COLOR CHANGES OF TEETH AFTER USING DOXYCYCLINE VERSUS MINOCYLCLINE AS INTRACANAL MEDICAMENT

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ABSTRACT

Background and Aim: To evaluate the discoloring effect of doxycycline versus minocycline in triple antibiotic paste (TAP) and, to compare the efficiency of light-activated bleaching on tooth discoloration after dressing with these medicaments.

Materials and Methods: Forty simulated immature permanent teeth were randomly assigned into four groups (n=10), and dressed by different antibiotic pastes as follows: Minocycline, Doxycycline, TAP with minocycline (Minocycline+), TAP with doxycycline (Doxycycline+). Following 15 days of intracanal dressing, the medicaments were removed and light-activated 35% hydrogen peroxide was applied for the bleaching purpose. Tooth color changes were measured by detecting L*, a*, and b* values with a colorimeter and ΔE value was calculated.

Results: Minocycline or Minocycline+ showed more discoloration than Doxycycline or Doxycycline+ at 15 days of medication (p<0.05). The discoloration in Doxycycline+ decreased with time while in Minocycline or Minocycline+ continued to increase discoloration (p<0.05). The highest bleaching effect was obtained in Doxycycline+ (p<0.05).

Conclusions: Doxycycline use in TAP as an alternative to minocycline caused less discoloration that was removed more effectively by the laser activated bleaching procedure.

Keywords: Bleaching, Discoloration, Doxycycline/Minocycline, Immature Permanent Teeth, Triple Antibiotic Paste
İNTRAKANAL MEDİKAMENT OLARAK KULLANILAN MİNOSİKLİNE ALTERNATİF DOKSİSİKLİN KULLANIMININ DIŞLERDEKİ RENK DEĞİŞİMİNE ETKİSİ

ÖZ

Amaç: Doksisiklin ve minosiklin içeren üçlü antibiyotik patının (ÜAP) renklendirici etkisinin ve ışınla aktive edilmiş beyazlatma işleminin bu renklenme üzerine etkisinin değerlendirilmesidir.

Gereç ve Yöntemler: 40 adet simüle edilmiş immatur daimi diş rastgele dört gruba ayrılmış (n=10) ve kök kanallarına farklı antibiyotik patları şu şekilde uygulanmıştır; Minosiklin, Doksisiklin, Minosiklinli ÜAP (Minosiklin+), Doksisiklinli ÜAP (Doksisiklin+) grubu. 15 günlük kanal içi uygulama takiben, antibiyotik patları uzaklaştırılmış ve %35’lik hidrojen peroksit ışınla aktive edilmiş beyazlatma işlemi uygulanmıştır. Dişteki renk değişiklikleri, kalorimetre ile L*, a* ve b* değerlerinin belirlenmesi ile ölçülmüş ve ΔE değeri hesaplanmıştır.

Bulgular: Minosiklin ya da Minosiklin+ gruplarını, 15 günlük uygulama sonrasında Doksisiklin ya da Doksisiklin+ gruplarına göre daha fazla renklenme göstermiştir (p<0.05). Doksisiklin+ grubunda renklenme zamanla azalırken, Minosiklin ya da Minosiklin+ grubunda renklenme artırma devam etmiştir (p<0.05). En yüksek beyazlatma etkisi Doksisiklin+ grubunda görülmüş (p<0.05).

Sonuç: ÜAP içerisinde minosiklin yerine alternatif olarak doksisiklin kullanımı daha az renklenmeye neden olur ve bu renklenme ışınla aktive edilmiş beyazlatma işlemlerini daha etkin bir şekilde geri dönebilir.

Anahtar Kelimeler: Beyazlatma, Renklenme, Doksisiklin/Minosiklin, İmmatür Daimi Diş, Üçlü Antibiyotik Patı

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INTRODUCTION

Dental trauma, caries and dental anomalies can result in necrosis of immature permanent teeth. In this case, conventional root canal treatment can remove the infection, however it leaves the root short, weak and prone to fracture. Although calcium hydroxide apexification or an apical plug with mineral trioxide aggregate can overcome some of the technical challenges during obturation of the root canals, the risk of tooth fracture and mobility still remains. Endodontic revascularization is a biologically-based alternative treatment method for the infected immature permanent teeth. Revascularization treatment provides the maturation of the root canals and so reduces the tendency of root fracture by increasing the length and thickness of root canal walls. In this treatment protocol, mechanical instrumentation is limited since it may further weaken the thin root canal walls. For this reason, the root canal disinfection mainly depends on the use of irrigation solutions and antimicrobial medicaments. Triple Antibiotic Paste (TAP) including minocycline, metronidazole and ciprofloxacin has been widely used as an intracanal medicament in revascularization. It is effective in complete removal of bacteria inside the root canal also in the deep layers of root canal dentin. However, the minocycline ingredient of the paste results in severe discoloration of the tooth crown. For this reason, other combinations of the paste or additional bleaching procedures might be considered as a further requirement for this current treatment protocol. Indeed, discoloration of minocycline, a tetracycline derivative arises from the chelating mechanism with calcium ions resulting in stable tetracycline-calcium-orthophosphate complex depositing into bone and teeth. On the other hand, doxycycline, a semi-synthetic tetracycline congener, and an active ingredient of MTAD (commonly used irrigation solution) binds less calcium and so results in less discoloration. The aim of this study was to investigate the discoloring effect of doxycycline versus minocycline in TAP and, to compare the efficiency of bleaching treatment on dentin discoloration after dressing with these intracanal medicaments.

MATERIALS AND METHODS

All experiments in the study were approved by the Ethical Committee of Hacettepe University with the project number of 014/71.

Tooth Selection and Specimen Preparation

Forty freshly extracted human maxillary incisors with no cracks, fractures, caries, abrasions and discoloration were selected for the study. The soft tissues around each tooth root were removed and the teeth were sectioned at 3 mm above and 5 mm below the cementoenamel junction using water-cooled diamond discs to obtain the standardized 8 mm length of the specimens. The outer root surfaces were polished using aluminium oxide abrasive discs from coarse to fine grit. The teeth were then stored in 0.2% thymol solution to inhibit bacterial growth. Endodontic access cavities were prepared, and the root canals of the teeth were enlarged using Gates-Glidden burs (Maillefer, Switzerland) up to #6 for the simulation of immature root canals. The specimens were then irrigated using 5 ml of 17% ethylenediaminetetraacetic acid (Werox, Izmir, Turkey) and 10 ml of 2.5% sodium hypochlorite (NaOCl) (ACE; P&G, Istanbul) to remove the smear layer and then washed with 5 ml of distilled water. After that, the prepared specimens were randomly divided into four groups according to intracanal medicaments used (n=10). TAP, a mixture of ciprofloxacin, metranidazole and minocycline/doxycycline in the proportion of 1:1:1 was prepared and applied into the root canals as follows; Minocycline (Minocin; SK Chemicals, Osan, Korea), Doxycycline (Monodoks; DEVA, Istanbul, Turkey), TAP with minocycline (Minocycline+), TAP with doxycycline (Doxycycline+). All medicaments were applied into the root canals using a lentulo spiral (Mani Inc, Toshigi-Ken, Japan) until medicament extrusion was seen from the apex to ensure that the entire volume of the root canal was filled. The coronal and apical access cavities were both temporarily sealed with ColtOsol (Coltene-Whaledent, Langenau, Germany) and the specimens were stored in dark medium with 100% humidity during the experimental procedures. After 15 days, the intracanal medicaments were removed by passive ultrasonic irrigation via a smooth ultrasonic file (size #15 K-file, 0.02 taper) coupled to the file-holding adapter of a Satelec P5 Newton XS ultrasonic system handpiece (Acteon Group, Merignac, France) using 10 ml of 2.5% NaOCl. Following the removal of TAP, 35% hydrogen peroxide (Opalescence Endo, Ultradent; South Jordan, UT, USA) was applied for the bleaching process under the light activation (Elipar 2, 3M/ESPE, Seefeld, Germany) for 20 minutes for two times.

Color Change Evaluation

Tooth colors were measured with a colorimeter, Vita Easyshade (Viadent, Brea, CA, USA) before procedures...
(baseline) and 5, 10 and 15 days after the medicament treatment. Before the measurements, the samples were mounted on a specific sample positioning system for consistent assessments.

The records with the colorimeter were obtained in terms of the CIE L*a*b* system introduced by the Commission Internationale de l’Eclairage in 1967, which allows for a numeric definition of shade and its three dimensional representation. Color is defined by the coordinates L*, from 0–100, which represents shade alterations in the black and white scale; a*, which represents shade and saturation in the red-green axis; and b*, which represents saturation in the blue-yellow axis. These three parameters for measuring the color changes (ΔL, Δa, Δb) were calculated by subtracting the baseline values from the values taken at each time. In addition, the ΔE* values, which are used to assess the color differences between 2 samples, were obtained by using the following equation:

\[ \Delta E* = \sqrt{(L_{a2} - L_{a1})^2 + (a_{a2} - a_{a1})^2 + (b_{a2} - b_{a1})^2} \]

The test groups were compared for statistical differences in the baseline L*, a*, and b* scores using one-way ANOVA while two-way ANOVA with repeated measurements was used for differences in different time intervals. The overall analysis was performed with SPSS software (version 21.00, SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at p<0.05. For clinical considerations, the human perceptibility threshold was set at 3.7 units and the differences beyond this value were considered clinically perceptible.

**RESULTS**

The mean values of the ΔE for the test groups at all time intervals are presented in Table 1 and Figure 1. Statistical analysis showed no significant difference among the baseline CIE L* a* and b* values of the test groups (p>0.05) showing homogeneous distribution of teeth in experimental groups. Regarding to the experimental groups, all groups induced color change exceeding the human perceptibility threshold (p<0.05). Doxycycline+ caused more discoloration than Minocycline after 5 days (p<0.05) while no significant difference was observed among the other groups after 10 days (p>0.05). Minocycline or Minocycline+ showed more discoloration than Doxycycline or Doxycycline+ at 15 days of medication (p<0.05).

The highest bleaching effect was obtained in Doxycycline+ and this was significantly different than the other groups (p<0.05). Minocycline, Doxycycline alone and Minocycline+ continued to increase discoloration even after bleaching procedure (p<0.05) while the discoloration in Doxycycline+ decreased with time (p<0.05).

**DISCUSSION**

Disinfection of the root canal system in revascularization treatment is mainly achieved by intracanal medicaments. Previous studies showed that minocycline content of TAP is substantially responsible for the discoloration of the medicament. This study provides insights into the comparison in potential discoloration of minocycline and doxycycline alone or when used in TAP and the bleaching effect after discoloration.

Since the variability in tooth morphology can affect the results of the study, in the present study, the teeth with similar shape and size among the groups was selected and confirmed with the similar baseline color values in all groups. For the measurement of color changes, Vita Easyshade Compact device was used as a colorimeter. Colorimeters have color filters that approximate are generally designed to measure color in X; Y; Z tristimulus terms or in CIE L* a* b* values. Colorimeter measurements when compared with spectrophotometer readings deemed reliable and accurate method for color difference measurements. In addition, colorimeters were shown good repeatability of natural

<table>
<thead>
<tr>
<th>Groups</th>
<th>ΔE5</th>
<th>ΔE10</th>
<th>ΔE15</th>
<th>ΔE-Bleach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minocycline</td>
<td>24.00 ± 7.79*</td>
<td>26.40 ± 6.03</td>
<td>29.60 ± 7.58*</td>
<td>37.30 ± 7.18*</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>24.66 ± 11.01</td>
<td>25.60 ± 9.74</td>
<td>23.90 ± 6.56*</td>
<td>28.91 ± 6.29*</td>
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<tr>
<td>Minocycline +</td>
<td>28.47 ± 8.70</td>
<td>30.00 ± 9.40</td>
<td>32.10 ± 7.69*</td>
<td>28.94 ± 9.62*</td>
</tr>
<tr>
<td>Doxycycline +</td>
<td>32.78 ± 9.50*</td>
<td>25.0 ± 6.00</td>
<td>26.50 ± 7.52*</td>
<td>22.36 ± 4.85*</td>
</tr>
</tbody>
</table>

* Different labels (*,#) in each column showed significant difference (p<0.05).
Discoloration Effects of Intracanal Medicaments

As an intracanal medicament, TAP consisting of ciprofloxacin, metronidazole, and minocycline is mostly used in regenerative endodontic cases due to its desirable antibacterial properties in infected root canal. Alternatively, doxycycline has been used in TAP instead of minocycline. Akçay et al. investigated the effect of various antibiotic pastes used in revascularization treatment and showed that TAP with minocycline and doxycycline, induced coronal discoloration exceeding color perceptibility threshold (3.7 units). This finding was in agreement with the result of the present study. The present study also showed that the bleaching procedure was not effective on the discoloration caused by doxycycline and minocycline used alone and, the discoloration continued to increase over time. The increasing of discoloration in despite of bleaching might stem from the severity and location of the tetracycline staining that was more difficult to bleach. It has been reported that more than 80% of the triple antibiotic paste that can penetrate 350 μm through the cementum was remained within dentin despite copious irrigation with different methods and protocols. This may explain why the minocycline and doxycycline is not completely resolved by the bleaching process and the remaining antibiotics in the dentinal tubules might cause further discoloration.

The present study showed that minocycline or doxycycline used alone or within TAP caused color changes exceeding the perceptibility threshold of the tooth color, and bleaching procedure was found to reduce discoloration in TAP groups. This might have been related to the use of relatively low concentration of tetracycline in TAP compared to the groups where minocycline and doxycycline are used alone. For tetracycline stained teeth, the color is derived from the photo-oxidation of the tetracycline molecule. Peroxide has been considered to decrease tetracycline discoloration by chemical degradation. In this study, light-activated hydrogen peroxide tooth bleaching system was used to accelerate the bleaching process. Laser application has been recommended for severe discoloration by increasing the bleaching properties of the hydrogen peroxide. It also accelerates the bleaching effect, allows simple and short application of the bleaching agents, and so prevents the long term detrimental effects on dental structures. The present study showed that the laser activated peroxide bleaching significantly decreased the discoloration of TAP with doxycycline even it was still beyond the human perceptibility threshold.

CONCLUSION

Doxycycline and minocycline caused severe discoloration, especially used alone. Hydrogen peroxide bleaching activated with laser seems more effective on the discoloration by doxycycline containing TAP and is not a convenient method for the discoloration of the minocycline containing medicaments. Subsequent studies on the factors which can reduce the discoloring effects of tetracycline containing medicaments should be investigated.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

5. Cehreli ZC, Isbitiren B, Sara S, Erbas G. Regenerative endodontic treatment (revascularization) of immature necrotic molars


