3) and group 3 (19.12 ± 4.06 mm^3) (Figs. 3B, 4, and 5).

VBH

The mean VBH was significantly higher around dehiscence defects in group 2 (6.36 ± 1.37 mm) compared to the control group (group 3) (0.00 ± 0.00 mm) (P <0.001). The mean VBH was significantly higher around dehiscence defects in group 1 (3.91 ± 2.68 mm) compared to the control group (group 3) (0.00 ± 0.00 mm) (P <0.05). VBH was significantly higher in group 1 (3.91 ± 2.68 mm) compared to group 3 (0.00 ± 0.00 mm) (P <0.05). There was no significant difference in the VBH between group 1

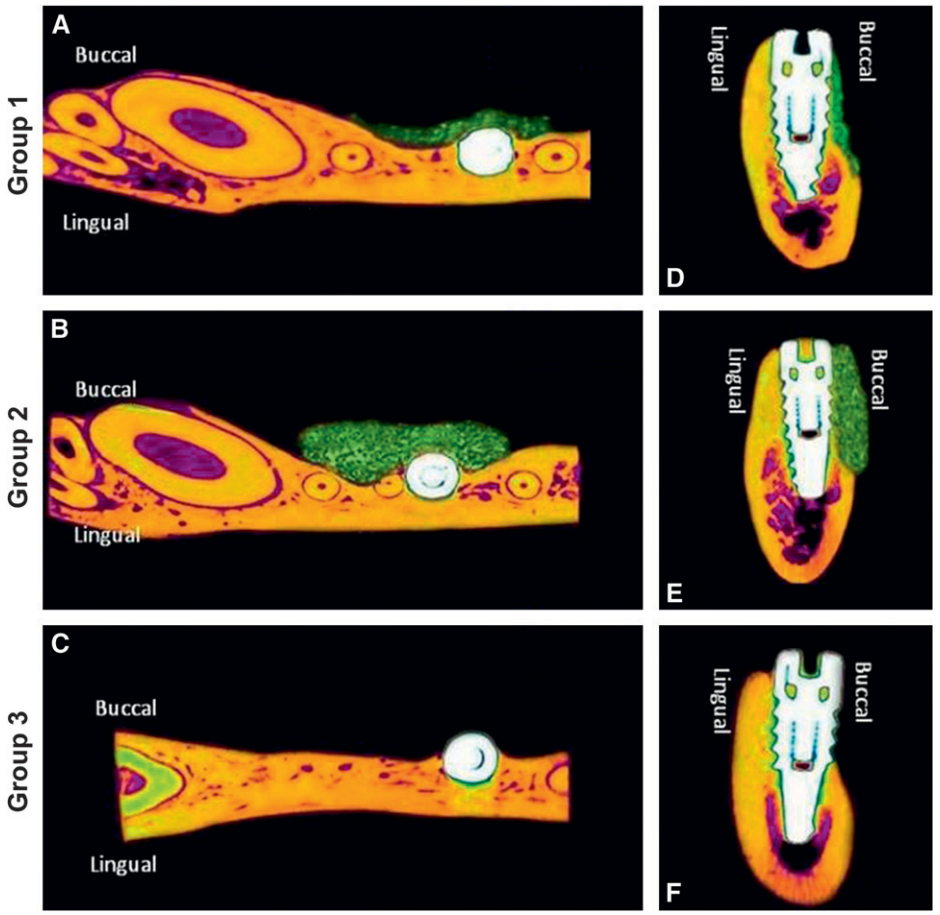

Figure 4.
A through C) *A series of reconstructed axial microCT images illustrating the thickness of the newly formed buccal bone (green) around immediate implants with dehiscence defects in groups 1 through 3.* ***D through F)*** *A series of reconstructed sagittal microCT images illustrating the vertical height of the newly formed buccal bone around immediate implants with dehiscence defects in groups 1 through 3.*

(3.91 ± 2.68 mm) and group 2 (6.36 ± 1.37 mm) (Figs. 3C and 4).

BIC

The mean BIC was significantly higher around dehiscence defects in group 2 (67.25% ± 13.42%) compared to that in group 1 (36.25% ± 12.78%) (P <0.05) and group 3 (30.25% ± 7.27%) (P <0.01) (Figs. 3D and 4). There was no significant difference in the mean BIC among sites in group 1 (36.25% ± 12.78%) and group 3 (30.25% ± 7.27%) (Figs. 3D, 4, and 5).

There was no significant difference in the BBT, BBV, VBH, and BIC on the lingual surface of the implants among the three groups.

DISCUSSION

The present microcomputed tomographic results demonstrated that GBR around immediate implants with buccal dehiscence-type defects was enhanced when treated merely with xenograft and PDGF compared to when a CM was placed over the xenograft soaked in PDGF. These results are in accordance with studies[27-32] that demonstrated that growth factors exhibit the potential to regenerate bone in dehiscence-type defects around implants. It has been hypothesized that the gel-like consistency of growth factors provides a space-making potential to the growth factor, and simultaneous use of graft material may hinder the collapse of the flap into the bone defect during the early healing phase.[32] Likewise, in a recent systematic review,[29] the authors reported that treatment of periodontal osseous defects with enamel matrix derivative (an amelogenin-rich growth factor) is as effective as when resorbable membranes are used during GBR. Simion et al.[16,18] hypothesized that barrier membranes obstruct the chemotactic effect of the growth factor on periosteal pluripotential mesenchymal cells. Similar results were reported by Kanou et al.[33] This may be an explanation for our results that demonstrated a higher BBT, BBV, and BIC around dehiscence treated with PDGF and xenograft alone compared to those covered with CM after placement of PDGF and xenograft over the defect. However, additional studies are warranted to investigate the influence of barrier membranes on the periosteal pluripotential mesenchymal cells.

Several studies[18-22] have shown that PDGF enhances periodontal regeneration by accelerating events, such as cellular chemoattraction, differentiation, and proliferation. Mott et al.[34] used fluorescence effects to investigate the effect of bone graft soaked in PDGF on osteoblastic proliferation around rat calvaria defects. The results demonstrated that use of bone grafts soaked in PDGF significantly enhanced osteoblastic proliferation in the defect sites compared to sites merely treated with bone graft.[34] In another study, Sanchez-Fernandez et al.[27] tested the

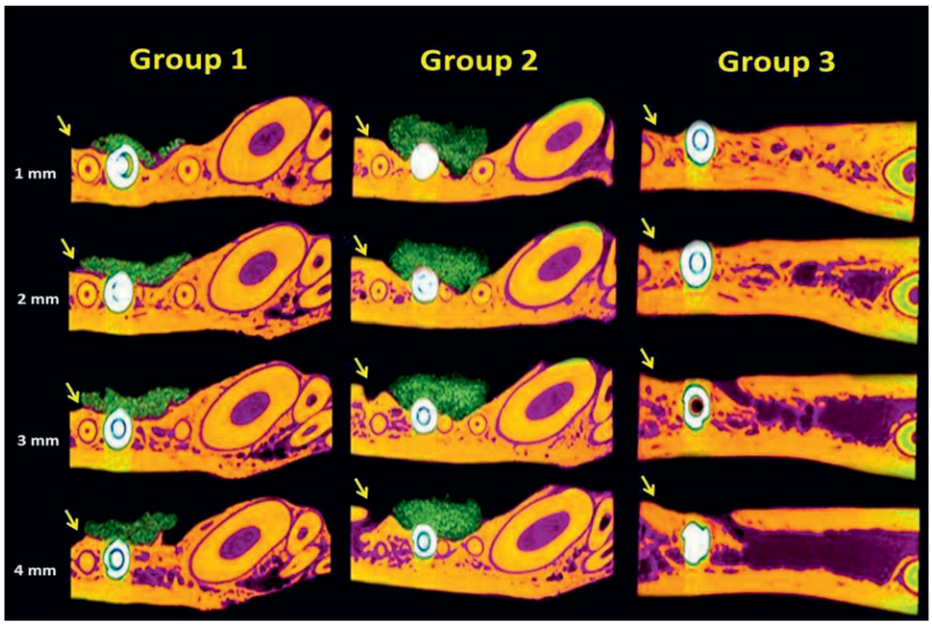

Figure 5.
A series of reconstructed axial images (at four different sections of 1-mm intervals starting 1 mm below the cemento-enamel junction) illustrating the thickness of the newly formed buccal bone (green) among the three groups. In group 2 (PDGF + xenograft), bone regeneration around immediate implants with dehiscence defects was significantly higher in group 1 (PDGF + xenograft + CM) and group 3 (control/no treatment). Yellow arrows indicate the buccal surface.

hypothesis that osteoclasts can regulate the chemotaxis of osteoblasts. The results demonstrated that mature osteoclasts produce factors including the PDGF that attract osteoblasts toward sites with osseous defects, thereby promoting new bone regeneration in the target tissues.[27] Similar results were reported by Park et al.[35] Likewise, Howes et al.[36] reported that PDGF enhances demineralized bone matrix-induced cartilage and bone formation. The present microCT results support these studies[27,35,36] because dehiscence defects treated merely with xenograft and PDGF displayed significantly more osseous regeneration compared to the defects treated with xenograft, PDGF, and CM. This reflects that the osteopromotive effects of PDGF are significant enough to induce new bone formation, and the contribution of a CM in this regard is redundant.

According to the present results, VBH and BIC were significantly higher around immediate implants where dehiscence sites were treated merely with xenograft and PDGF compared to sites covered with a CM after placement of PDGF and xenograft. A possible explanation in this regard may be extracted from a histologic study[37] in which the authors demonstrated that CMs have a short half-life and are susceptible to resorption. Early resorption of a CM may contribute to impeding the osteogenic activity taking place in the space beneath the membrane.

CONCLUSION

Within the limits of the present microCT experiment, it is concluded that GBR around immediate implants with dehiscence defects using PDGF and xenograft alone resulted in higher BBT, BBV, VBH, and BIC than when performed in combination with a CM.

ACKNOWLEDGMENTS

This research was registered at the College of Dentistry Research Center, King Saud University, Riyadh, Saudi Arabia (#NF 2364). The authors report no conflicts of interest related to this study.

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ORIGINAL ARTICLE

PERCEPTION OF FEMALE DENTAL STUDENTS TO SOME GINGIVAL DEFECTS

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ABSTRACT

The main objective of this study was to assess the perception of smile attractiveness towards four periodontal defects; namely: gingival recession (GR), gingival pigmentation (GP), black triangle (BT) and gummy smile (GS) among female dental students (n=100) in five academic levels at College of Dentistry, King Saud University, Saudi Arabia. Fifteen standardized altered smile images, representing the four defects at varying severities, were displayed to the students in a power point. A questionnaire with visual analog scale (VAS) was used to estimate the perception to each defect at each severity (1500 responses). The perception score was based on a scale of 0-100, where 0= the defect is strongly unattractive, and 100= the defect is relatively attractive. Results showed that PG defect was the relatively most ($p \leq 0.05$) attractive defect, whereas GR was the most unacceptable defect. Generally, perception scores decreased significantly ($p \leq 0.05$) as the severity of each defect was increased. Education level of students had a strong effect; students at higher academic levels were more accurate and have more critical eyes than students in lower level.

Key Words: *Black triangle; Dental education; Gingival pigmentation; Gingival recession; Gummy smiles; Perception; Saudi students.*

INTRODUCTION

Undoubtedly, aesthetic demands have been greatly increasing in this century. Several factors, such as mass media and internet, have played major role in the perception of beauty in modern cultures.[1] The perception of dental aesthetics varies greatly from person to person. This perception is influenced by different factors, such as personal experience, culture, time and dental education.[2-7] For example, Musskopf et al. (2013) compared the perception of smile aesthetic among some patients, dental students and dentists.[7] They found that patients were less critical in their perceptions than the professionals (dentists and dental students). It has been found that age also has an impact on the perception of smile esthetics in a study which evaluated the differences in smile esthetic perception between a younger and older age group of laypeople.[8]

Dental profession plays a major role in building the aesthetic standards. It is very interesting to see how the future dental professionals evaluate the various aesthetic situations, and how can dental education alter their perception of smile esthetics. A thorough knowledge of the perception of smile components may guide professionals to prepare appropriate treatment plans and to recognize what is most likely to be understood as good appearance. Several studies to evaluate aesthetic perception of the components that comprise the smile (the teeth, the lip and the framework of the gingival scaffold)[9] have been conducted.[10-15] Information available in literature about the perception of dental students to altered smile are few and scattered. Perception of dental students towards some parameters of altered smile and the effect of abnormal deviations of these parameters was studied by Nabil et al. (2016). They found that senior students were more critical in their evaluation than junior students.[16] Another study was conducted by Rocha et al. (2011)[17] to assess perception of dental students towards changes in some features of smile.[17] These researchers found that uneven gingiva had the worst perception in periodontal aesthetic, however, the perception of localized and generalized gingival recession did not differ significantly.

Most studies to evaluate the perception of altered smile features have been conducted on orthodontic variables. There is scarcity of information on evaluating the perception of altered smile on periodontal variables. Therefore, the present study was conducted: 1) to assess the perception towards four classic periodontal defects at different severities among female dental students at College of Dentistry, King Saud University in Riyadh, Saudi Arabia and 2) to determine the effect of the students' academic level (five academic years) on their

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perception towards the selected periodontal defects.

METHODOLOGY

The present study was approved by the College of Dentistry Research Center (CDRC) at King Saud University, Riyadh, Saudi Arabia. Each participant in the study signed an informed consent.

Participant:

A total of one hundred female students at the College of Dentistry, King Saud University participated in this study. Twenty female students from each of the five academic levels were randomly selected using Research Randomizer Program (copy right © 1997-2018 by Geoffrey C. Urbaniak and Scott Plous).

Variables

Three female students and one female patient were first chosen for their smiles. The smiles had little gingival exposure to give a space for altered gingival defects that will be manipulated later. Informed consent forms were obtained from them to digitally manipulate their smiles and to use them in this study. A colored smile photograph was obtained from each of the four smiles using a digital camera (KODAK easy share p712 camera - dental flash & close-up lens- Eastman Kodak Company Rochester NY 14650-made in Korea) in the frontal pose by the same photographer (Figure 1). Each original smile photograph was obtained by positioning the subject 5 feet. from the camera with the head in the natural position.[18] The original photographs were then manipulated using image processing software (Adobe Systems, Photoshop version CS2, San Jose, California, USA) to produce a series of images with the nose and chin removed from the images to reduce the number of confounders.

Study design

This study was a cross sectional study to verify the students' perception towards four gingival defects; namely: gingival recession (GR), black triangle (BT), gingival pigmentation (GP) and the gummy smile (GS). The defects GR, GP and GS were at four severities (classes), whereas the defect BT was at three severities. The original smile photographs (Fig. 1) were altered based on the following classifications;

1. The first original photo (Fig. 1A) was manipulated to a series of four images (Fig. 2) to create GR according to Miller classification for gingival recession.[19]
2. The second original photo (Fig. 1B) was manipulated to a series of four images (Fig. 3) to create GP following the Melanin Index.[20]
3. The third original photo (Fig. 1C) was manipulated to a series of three images (Fig. 4) to create BT according to Nordland and Tarnow classification system for loss of papillary height.[21]
4. The fourth original photo (Fig. 1D) was manipulated to a series of four images (Fig. 5) to create GS based on gummy smile scale proposed by Kurpis.[22] This scale measures the amount of gingival tissue displayed as a percentage of tooth height which classify it into: a) Mild: where the amount of gingival tissue shown during smiling is 1-25% of tooth length, b) Moderate: where the amount of gingival tissue shown during smiling is 25-50% of tooth length, c) Advanced: where the amount of gingival tissue shown during smiling is 50-100% of tooth length, and d) Severe: where the amount of gingival tissue shown during smiling is more than 100% of tooth length.

All alterations were selected after consultation with clinically experienced periodontist.

Questionnaire

A questionnaire was developed and distributed to the selected female students. Students were asked to score the attractiveness / unattractiveness of each smile image separately, using a visual analog scale (VAS). This scale was graded from 0 to 100; where 0 was strongly unattractive and 100 was considered to be relatively attractive. The questionnaire consisted of two parts: 1) introduction of the students and their academic level and 2) visual analog scales (VAS). A 10-cm VAS was used for ratings. It has a graded scale, each 1 cm represents 10 reading (10, 20, 30...100). Each student was asked to mark along the VAS according to her perception of the smile aesthetics.

Settings

The questionnaire was distributed to the selected students in a lecture room, each academic level alone. An introduction was first given to the students, and then they were asked to fill their demographic data. Then, the fifteen smile pictures were displayed with a power point presentation on a smart board, one picture at a time. These fifteen pictures were randomly displayed, each for 30 seconds.

Statistical analysis

SPSS, version 22.0 (IBM Corp, 2013) was used. Analysis of variance (ANOVA) was utilized to determine the significant differences. When F values were significant ($p \leq 0.05$), Duncan's multiple-range test was used to separate means. Linear correlation analysis was performed to determine the relationship between the academic level of the participant female students and their perception scores.

RESULTS

A total of 100 female dental students, from the five

different academic levels, were randomly selected in this study. Twenty students were selected from each academic level. Their age ranged from 19 to 24 years. The students were asked to give their perception towards four main clinical gingival defects at varying severities. The four gingival defects were displayed in different situations according to their severities. A total of 15 smile photos were displayed, and a total of 1500 responses were obtained.

Perception to the different defects and severities

The overall perception to the four gingival defects, at all severities (classes), is shown in Table 1. The gingival pigmentation (GP) was the relatively most ($p \leq 0.05$) attractive defect among all participated female students, whereas the gingival recession (GR) was the most unattractive defect. The other two defects (BT, GS) were in the middle, with no significant ($p \leq 0.05$) differences between these two defects (Table 1). Table 2 represents the effects of the defect severities on perception. In general, perception scores decreased ($p \leq 0.05$) (i.e. least attractive) as the severity of each defect was increased (Table 2).

Effect of students' education on perception

The level of students' education showed a strong effect on their perception towards the four gingival defects (Table 3) and at different severities (Figs.6, 7, 8, 9). Female students in higher academic levels (i.e. third, fourth and fifth) showed greater ($p \leq 0.05$) accuracy and have more critical eyes than students in lower academic levels (i.e. first and second levels) (Table 3). This is also true with regard to increasing severities of the four defects (Figs. 6, 7, 8, 9).

TABLE 1: PERCEPTION TO THE FOUR GINGIVAL DEFECTS AMONG FEMALE STUDENTS IN COLLEGE OF DENTISTRY, KING SAUD UNIVERSITY

Gingival defect	n	Perception (0.0 – 100)	SD
GP	400	43.26 a	± 22.50
BT	300	35.51 b	±19.10
GS	400	33.95 b	±23.80
GR	400	17.54 c	±17.51

- Means within a column followed by the same letter are not significantly ($p \leq 0.05$) different, according to Duncan's multiple range test.

- Perception score was based on a scale of 0.0-100, where: 0.0=defect is strongly unattractive, and 100=defect is relatively attractive.

- Gingival defects: GP= gingival pigmentation, BT= black triangle, GS=gummy smile and GR= gingival recession.

TABLE 2: PERCEPTION TO THE FOUR GINGIVAL DEFECTS AT DIFFERENT SEVERITY CLASSES AMONG FEMALE STUDENTS IN COLLEGE OF DENTISTRY/ KING SAUD UNIVERSITY

Severity Levels	Perception (0.0-100)			
	GR	GP	GS	BT
Class I	32.22 a (±15.61)	56.85 a (±21.01)	47.30 a (±21.36)	37.30 a (±17.63)
Class II	18.70 b (±15.61)	45.15 b (±20.14)	41.10 b (±21.83)	42.15 a (±19.60)
Class III	12.70 c (±15.47)	39.90 b (±19.70)	22.90 c (±21.89)	27.07 b (±16.92)
Class IV	6.53 d (±11.99)	31.15 c (±21.31)	24.50 c (±20.53)	_

- Values are means of 100 responses. Means in the same column with the same letter are not significantly ($p \leq 0.05$) different, according to Duncan's multiple range test.

- Gingival defects: GP= gingival pigmentation, BT= black triangle, GS=gummy smile and GR= gingival recession.

- Perception was based on a scale of 0.0-100, where 0.0= strongly unattractive and 100=relatively attractive.

TABLE 3: PERCEPTION TO THE FOUR GINGIVAL DEFECTS AMONG FEMALE STUDENTS IN EACH OF THE FIVE ACADEMIC LEVELS

Academic level	Perception (0.0-100)				
	GR (n = 80)	GP (n = 80)	GS (n = 80)	BT (n = 60)	All defects (n=300)
First	20.69 a (±15.87)	51.13 ab (± 18.62)	40.75 ab (± 17.49)	43.33 a (± 17.34)	38.68 a (± 20.78)
Second	21.88 a (±19.037)	52.19 a (± 25.04)	45.75 a (± 24.89)	43.58 a (± 21.45)	40.67 a (± 25.59)
Third	19.63 ab (±21.71)	44.94 b (± 24.12)	34.44 ab (± 26.78)	35.37 b (± 18.58)	33.47 b (± 24.97)
Fourth	14.63 bc (±14.92)	37.00 c (± 18.05)	29.75 c (± 22.33)	30.17 bc (± 14.90)	27.73 c (± 19.79)
Fifth	10.88 c (±12.42)	31.06 c (± 18.40)	19.06 d (± 16.86)	25.08 c (± 15.88)	21.28 d (± 17.72)

- Means in the same column with the same letter are not significantly ($p \leq 0.05$) different, according to Duncan's multiple range test.

- Gingival defects: GP= gingival pigmentation, BT= black triangle, GS=gummy smile and GR= gingival recession.

- Perception was based on a scale of 0.0-100, where 0.0= strongly unattractive and 100= relatively attractive.

Fig 1: The original smile photos. A) This photo was used to manipulate to GR. B) This photo was used to manipulate to GP. C) This photo used to manipulate to BT. D) This photo was used to manipulate to GS

Fig 2: Classes (severities) of gingival recession (GR). A) Class I. B) Class II. C) Class III and D) Class IV

Fig 3: Classes (severities) of gingival Pigmentation (GP). A) Class I. B) Class II. C) Class III and D) Class IV

DISCUSSION

Although many studies have been conducted to evaluate different dentofacial aspects that affect smile attractiveness, the perception of different gingival defects is not yet discussed in the periodontal literature. The present study was conducted to evaluate the perception towards four classic clinical defects at varying severities. Female dental students (n = 100), in five academic levels, were asked to evaluate fifteen

Fig 4: Classes (severities) of black Triangle (BT). A) Class I. B) Class II and C) Class III

Fig 5: Classes (severities) of gummy Smile (GS). A) Mild. B) Moderate. C) Severe and D) Advanced

altered smile images, using the visual analogue scale (VAS). VAS has been used successfully and widely for the purpose of evaluating subjective feelings and has showed good levels of reproducibility and validity.[7,17,23]

Results of this present study indicated that, among the four gingival defects, the gingival recession (GR) was the most unattractive defect, whereas the gingival pigmentation (GP) was the relatively most attractive. As defect severities were increased, the perception scores decreased, as expected. GR is a common clinical feature in poor and high populated regions of the world.[24,25] It has been reported that patients are often unaware of buccal gingival recessions due to the fact that most of these defects are asymptomatic [26], and only 28% of the clinically-identified recession sites were perceived by patients. Laypersons (unlike professionals and dental students) cannot recognize gingival recession (GR) of less than 2mm.[7] This study of Musskopf and his co-workers (2013)[7], is in contrast to the present study, that examined GR as a result of soft tissue inflammation and periodontal disease that comprise bone destruction. All recessions here were symmetrical. This fact assist professionals to understand the reason behind the lowest perception, by raters, for GR.

Gingival pigmentation (GP), in contrast to GR, was found in this study as the relatively most attractive

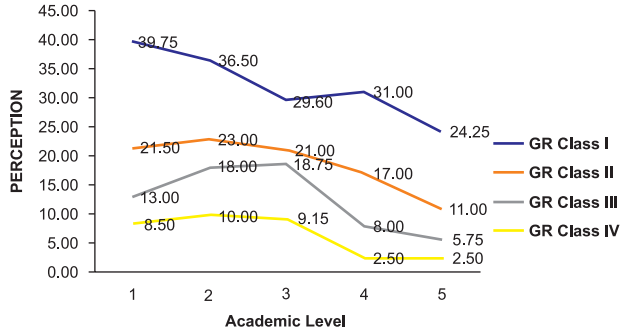

Fig 6: Relationship between academic levels and perception toward gingival recession (GR) at different classes (severities). Coefficient correlation (CF) for Class I=-0.95*, (CF) for Class II= -0.88*, (CF) for Class III = -0.66 and (CF) for Class IV = -0.83

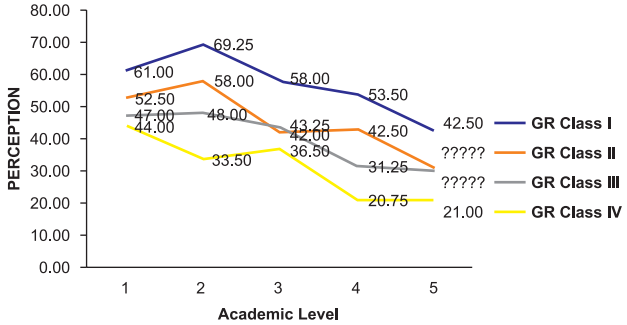

Fig 7: Relationship between academic levels and perception toward gingival pigmentation (GP) at different classes (severities). Coefficient correlation (CF) for Class I= -0.85, (CF) for Class II= -0.89*, (CF) for Class III = -0.93* and (CF) for Class IV = -0.92*

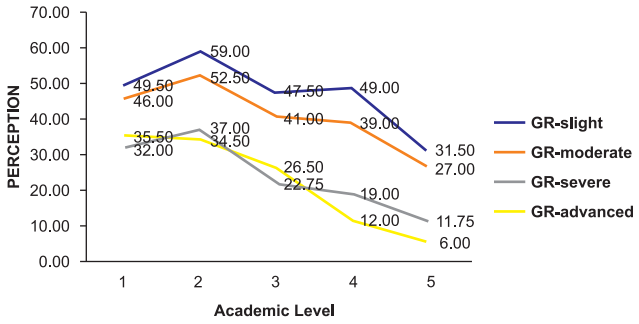

Fig 8: Relationship between academic levels and perception toward gummy smile (GS) at different severities. Coefficient correlation (CF) for slight GS= -0.73, (CF) for moderate GS= -0.86, (CF) for severe GS= -0.97* and (CF) for advanced GS = -0.92*

defect. GP is well-known to affect the colour of the gingiva; it will turn the colour to darker instead of normal pale pink. However, change in colour does not affect any function or causes physiological impairment. In the Middle East, especially in the Gulf countries (GCC), most of the people have darker skin, and subsequently have darker gingival colour than Caucasian people. The fact that ethnic and social differences make people more familiar with darker gingiva, GP images

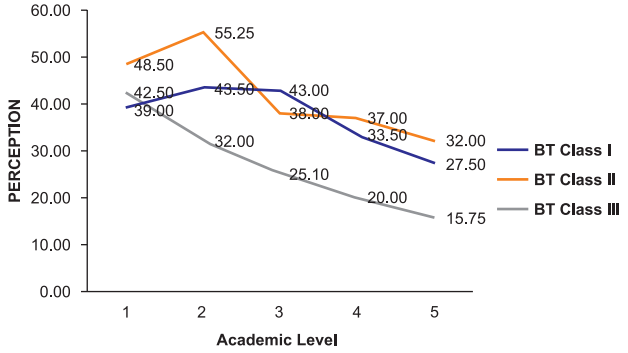

Fig 9: Relationship between academic levels and perception toward black triangle (BT) at different classes (severities). Coefficient correlation (CF) for Class I= -0.77, (CF) for Class II= -0.86, and (CF) for Class III = -0.98*.

are more acceptable, as was found in this study. The present study also found that severity of PG increased the perception scores decreased. The used severity level for GP was based on Melanin Index by Hedin (1977) which categorize the smoker's melanosis. To my knowledge this index is the only classification found for GP in the periodontal literature.

The perception scores towards the other two defects of gummy smile (GS) and black triangle (BT) were in the middle (33.9 and 35.5) respectively. Gummy smile (GS) represent a condition considered anti-aesthetic.[9, 27] Normally, the individual exposes 1-3 mm of gum at smiling. When she/he exposes a large extension of gum more than 3mm, this individual has a condition of gummy smile. Using a series of extraoral front-view-photographs of a gingival smile before and after surgical corrections of gummy smile, Pithon et al. (2014) found that photos which showed 2.5mm of gingiva when smiling scored as the most attractive by the dental professional and students, whereas the image that showed 3mm of gingiva when smiling was most attractive to the laypersons.[28]

The present study shows that as the severity of GS increased, the perception of attractiveness decreased (Table 2, Fig. 8). The severity of gingival exposure depends on distance between the upper lip and the gingival margins of central incisors. Perceptions of gingival display and gingival design or height are reported in several articles and reviewed by Parrini et al. (2016).[29] In their review article, Parrini and his Colleagues looked for thresholds of acceptance for gingival exposure and reported many measurements. They indicated that perception scores decreased with increased gingival display, as confirmed by the current study.[29] Some researchers[10] have stated the gingival display is often aesthetically appealing because it corresponds with a more youthful appearance.

Black triangle (BT) was found in the present study

to affect the smile attractiveness. BT is a result of loss of interdental papilla height, resulting in embrasure not being filled with soft tissue and bone. This small space occurs in more than one third (1/3) of adults. In present study, the perception toward BT scored intermediate (35.5). Unlike the other studies, BT, in our study was applied between all upper anterior teeth and it was symmetrical. Generally, perception decreased as BT severity was increased. However, no difference ($p \leq 0.05$) was found between the classes I and II, and this might be due to the small differences detected in black spaces which happened due to minor loss of soft tissues and bone. In contrary, in class III, the papilla loss (BT) has more bone loss which negatively affect the aesthetic smile. Pithon and his colleagues (2013) evaluated the aesthetic perception of the smile by laypersons at three age groups (15-19, 35-44, and 65-74 years) with regard to black spaces between the maxillary central incisors.[30] They found that younger people are more likely, than older people, to perceive black spaces in maxillary incisors, and also found that the larger the black spaces, the less attractive the persons rate the smile. Our results about BT confirm the findings by Sriphadungporn and Chamnannidiadha (2017) that the presence of a black triangle between maxillary central incisors was more attractive by older people than younger ones.[8] Based on their assumption, a 0.05mm black triangle represented the threshold of acceptability in younger group, whereas in the older group, 1.5mm was the limit of acceptability.

The other factor that play very important role in the perception to the aesthetic smile is the level of dental education. Our results show that as the academic level of the female dental students increased, these students became more aware and have much critical eye in their perception to the smile, especially in the third, fourth and fifth academic years. There was a linear improvement from the first academic year to the fifth academic year. Our results confirm those by Ayyıldız and his colleagues (2017) who found increased aesthetic awareness among students after the second year.[31] However, a study by España and others (2014) failed to find linear improvement from year 1 to year 5 or any significant between genders.[32] They, however, evaluated aesthetic perception toward altered: midline diastema, upper and lower midlines, crown length of the maxillary right central incisor, occlusal cant and gummy smile.

In College of Dentistry at King Saud University dental students start periodontics courses and clinics from third year. This may explain why students in the third, fourth and fifth academic years found the altered smile features photos less attractive compared to students in the first and second years who showed no significant differences in perception toward the four gingival defects (GR, GP,GS and BT).

Females are known to have more critical eye and vision when it comes to aesthetic evaluation. Therefore, it would be interesting to compare the relative perception between male and female dental students. It is desirable to expand study sample and include more categories such as periodontists and laypeople to identify levels of acceptance, attractiveness and unattractiveness and treatment needs for each defect. Such useful information is needed to help periodontists to direct proper treatment and to develop more strategic procedures to increase the beauty of smiles.

CONCLUSION

Gingival recession (GR) affect greatly the smile attractiveness compared to the other gingival defects (GP, GS and BT). Gingival pigmentation (GP) show the highest perception, among the others, in altered smile images. As the severity of periodontal defects increases, the perception of attractive smile decreases. Dental education plays an important role in the development of aesthetic perception of dental students.

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Case Report

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A conservative approach for treating excessive gingival display: a clinical report

Abstract

Excessive gingival display (EGD) namely "the gummy smile" is unattractive smile for some patients. These patients seek treatment and request an attractive smile in dental clinics. The excessive gingival display could be a result of multiple factors and usually its treatment with orthognathic surgery is aggressive and has high morbidity rate.

Aim: The aim of this clinical report is to present a conservative and combined treatment approach to a case with an excessive gingival display of multiple etiologies.

Materials and methods: The patient had EGD due to vertical maxillary excess and hypermobile upper lip. The preferred treatment was conservative with minimal side effects. The management began with aesthetic crown lengthening conducted with osteotomy and buccal bone re-contouring. Then, after 6 months the patient underwent a lip repositioning surgery.

Results: Reduction of EGD and restricted muscle pull of upper lip.

Conclusion: Gummy smile can be treated conservatively with combined approach. Identifying the causative factors and proper case selection are the key elements for good management.

Keywords: Gummy smile; Hypermobile lip; Lip repositioning; Vertical maxillary excess

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Introduction

Excessive gingival display (EGD) is one of the major causes of patient embarrassment. An imbalance in the gingiva-tooth ratio results in dominance of gingival appearance often referred to as "gummy smile." A normal gingival display between the inferior border of the upper lip and the gingival margin of the central incisors during a normal smile is 1-2 mm. Whereas, excessive gingivae-to-lip distance of 3 mm or more is considered as unattractive.[1] A gummy smile is prevalent in 10.5-29% of the population.[2] It is highly prevalent among women and the excessive gingival exposure decreases with age due to loss of muscle tone in both upper and lower lips.[3] Gummy smile has a variety of possible etiologies that can act alone or in combination. First, it may be a result of delayed eruption in which the gingiva fails to complete the apical migration over the maxillary teeth to a position that is 1 mm coronal to the cement-enamel junctions.[4] In this case of delayed tooth eruption, restoring the normal dentogingival relationships can be achieved with an aesthetic crown lengthening.[5] The procedure involves moving the gingival margins apically through soft and possibly hard tissue resection. The second possible cause is gingival enlargement.[2] Gingival enlargement could be due to dental plaque, hereditary gingival fibromatosis, medications or hormonal changes.[6,7] The management depends on periodontal therapy to remove plaque and plaque retentive factors and modification of medication regimen. Gingivectomy and gingivoplasty surgeries are possible to deal with enlarged soft tissues.[8] The third possibility is vertical maxillary excess in which there is an enlarged vertical dimension of the midface and incompetent lips.[9] Treatment involves orthognathic surgery. It involves hospitalization and significant morbidity for patients. The Fourth possibility is the hypermobility of upper lip caused by the lip elevator muscles.[2] Botox injections may be used as a temporary solution to the problem,[10] or for more stable results, surgical lip repositioning, could be utilized to reduce the labial retraction of the elevator smile muscle and minimize the gingival display.[11] Finally, another cause is the deficient lip length that can be managed with lip training exercises.[2] The average length of the maxillary lip is 20 to 22 mm in young adult females and 22 to 24 mm in young adult males.[12]

During patient examination, it is important to establish the etiology responsible for the excessive gingival display. Cases of excessive gingival display with multiple etiologies require more than one technique to achieve desirable outcomes. The aim of this clinical report is to present a conservative combined treatment approach to a case with an excessive gingival display of multiple etiologies. An aesthetic crown lengthening was performed in conjunction with lip repositioning surgery.

Case report

A forty year old woman, with no significant medical history, came to our clinic with a chief complain of an undesired gummy smile and square anterior teeth. During the clinical extra-oral examination, symmetric facial features were found with a normal upper lip length of about 20 mm (Figure 1A). Patient has longer lower third of the face and hypermobile upper lip that caused an excess gingival display of approximately 6 mm at dynamic smiling (Figure 1A) (Figure 1B). A periodontal examination revealed healthy non-inflamed gingiva with an adequate width of attached gingiva on the facial aspect and prominent canine eminence bilaterally. There was a deep bite, and the upper central incisors were not short (9 mm). Based on Bhola et al. classification,[2] excessive gingival display was diagnosed, caused by a combination of a moderate bony maxillary excess EGD (B) degree 2, and a hypermobile lip EGD (E) subclass 2 that revealed 4 to 8 mm of gingiva.[2] Different treatment plan options were presented to the patient.

Patient preferred conservative and less morbidity approach to treat her gummy smile and square teeth. In order to make a final decision and to involve patient's opinion in the treatment plan, a wax- up and transparent stent of upper teeth were made. The wax-up represents the upper teeth from second premolar to collateral after aesthetic crown lengthening with 3 mm longer crowns (Figure 2A). Patient tried the stent and liked the future results of esthetic crown lengthening (Figure 2B). After evaluation and discussion the exact sequence of the therapy and the possible complications, the procedures of the aesthetic crown lengthening with osteotomy and lip repositioning were selected.

Figure 1 Preoperative smiles. A: Static smile; B: Dynamic smile.

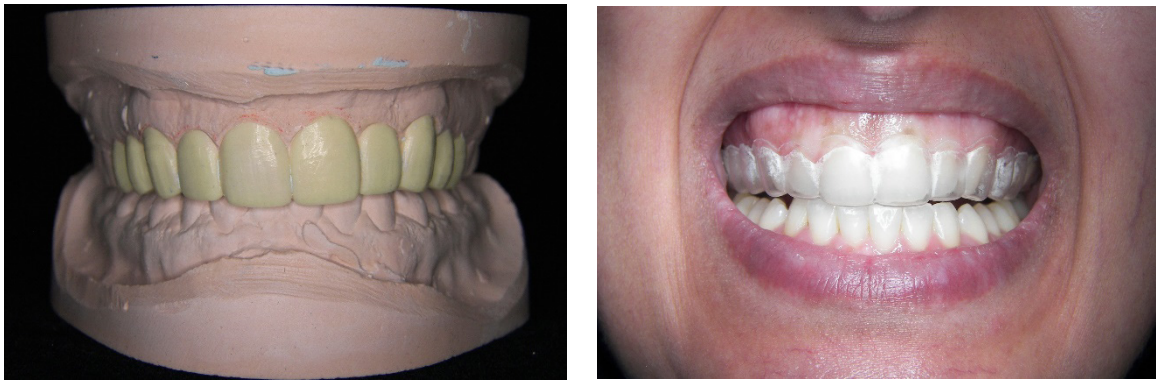

Figure 2 A: Wax-up of the upper teeth with 3mm longer crowns; B: Patient is trying the upper stent that represent the final teeth shape after aesthetic crown lengthening.

Surgery one (aesthetic crown lengthening)

The objectives of aesthetic crown lengthening were to reshape the square upper teeth to a longer ones; as the shape of patient's face and to reduce from the excessive gingival exposure during dynamic smiling. Local anesthesia was given via local infiltration with Xylocaine 2% with Adrenaline 1:80,000 (XYLOCAINE® Dental Adrenaline 2%, 20mg/ml + 12.5 µg/ml, 1.8 ml, DENTSPLY). Demarcation of cemento-enamel junction and gingivectomy were performed from second premolar to collateral via internal bevel incision. The incision line followed the cemento-enamel junction without disturbing the proximal papilla (Figure 3A). A full-thickness flap was, then, elevated from the second premolar to collateral via intra-sulcular incision (Figure 3B). An ostectomy was carried out to remove tooth-supporting bone 3 to 4 mm from cemento-enamel junction to re-establish the biologic width from the future gingival margins. In addition, canine eminence and buccal bone were relieved and re-contoured. The flap was repositioned at its original position and sutured using vicryle 5-0 sutures (Coated VICRYL®, polyglactin 910, Sutures, ETHICON, JOHNSON & JOHNSON HEALTH CARE) with single interrupted sutures (Figure 3C). The postsurgical instructions included a diet of soft foods, intermittent icing of the upper lip for the first day, avoidance of tooth brushing around the surgical site, and gentle rinsing with 0.12% chlorhexidine gluconate twice daily for 14 days. Ibuprofen 400 mg bid were prescribed for 7 days. After 2 weeks, healing was uneventful and the sutures were removed. Improvement of the gummy smile was achieved immediately (Figure 3D). At 2 months of healing, the exposed root surfaces were completely covered and final gingival margins were aesthetic and stable (Figure 3E). After 6 months, the tissue maturation was completed, and the patient was ready for the modified lip repositioning surgery. The amount of epithelium to be excised was determined by doubling the amount of gingival display. In this case, the band was approximately 10 to 12 mm wide.

Surgery two (lip repositioning)

Under local anesthesia Xylocaine 2% with Adrenaline 1:80,000, the surgical area was demarcated with marker as an elliptical shape (Figure 4A). The incision outlined from right first molar to left first molar. A partial-thickness incision was made along the mucogingival junction. Second parallel incision was made at the labial mucosa at approximately 10-12 mm distance from the first incision (Figure

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4B) (Figure 4C). The two incisions were connected at the distal ends. The epithelium was removed in the incision outline, leaving the underlying connective tissue exposed (Figure 4D). Middle high frenum attachment was removed. Bleeding was controlled by an additional local anesthesia infiltration and the use of pressure. Care was taken to avoid damage to the muscle tissue, nerves, and any minor salivary glands in the submucosa. The parallel incision lines were approximated with interrupted stabilization sutures with, first, midline suture then, alongside the borders of the incision. These sutures were made to ensure proper alignment of the lip midline and to approximate both flap horizontal borders using Vicryl 4-0 (Figure 4E). Other than limited facial movements during healing, postsurgical instructions and medications were the same as previously noted. The patient was seen for a follow-up at 1, 2, 6, and 12 weeks after surgery. At 1 week, healing was uneventful and mild pain and tension and moderate swelling of the upper lip were reported. At 2 weeks, the sutures were removed and the slight tension and soreness below the upper lip were reduced. The suture area of the lip repositioning healed uneventfully in the form of a scar (Figure 4F), which was not apparent when the patient smiled (Figure 5A). At 12 weeks, the patient was very satisfied with the esthetic outcome and her harmonic smile, revealing adequate gingival display and desired tooth proportion (Figure 5A) (Figure 5B).

Figure 3 Aesthetic crown surgery (ECL). A: Gingivectomy at upper teeth from second premolar to collateral; B: Intra-sulcular incision and full-thickness flap at upper teeth from second premolar to collateral. C: Suturing with interrupted single sutures using vicryle 5-0. D) Teeth and soft tissue at Follow-up after 2 weeks of ECL. E) Smile at follow-up after 2 months of ECL.

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Figure 4 Lip repositioning surgery (LRP). A: Demarcation of incision outline as elliptical form; B: Partial-thickness incision was made along the mucogingival junction and labial mucosa. C: Dissection and removal of epithelium layer; D: Exposed connective tissue; E: Wound suturing with single interrupted sutures; F: Tissues healing after 2 weeks of LRP.

Figure 5 postoperative smiles at 12 week of lip repositioning surgery. A: Dynamic smile; B: Static smile.

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Discussion

Lip repositioning was first reported as a corrective method for a gummy smile in 1973 by Rubinstein and Kostianovsky.[13] Then, a modification to the original surgical technique was introduced by Silva et al.[14] who proposed maintaining the attachment of the upper maxillary frenum; this to maintain the position of the labial midline and to reduce the morbidity. The modified lip repositioning surgery is considered safer and designed to have fewer complications compared to muscle dissection and repositioning as well as orthognathic surgery.[14] Complications from lip repositioning surgery can occur and include discomfort, ecchymosis, swelling of the upper lip, relapse, mucocele formation, paresthesia and an asymmetric smile.[2] Relapse following lip repositioning technique was found to occur in 8% of the cases treated.[15] Patient satisfaction also may be limited; at 3 months post-surgery with an average outcome of a 3-mm gingival display, only 66% of patients were satisfied with their outcome.[15] Sliva and his colleagues[14] conducted a survey to evaluate patients underwent lip repositioning surgery after 2.5 years. They found that there were 90% of patients who want to repeat the procedure and 70% considered the post-operative amount of gingival display to be "about right'.

Ishida et al.[16] have described a more invasive combined approach for treating excessive gingival display that included myotomy of the levator labii superioris muscle. One of the disadvantages of their technique is the high morbidity and irreversible outcome. In some other studies,[10,17–19] botulinum toxin has yielded satisfactory results, given that it blocks the muscular activity. However, Botulinum toxin technique has a transitory effect (6–7 months) and for this reason, the toxin must be reapplied periodically to maintain the desired outcome. In this present case, there was a risk of root surfaces exposure after gingivectomy and osteotomy. Osteotomy was made to achieve a biological width and to create healthy aesthetic gingival margins. To avoid this problem, the interproximal papilla and its underlying bone were left unchanged. However, the minor root surfaces exposure, were covered again with gingival tissues after 2 months of soft tissue remodeling (Figure 5A) (Figure 5B). Buccal bone and canine eminence were re-contoured to minimize the bulbous appearance of the soft tissue architecture and to allow a more relaxed, fuller upper lip at smile.

Conclusion

Gummy smile can be treated conservatively with a combined approach. Identifying the causative factors and proper case selection are the key elements for good management.

Acknowledgment

None.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Management of Nifedipine-Induced Gingival Overgrowth with Drug Substitution: A case report

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Abstract

Nifedipine-induced gingival overgrowth (NIGO) is an abnormal growth of the gingival tissues in response to an adverse drug reaction in some patients treated for hypertension. The prevalence of gingival overgrowth associated with calcium channel blockers has been reported to be 15 - 85% with an average composite of around 42%, in patients taking nifedipine.

Aim: The aim is to present a non-surgical management for NIGO, with medication substitution.

Material and Methods: a forty-one-year-old lady, showed up at periodontics clinic complaining of gingival tissue overgrowth. She has a history of blood hypertension and she has been treated for four years with Adalat CC 60 mg and Concor 10 mg daily. After comprehensive examination, she was diagnosed with NIGO. The patient was referred to her physician, and Adalat was replaced with Diovan 80 mg and Natrilix SR 1.5 mg once daily. Periodontal management included scaling and root planing. Patient was instructed for meticulous plaque control measures and recalled every three months for maintenance.

Results: The tissue responded excellent to non-surgical treatment with quite tissue shrinkage.

Conclusion: The most effective treatment for patients with gingival enlargement is the possibility of withdrawal of the medication and substitution with others. In some cases, this substitution is not possible.

Keywords: *Calcium Channel Blockers; Gingival Overgrowth; Medication Substitution; Nifedipine*

Abbreviation

NIGO: Nifedipine-Induced Gingival Overgrowth

Introduction

Patients using medications have been increasing in numbers at dental clinics. Some of these medications have side effects to the oral cavity and periodontal tissues. One of the pharmacologic unwanted side effects of these medications is gingival overgrowth [1]. Several factors namely; age, genetic predisposition, presence of preexisting plaque, immunological changes, pharmacokinetic variables and gingival inflammation influence the relationship between the medications and gingival tissue [2]. Gingival enlargement may create speech, mastication and esthetic problems [3]. However, not all patients taking these drugs develop drug-induced gingival overgrowth. The incidence of gingival overgrowth can be 50% in epileptics, 30% in transplant patients, and 20% in hypertension subjects treated with calcium-channel blocking agents [4].

Nifedipine, sold under the brand names: Adalat, Procardia and others. It is a calcium-channel blocking agent and dihydropyridine derivative. Nifedipine is a medication used to manage angina, high blood pressure, Raynaud's phenomenon, premature labor and prinzmetal angina [5]. It was discovered in 1969 and approved for use in the United States in 1981. It is on the World Health Organization's List of essential medicines, the most effective and safe medicine needed in a health system [6].

The prevalence of gingival overgrowth associated with calcium channel blockers has been reported to be 15 - 85% with an average composite of around 42%, in patients taking nifedipine (Adalat, Procardia). However, the prevalence with other calcium channel blockers, such as Varapamil, Dilatiazem, Felodipine, or Amlodipine, is significantly less and reported to be around 5% [7].

Although there are previous reports of nifedipine-induced gingival enlargement that managed with non-surgical therapy, there are no comprehensive description of cases managed effectively with drug substitution. Therefore, the aim of this case report is to present a careful management of nifedipine-induced gingival overgrowth with medication substitute and periodontal treatment including surgical and non-surgical management.

Case Report

A forty-two-year-old lady showed up in the periodontal clinic at Dental College of King Saud University, complaining of gingival overgrowth and bleeding gums during brushing in the mandibular and maxillary regions. The swelling is progressively increasing causing difficulty in mastication and oral hygiene. Past medical history revealed a history of hypertension for the last four years, for which she was receiving Adalat CC 60 mg and Concor 10 mg daily. There is a family history of blood hypertension in her father and mother.

Patient noticed gradual increase in the size of gingiva at maxillary right region after a year of anti-hypertension medications administration. Later, the enlargement spread gradually to other teeth causing esthetic disfigurement.

On examination, generalized gingival enlargement was noticed in the upper and lower arches, with an isolated nodular growth observed in the right side of the upper arch. Generally, the enlarged gingiva was firm, pale pink and resilient with a minutely lobulated surface. However, there were few red spotted areas scattered in the upper arch. The gingiva showed a tendency to bleed (Figures 1A, B, C, D and E). There were accumulations of plaque at the gingival margins and deposits of calculus subgingivally. The pockets depth ranged from 3 to 4 mm. Upon radiographic examination, there was a generalized 30% horizontal bone loss with localized vertical defects in teeth # 16 mesially and # 47 mesially (Figure 2). A remaining root was noticed at # 15 area.

Figure 1: *Initial Intra-Oral Photos Showing the Gingival Overgrowth. A) Frontal View. B) Right Side View. C) Left Side View. D) Upper Occlusal View. E) Lower Occlusal View.*

Figure 2: *Panoramic view x-ray.*

Based on the clinical presentation of the gingival enlargement and a history of nifedipine intake, the case was diagnosed as Nifedipine-induced gingival overgrowth. The plaque is the primary risk factor and calculus is a secondary risk factor.

The patient was referred to her physician for nifedipine substitute to other anti-hypertension medications. Then, an emergency gingivectomy was performed around tooth # 16 because the gingival over-growth there was interfering with occlusion. Also, the remaining root was extracted. The nifedipine (Adalat CC 60 mg) was replaced with Diovan 80 mg once daily. Diovan (valsartan) is an angiotensin II receptor antagonist. Diovan keeps blood vessels from narrowing, which lowers blood pressure and improves blood flow. Natrilix SR 1.5 mg (indapamide) was added later to improve the control over blood pressure. Natrilix SR is a thiazide diuretic. It lowers blood pressure and fluid retention in edema by removing the extra water and certain electrolytes from the body.

Periodontal management consisted of supra and subgingival scaling and root planning, followed by careful instructions on oral hygiene procedures. The case was reviewed for any signs of improvement after a period of two months. The tissue responded excellent to nonsurgical treatment and medication replacement with quite volume shrinkage. The blood pressure was 134/79. Gingiva looked healthy regarding its colour, shape and texture except the upper right area which displayed slight gingival irregularities (Figures 3A, B). A gingivoplasty was performed using gingival knife to the upper right area to reshape the gingival tissues irregularities. The patient was reinforced on oral hygiene instructions Chlorhexidine mouth rinse 0.2% twice daily for 15 days, followed every three months with hygienist. After seven months, the gingival tissue was well maintained, and the patient did not show any recurrence of enlargement (Figures 4A, B, C, D, and E). Patient is on Diovan 80 mg, Natrilix SR 1.5 mg, Concor 10 mg and Lipitor 10 mg, and the blood pressure is now 135/83.

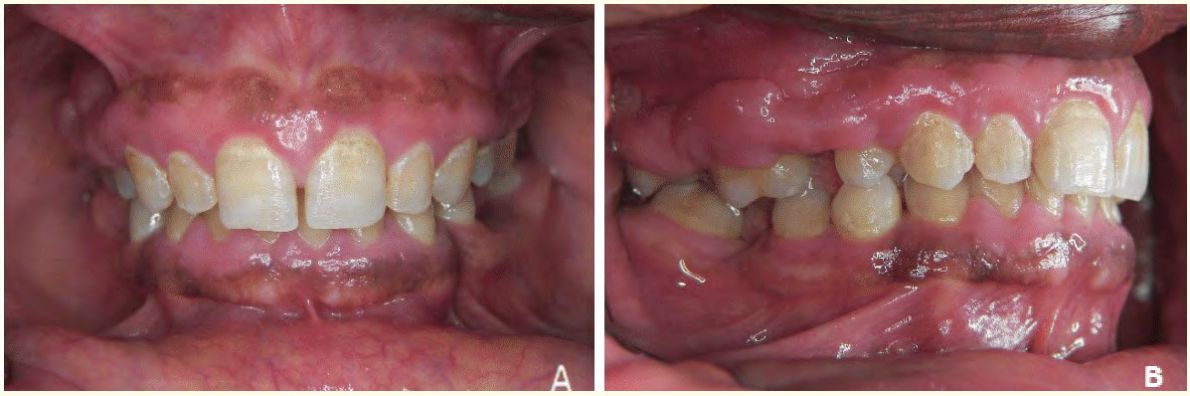

Figure 3: *A) The Gingival Tissue Healing after two Months. B) Notice the Gingival Tissue Irregularities at the Upper Right Side*

Figure 4: *Follow-Up Photos After Seven Months. A) Frontal View. B) Right Side View. C) Left Side View. D) Upper Occlusal View. E) Lower Occlusal View.*

Discussion

The pathogenesis of drug-induced gingival overgrowths is not completely understood. It has been hypothesized that the mechanism through which these medications trigger the connective tissue response could be an abnormal susceptibility of fibroblasts to these medications [4]. When an interaction occurred between nifedipine and gingival fibroblasts, overproduction of collagen and extracellular ground substance occurs and leads to increase in the gingival size. The drug interferes with the calcium metabolism of fibroblast cells and hence reduces the production of the degrading enzyme collagenase [4].

According to the Academy of Periodontology report, the patient's oral hygiene represents a significant risk factor for drug-induced gingival overgrowth. Plaque-induced inflammation can exacerbate the effect of medications, leading to a combined effect on the gingival tissues. Some investigators believe that inflammation is a prerequisite for gingival overgrowth that could be prevented by proper plaque removal [3,4]. This is supported by the fact that edentulous areas did not show signs of enlargement in most reported cases. In the present case, the gingival overgrowth has improved much after periodontal therapy and plaque removal. With gingival tissue shrinkage, the patient was able to perform her oral hygiene properly.

The daily dose, blood level, salivary levels, and gingival crevicular levels of the drugs have been related to the presence of gingival overgrowth. This effect is dose-related, with minimum baseline and threshold level required to induce gingival changes. In the case of calcium channel blockers, Ellis., *et al*. [7] assayed nifedipine levels in the plasma and gingival crevicular fluid and found that patients with high drug concentration in the crevicular fluid developed gingival enlargement, in contrast to patients where the drug could not be detected in the gingival crevicular fluid and the patients failed to develop gingival overgrowth [8].

There is little awareness about nifedipine-induced gingival overgrowth in medical field. There is a need to make a coordinated treatment plan between physicians and dentists for patients who are taking nifedipine, phenytoin and cyclosporine therapies.

Conclusion

The most effective treatment for patients with gingival enlargement caused by Nifedipine therapy is the possibility of withdrawal of the medication and substitution with others. In some cases, this substitution is not possible. Meticulous plaque control measures, combined with strict maintenance therapy, will be one of the essential methods of prevention and management of these cases.

Conflict of Interest

Author has none to declare.

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