

Original Article**Effect of topical phenytoin on creeping attachment of human gingiva:  
A pilot study**

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**Abstract**

**BACKGROUND AND AIM:** The aim of this study was to evaluate the effect of topical phenytoin on creeping attachment.

**METHODS:** In this pilot quasi-experimental study, 8 patients referring to Kerman School of Dentistry, Kerman, Iran with Miller class I or II gingival recessions were selected using convenient non-random sampling if they needed root coverage and met the study's inclusion criteria. The patients applied phenytoin mucoadhesive paste 1% on the surface of the deepithelialized gingiva of the tooth with gingival recession, twice a day for two months. Data was analyzed with paired t-test using SPSS version 17.

**RESULTS:** According to our findings, the width of keratinized gingiva at the baseline was 3 mm, and after 2 months it increased to 3.1 mm. The mean baseline height and width of gingival recession were 1.9 mm and 3 mm, respectively, and after 2 months they decreased to 1.8 mm and 2.9 mm accordingly. There was no significant difference in any of the aforementioned parameters before and after treatment ( $P > 0.05$ ).

**CONCLUSIONS:** The results of this study showed that topical application of phenytoin mucoadhesive paste can not initiate and promote creeping attachment.

**KEY WORDS:** Creeping Attachment, Phenytoin, Gingival Recession

J Oral Health Oral Epidemiol 2012; 1(2): 65-69

Creeping attachment is the postoperative migration of the gingival marginal tissue in a coronal direction over portions of a previously denuded root.<sup>1-3</sup> This phenomenon was first described by Goldman and Cohen following usage of free gingival grafts in some cases.<sup>1</sup> Creeping attachment is reported by several clinicians and is apparently best observed on mandibular anterior teeth with narrow recessions.<sup>1-3</sup> This phenomenon can be detected 1 to 12 months after graft surgery with an average coverage of about 1 mm.<sup>4</sup> Creeping attachment is reported following free gingival grafts, free connective tissue grafts, acellular dermal matrix grafts, and subepithelial connective tissue grafts.<sup>2,3,5-8</sup> The onset of creeping attachment is not an immediate mechanism,

and sometimes occurs following the initial healing.<sup>5,6</sup>

Phenytoin was first introduced as an antiseizure medication in 1973.<sup>9</sup> Its chemical structure is similar to barbiturates.<sup>9</sup> Gingival enlargement is a common complication of long-term oral phenytoin treatment.<sup>10</sup> This finding generated interest in using this drug to promote wound healing.<sup>11</sup>

Shapiro carried out the first study to evaluate the effects of oral phenytoin on periodontal wounds and reported that phenytoin accelerates wound healing and reduces pain and inflammation.<sup>12</sup> Some investigators have used topical phenytoin to accelerate healing in chronic wounds, leg ulcers, leprosy wounds, burns, diabetic foot wounds, skin graft donor sites, and war wounds.<sup>13</sup>

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Topical phenytoin increases fibroblast proliferation, extracellular matrix production, collagen synthesis, and causes granulation tissue to form significantly earlier.<sup>11,14,15</sup>

Based on the results of the studies on this subject, creeping attachment is not predictable, and the onset and mechanism of development of this phenomenon has not been recognized until now.

Therefore, based on the effects of phenytoin on wound healing and the information related to creeping attachment, we decided to apply a phenytoin mucoadhesive paste on deepithelialized gingiva to initiate and promote creeping attachment. The aim of this study was to evaluate the effect of phenytoin mucoadhesive paste on creeping attachment.

## Methods

In this pilot quasi-experimental study conducted in 2010, 8 patients (8 sites), four males and four females aged 23 to 47 years, who had Miller class I or II gingival recessions on one of premolar, canine, or incisor teeth and needed root coverage either for cosmetic reasons or dentinal hypersensitivity, were selected from the patients referred to the School of Dentistry of Kerman University of Medical Sciences, Kerman, Iran. These patients were selected using convenient non-random sampling (available samples).

The inclusion criteria of the study were no systemic diseases, no medications affecting the periodontium, no pregnancy or lactation, no periodontal diseases, no smoking, no occlusal trauma in the region under study, full-mouth plaque score and full-mouth bleeding score < 20%, recognizable cemento-enamel junction (CEJ) of the tooth under study, and no root decay and restoration. If the participants needed scaling and root planing, it had to be performed. Bass method of tooth brushing and dental flossing was instructed to all participants in this study.

These patients were informed of the purpose of the study and were required to sign an informed consent. The study design

and consent form were approved by the ethical committee of Kerman University, School of Medical and Dental Sciences.

## Clinical Measurements

Probing depth and keratinized gingival width (the distance between gingival margin and mucogingival junction) were measured at the midfacial aspect of the tooth in need of root coverage to the nearest millimeter with a Williams periodontal probe. In addition, height of gingival recession (the distance between gingival margin and CEJ of the tooth in midfacial region) and width of gingival recession at CEJ (the mesiodistal distance of gingival recession between interdental papilla at the level of CEJ) were measured to the nearest millimeter with a Williams periodontal probe.

This single-blind study was done by two clinicians. A periodontist who was blind to the study confirmed the need for root coverage in each patient and measured all clinical parameters at baseline and 2 months after application of topical phenytoin. Application of phenytoin mucoadhesive paste 1% was instructed to the patients by the second clinician that was not blind to the study. In this study, patients were not blind to the study.

## Preparation of phenytoin mucoadhesive paste 1%

Phenytoin mucoadhesive paste 1% was prepared in Kerman School of Pharmacy. To prepare this paste, one gram of phenytoin powder was mixed with 100 grams of mucoadhesive paste compositions (including polyethylene LD, liquid paraffin, gelatin powder, lemon pectin powder, sodium carboxy methyl cellulose powder). The paste was then inserted into 100 mg tubes.

## Application of phenytoin mucoadhesive paste 1% on gingiva

After root planning, the sulcular epithelium of the facial gingiva of the tooth under study, was removed by a Gracey curette 1-2, like gingival curettage and the oral epithelium confined to free gingiva was removed by a

rotary surgical handpiece with a round diamond bur under local anesthesia with lidocaine injection 2% with epinephrine. After removing sulcular and oral epithelium, patients were instructed on the application of phenytoin mucoadhesive paste 1%.

Two tubes containing phenytoin mucoadhesive paste 1% were given to each patient and patients were asked to apply one pea-sized amount of this paste on the facial surface of the gingiva of the tooth with gingival recession twice a day for two months. Patients were also educated on how to apply the paste. This act was continued for two months and at the end of the second month, probing depth, keratinized gingival width, height of gingival recession and width of gingival recession at CEJ were recorded again.

### Statistical analysis

Data was analyzed using SPSS version 17. The normal distribution of collected data was tested by the one-sample Kolmogorov-Smirnov test. Paired t-test was used to compare the results of before and after the application of phenytoin mucoadhesive paste 1%.

### Results

Patients involved in the study did not report any complication of this treatment. The clinical parameters including width of keratinized gingiva, probing depth, height of gingival recession and width of gingival recession at CEJ, at baseline and 2 months after treatment are reported in table 1. The differences between the width of keratinized gingiva, probing depth, height of gingival recession and width of gingival recession at baseline and 2 months after the treatment were not significant ( $P > 0.05$ , Table 1).

### Discussion

The aim of this study was to evaluate the

clinical effect of topical phenytoin on creeping attachment. The results of this study showed that topical application of phenytoin mucoadhesive paste did not cause any statistically significant creeping attachment ( $P > 0.05$ ).

Matter and Cimasoni reported creeping attachment after free gingival graft.<sup>2</sup> The aim of this study was to determine which conditions predisposed to creeping attachment. In this study, factors which influenced the degree of creeping attachment were: width of recession, position of the graft, position of the tooth in the arch, bone resorption, and oral hygiene. In this study, more creeping attachment was developed following the treatment of a narrow type of gingival recession (less than 3 mm). However, creeping attachment was less successful in areas of wide recessions (0% to 33%).<sup>2</sup>

Matter in another study reported a mean of 0.89 mm of creeping attachment after 5 years of follow-up.<sup>3</sup> In this study, ten patients with areas of gingival recession of less than 3 mm in width were treated with free gingival graft (FGG).<sup>3</sup>

Haeri and Parsell compared the amount of creeping attachment following free gingival grafts and dermal matrix allografts.<sup>6</sup> An average of 1.23 mm of creeping attachment was measured on the FGG side, and 0.96 mm of creeping attachment was measured with the dermal matrix allograft.

Harris showed an average of 0.8 mm creeping attachment consequent to a connective tissue with partial-thickness double pedicle graft.<sup>5</sup> In this study, Harris did not find any factors that could be associated with creeping attachment.

Otero-cagide described a case with 5 mm of a unique creeping attachment that developed mesiobuccally oriented on a deep,

Table 1. The comparison between values of measured parameters at baseline and after two months

Parameter	Baseline (mean $\pm$ SD)	After 2 months (mean $\pm$ SD)	P*
Width of keratinized gingiva	3.0 $\pm$ 1.70	3.1 $\pm$ 1.70	0.34
Probing depth	1.6 $\pm$ 0.52	1.5 $\pm$ 0.52	0.34
Height of gingival recession	1.9 $\pm$ 0.87	1.9 $\pm$ 0.87	0.34
Width of gingival recession	3.0 $\pm$ 0.47	3.0 $\pm$ 0.47	0.34

SD = Standard deviation

\*Statistically significant at  $P < 0.05$

wide recession of a maxillary first molar subsequent to autogenous gingival grafting.<sup>7</sup>

Al-Rasheed in a case report described a creeping attachment that developed after using free connective tissue graft to treat a gingival recession on the lower left central incisor.<sup>8</sup> In this study, about 2 mm of coronal migration of the gingival margin was reported.

In all studies mentioned above, some factors that may have an effect on creeping attachment were reported, but the mechanism of this phenomenon was not identified.

Topical application of phenytoin will lead to an increase in production of fibroblasts, myofibroblasts, extracellular matrix, its proteins, and activity of growth factors.<sup>11-15</sup>

Topical effect of phenytoin on repairing periodontal wounds was evaluated and a rapid repair of periodontal wounds, and decrease in pain and inflammation were also reported.<sup>12</sup>

Keeping the hypothesis that "root coverage with non-surgical treatment may be accelerated with topical medication such as phenytoin" in mind, and based on the studies performed on wound healing following application of topical phenytoin, we decided to evaluate this treatment modality. However, the results of the present study did not confirm this hypothesis. The results of this study did not show any significant increase in the width of keratinized gingiva and probing depth improvement ( $P > 0.05$ ). Aimetti et al. evaluated root coverage following scaling and root planing.<sup>16</sup> In Aimetti's study, no significant differences were observed in keratinized tissue width and probing depth improvements.

In our study, at baseline, the mean recession height was  $1.9 \pm 0.87$ , which did not change significantly after 2 months of local phenytoin therapy ( $P > 0.05$ ). In Aimetti's study, at baseline, the mean recession height in the test group was  $1.64 \pm 0.37$  mm, and in the control sites it was  $1.43 \pm 0.42$  mm, which, respectively, decreased to  $0.78 \pm 0.60$  mm and to  $1.34 \pm 0.45$  mm, after 12 months. The

difference between the two groups was significant ( $P < 0.001$ ). These results occurred because of development of creeping attachment following root planing. The duration of Aimetti's study was 12 months and root surface instrumentation was repeated twice a month during the first 2 months and at 2-month intervals over the next 10 months. This treatment is time consuming and invasive because of repeated instrumentation. In the present study, we applied phenytoin mucoadhesive paste to accelerate creeping attachment following root planing and deepithelialization of gingiva, but we did not find the anticipated effect. However, further clinical testing is needed. We suggest the application of different concentrations of phenytoin mucoadhesive paste, application of phenytoin for more than two months, and using other drugs, in a single or combined form.

## Conclusion

The aim of this study was to evaluate the effect of topical phenytoin on creeping attachment. The results of this study showed that application of phenytoin mucoadhesive paste following root planing and deepithelialization of gingiva can not initiate and promote creeping attachment after 2 months. However, further studies should be designed to evaluate the mechanism of the development of creeping attachment.

## Acknowledgement

The authors would like to thank Dr. Payam Khazaeli, Pharmacologist, for his support and preparation of phenytoin mucoadhesive paste, from Pharmacology School, Kerman University of Medical Sciences. This study was supported by a grant from Kerman Dental and Oral Diseases Research Center.

## Conflicts of Interest

The authors declare that they have no conflicts of interests. This study was supported by a grant from Kerman Oral and Dental Diseases Research Center.

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