

Effect of two Percent turmeric extract gel on minor recurrent aphthous stomatitis

Nurdiana, Shamini Krishnasamy

Departement of Oral Medicine Faculty of Dentistry Universitas Sumatra Utara

ABSTRACT

Minor recurrent aphthous stomatitis (RAS) is recurrent oral ulcer with clinical features of shallow ulcer, round or oval shape, measuring less than 10 mm, covered with yellowish white pseudomembrane and surrounded by erythematous halo. Inflammation and pain that accompany the RAS make individual seek treatment to relieve these symptoms. Turmeric extract gel is a traditional medicine that can be used to cure RAS because it has anti-inflammatory, antibacterial, covering agents and antioxidants effect. The aim of this study was to explore the effect of 2% turmeric extract gel on minor RAS in reduction of erythematous halo, ulcer size, and pain intensity. This study was an experimental study using a pre test - post test control group design. The study involved 16 patients with minor RAS at University of Sumatera Utara Dental Hospital. Data collected by initial examination of RAS which included erythematous halo, ulcer size and pain intensity then controlled every day for the next three days. Analysis of the data in this study was used Friedman Test and Wilcoxon Signed Ranks Test to determine the difference between observations before and after RAS treatment. This study showed statistically significant results in reduction of erythematous halo at day of examination to first control with P value of 0.03 and first control to second control with P value of 0.025. Reduction of ulcer size showed statistically significant result at day of examination, first, second and third control with P value of 0.001 ($P < 0.05$). This study also showed statistically significant reduction in pain intensity with P value of 0.001 ($P < 0.05$) for day of examination to first control and first control to second control, as well as 0.014 ($P < 0.05$) for second control to third control. The results of this study showed a significant reduction in erythematous halo, ulcer size, and pain intensity.

Key words: Recurrent aphthous stomatitis, turmeric, erythematous halo, ulcer size, pain intensity

ABSTRAK

Stomatitis aphthous recurrent (RAS) minor adalah ulkus mulut berulang dengan gambaran klinis ulkus dangkal, bentuk bulat atau oval, diameter berukuran kurang dari 10 mm, ditutupi dengan pseudomembran putih kekuningan dan dikelilingi oleh halo eritematosa. Peradangan dan nyeri yang menyertai RAS membuat pasien mencari pengobatan untuk meringankan gejala-gejala tersebut. Ekstrak gel kunyit adalah obat tradisional yang dapat digunakan untuk menyembuhkan RAS karena memiliki efek anti-inflamasi, antibakteri, antioksidan dan dapat menyelimuti lesi. Tujuan dari penelitian ini adalah untuk mengeksplorasi efek ekstrak kunyit gel 2% pada RAS minor untuk mengurangi luas daerah halo eritematosa, ukuran ulkus dan intensitas nyeri. Penelitian ini merupakan penelitian eksperimental dengan menggunakan desain tes pra dan pasca untuk kelompok uji. Penelitian ini melibatkan 16 pasien dengan RAS minor di Rumah Sakit Gigi dan Mulut Universitas Sumatera Utara. Data dikumpulkan melalui pemeriksaan awal RAS meliputi luas daerah halo eritematosa, ukuran ulkus dan intensitas nyeri kemudian dikontrol setiap hari selama tiga hari ke depan. Analisis data dalam penelitian ini menggunakan Friedman Test dan Wilcoxon Signed Ranks Test untuk menentukan perbedaan antara pengamatan sebelum dan setelah pengobatan RAS. Penelitian ini menunjukkan hasil yang signifikan secara statistik pada pengurangan luas daerah halo eritematosa antara kunjungan pertama dengan hari kontrol pertama ($p = 0,03$) dan antara kontrol ke-1 dengan kontrol ke-2 ($p = 0,025$). Pengurangan ukuran ulkus menunjukkan hasil yang signifikan secara statistik pada kunjungan pertama, kontrol pertama, kontrol kedua dan ketiga dengan nilai $p = 0,001$ ($P < 0,05$). Penelitian ini juga menunjukkan penurunan signifikan secara statistik dalam intensitas nyeri dengan nilai $p = 0,001$ ($P < 0,05$) untuk kunjungan pertama dibandingkan dengan kontrol pertama dan antara kontrol pertama dengan kontrol kedua, serta $0,014$ ($P < 0,05$) untuk perbandingan kontrol kedua dengan kontrol ketiga. Hasil penelitian ini menunjukkan penurunan yang signifikan dalam hal luas daerah halo eritematosa, ukuran ulkus dan intensitas nyeri.

Kata kunci: *Stomatitis aphthous recurrent, gel kunyit, halo eritematosa, ukuran ulkus, intensitas nyeri.*

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is the most common disorders occurring in oral cavity. Recurrent aphthous stomatitis is classified into three types which is minor, major, and herpetiform.¹ Minor RAS is characterized by painful recurrent small, round, or ovoid ulcer, less than 1 cm in size with circumscribed margin, erythematous halo, and yellow or grey floor.^{1,2} The etiology of RAS is unknown but many possible etiologic agents and predisposing factors have been described in the literature.³ There is no curative treatment for RAS but treatment concentrated on promotion of healing and prevention of secondary infection, such as 3% hydrogen peroxide, water solution covering agents, topical analgesics, chlorhexidine mouthwashes, and localized steroid.⁴

Turmeric is a spice that comes from the root of *Curcuma longa*, a member of the ginger family, Zingiberaceae.⁵ In India, it has been used for centuries for its various medicinal

properties.^{1,5} Curcumin is a main pigment of turmeric and is known for its strong antioxidant, antiseptic, antibacterial, anti-inflammatory, immunomodulatory, and analgesic properties.^{1,2}

The use of turmeric in dentistry has been reported for treating toothache, gingivitis, periodontitis, and others.² A study by Marifar (2012) showed that 2% curcumin gel significantly reduced pain intensity and ulcer size of RAS compare to placebo.⁶ Another study by Al-Saffar (2006) revealed that topical application of viscous solution of curcumin at 10% and 50% concentration showed a good result of healing in patient with RAS.⁴ The aim of this study was to explore the effect of 2% turmeric extract gel on minor RAS in reduction of erythematous haloes, ulcer size, and pain intensity.

MATERIALS AND METHODS

The study was an experimental pre test - post test control group design. The subjects were

patients with minor RAS at University of Sumatera Utara Dental Hospital, Medan. The patients were selected with non probability sampling with purposive sampling. Patients were included if they presented with minor RAS with stress as the predisposing factor, and no history of systemic diseases and consumption of medicine. Patients were excluded from the study if they were not willing to be included in this study and wearing orthodontic appliance. The 2% turmeric extract gel was made at Traditional Medicine Laboratory, Faculty of Pharmacy, University of Sumatera Utara. The gel was made from 25 grams of carboxy methyl cellulose mixed with 1000 grams aquadest. Then, 35 grams turmeric extract diluted with a few drops of 70% ethanol and mixed with 1000 grams gel.

The trial was performed in approved by the Health Research Ethical Committee of North Sumatera. Written informed consent was obtained before entering the study. The data about RAS obtained with anamnesis and clinical examination. Anamnesis was done to evaluate the pain intensity in accordance with Verbal Descriptor Scale (VDS) with 0 means no pain, and 10 means uncontrollable pain. Clinical examination was done to assess erythematous halo, and ulcer size before treatment.

Patients were instructed to apply 2% turmeric extract gel 3 times a day (after breakfast, after lunch, and before sleep). The patients were advised not to eat or drink for 30 minutes to 1 hour after using the medication. Patients were also instructed to come every day for 3 days to evaluate the healing process of the ulcer in terms of erythematous halo, ulcer size, and pain intensity. Computer program was used for data entry and data analysis. Descriptive statistic of the study was calculated. The bivariate data were analyzed statistically using Friedman Test and Wilcoxon Signed Ranks Test with $P < 0.05$ was considered statistically significant.

RESULTS

This study was carried out from January to February 2015. A total of 16 patients were

participated in the study. The patients consist of 3 (18.80%) male and 13 (81.20%) female (Figure 1).

The reduction in erythematous halo was statistically significant in pre test - post 1 (day of examination to first control) with P value of 0.003 and post 1 - post 2 (first control to second control) with P value of 0.025. Meanwhile, no statistically significant reduction was note in post 2 - post 3 (second control to third control) with P value of 0.317 (Table 1).

The age range of the patients was 18 to 29 years. Patients at the age of 22 years was most commonly affected with 7 (43.8%) patients and patient age at the age 18 and 19 was the least affected with 1 (6.2%) patient (Figure 2).

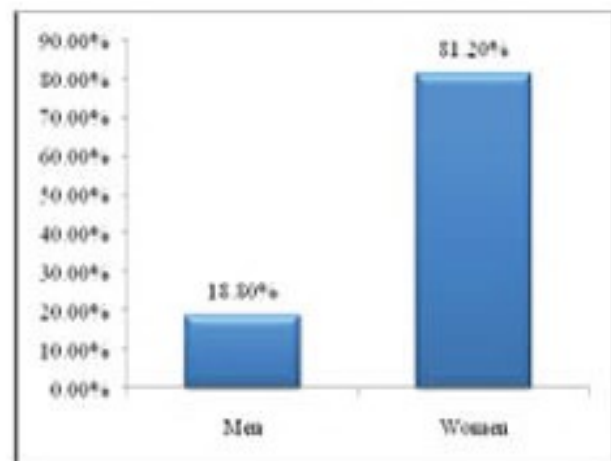


Figure 1. Distribution of the patients according to gender.

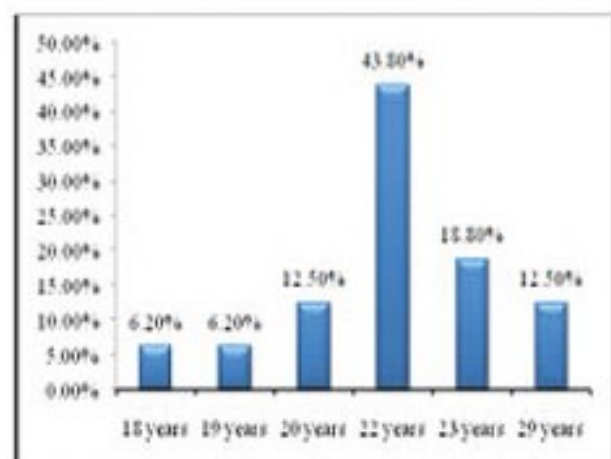


Figure 2. Distribution of the patients according to age.

Table 1. Analysis of erythematous halo at day of examination, first control, second control, and third control after given 2% turmeric extract gel.

Erythematous Halo	Mean	P value
Pre test - Post 1	1.31	0.003*
Post 1 - Post 2	2.44	0.025*
Post 2 - Post 3	3.06	0.317

* Significant

Ulcer was analyzed with Friedman Test and Wilcoxon Signed Ranks Test. Pre test - post 1 (day of examination to first control), post 1 - post 2 (first control to second control), and post 2 - post 3 (second control to third control) showed statistically significant with P value of 0.001 ($P < 0.05$) (Table 2).

Table 2. Analysis of ulcer size at day of examination, first control, second control, and third control after given 2% turmeric extract gel.

Ulcer Size	Median ± Interquartile Range	P value
Pre test - Post 1	3.00 ± 1.40	0.001*
Post 1 - Post 2	1.75 ± 1.50	0.001*
Post 2 - Post 3	0.00 ± 1.40	0.001*

* Significant

The reduction in pain intensity was statistically significant. Friedman Test and Wilcoxon Signed Ranks Test of pain intensity statistically significant with P value of 0.001 ($P < 0.05$) for day of examination to first control and first control to second control, as well as 0.014 ($P < 0.05$) for second control to third control (Table 3).

Table 3. Analysis of pain intensity at day of examination, first control, second control, and third control after given 2% turmeric extract gel.

Pain Intensity	Median ± Interquartile Range	P value
Pre test - Post 1	5.00 ± 2.00	0.001*
Post 1 - Post 2	3.00 ± 1.00	0.001*
Post 2 - Post 3	0.50 ± 1.00	0.014*

* Significant

DISCUSSION

Recurrent aphthous stomatitis is one of the most common painful oral disorder seen among patients that affects approximately 20% of the general population with minor RAS makes up more than 80% of all RAS cases.^{7,8} Recurrent aphthous stomatitis has a slight female predominance and typically starts in childhood or adolescence.³ In this study, the patients consist of 3 (18.8%) male and 13 (81.2%) female. The study done by Patil et al. showed that female (56.30%) were more frequently affected by RAS than male (43.70%) and this difference was statistically significant ($P < 0.005$).⁹ The result were similar to the findings by Safadi (2009) that reported female (82%) had RAS more than males (73%) and the difference between genders was statistically significant ($P = 0.003$).⁷ The current concept is that RAS is a clinical syndrome with several possible causes. Factors that have been suggested as being etiologic in RAS includes psychological stress and anxiety.⁸ Females are more prone to stress and emotional situations which can affect their immune response. Females also seek medical examination more frequently than males. The hormonal changes during pregnancy and menstruation also play a role in etiopathogenesis of RAS in female.¹⁰

The characteristic RAS initially present in the first or second decade of life, making this one of the few immune-mediated inflammatory conditions seen in both children and adults, and the frequency of episodes often diminishes sharply during the third decade.¹¹ Minor RAS in this study was most commonly seen in the patients aged 22 years with 7 (43.80%) patients, meanwhile the least commonly seen was in patients age 18 and 19 years with 1 (6.20%) patient. The result was similar to the study done by Abdullah et al. (2013) that showed RAS most commonly affected patient at an age range of 20 - 29 years.¹² Another study by Agustiar (2002) also revealed that RAS most commonly affect patients with age range from 21 - 41 years.¹³

Erythema is one of the five cardinal signs of inflammation. Erythema is caused by the dilation

of small blood vessels (vasodilation) in the area of injury which increasing blood flow into the area.¹⁴ In this study, all of the ulcers had erythematous halo at day of examination. Meanwhile, 7 patients had erythematous halo at first control, 2 patients had erythematous halo at second control, and 1 patient had erythematous halo at third control. Mean reduction of erythematous halo was 1.31 at first control, 2.44 at second control, and 3.06 at third control.

The number of erythematous halo showed decrease with application of 2% turmeric extract gel every day for 3 days. The bivariate analysis of erythematous halo showed statistically significant at day of examination to first control with P value of 0.003 ($P < 0.05$). Analysis of first control to second control showed P value of 0.025 ($P < 0.05$) that indicate statistically significant reduction in erythematous haloes. At second control to third control after application of 2% turmeric extract gel P value was 0.317 ($P > 0.05$) that indicate no statistically significant decrease. However, at third control 15 patients no longer showed erythematous halo. In the previous study conducted by Halim et al. (2013) found that curcumin accelerate healing process of ulcer by increasing cell proliferation and collagen synthesis which was shown by increasing of DNA (deoxyribonucleic acid), protein total, and type III collagen in wound tissue.²

Once acute inflammation has begun, a number of outcomes may follow including healing and repair. During healing process, damaged cells capable of proliferation regenerate.¹⁴ The analysis of ulcer size at day of examination, first control, second control, and third control showed reduction in Median \pm Interquartile Range. After application of 2% turmeric extract gel there was a reduction in ulcer size from 4.00 ± 1.80 at day of examination to 3.00 ± 1.40 mm at first control, 1.75 ± 1.50 mm at second control and 0.00 ± 1.40 mm at third control. Deshmukh et al. (2014) stated that curcumin can reduce ulcer size with complete healing (0 mm) in 7 days.¹ The curcumin extract gel act as covering agent because of its high viscosity (thick). The gel will adhere to ulcer and heal without any disruption therefore ulcer will heal faster.^{14,6} Study by Al-Saffar (2006) revealed curcumin as a strong antioxidant compare to vitamin E which also help accelerate repaired of damaged tissue.⁴ Moreover, antibacterial activity

of turmeric prevent bacterial growth around ulcer therefore ulcer will heal faster.¹

The analysis of ulcer size with Friedman Test and Wilcoxon Signed Ranks Test showed P value of $P = 0.001$ ($P < 0.05$) which means there was statistically significant difference in ulcer size at day of examination, first control, second control, and third control after application of 2% turmeric extract gel for 3 days. In this study known that 9 patients healed completely after application of 2% turmeric extract gel for 3 days. The application of 2% turmeric extract gel accelerate the healing of SAR like shown in study by Deshmukh et al. in which curcumin reduce the inflammation by increasing the epithelisation level.¹

Recurrent aphthous stomatitis often cause pain.³ The pain results in part from the distortion of tissues, and also induced by certain chemical mediators of inflammation, such as bradykinin, serotonin, and the prostaglandin.¹⁴ In this study, pain was measured with Verbal Description Scale. This scale can be used objectively to measure pain. It is consists of pain description that arranged in the same distance along a line. The patients were then asked to describe the most appropriate scale for perceived pain. The description is ranked from 0 as no pain, 1-3 as mild pain, 4-6 as moderate pain, 7-9 as severe controllable pain, and 10 as uncontrollable pain.¹⁵ The result of this study showed Median \pm Interquartile Range value was 5.00 ± 2.00 for day of examination to first control (moderate pain). The pain intensity was reduced after application of 2% turmeric extract gel, Median \pm Interquartile Range of pain intensity was 3.00 ± 1.00 (mild pain) for first control to second control, and 0.50 ± 1.00 (mild to no pain) for second control to third control.

The statistic analysis of pain intensity with Friedman Test and Wilcoxon Signed Ranks Test showed P value of 0.001 ($P < 0.05$) which means there was statistically significant reduction in pain intensity of minor RAS at day of examination, first control, second control, and third control. Based on statistic analysis of this study the result showed that turmeric extract gel can reduce pain intensity. In this study 13 out of 16 patients experienced no pain after application of 2% turmeric extract gel for 3 days. In study by Marifar et al. (2012) revealed that curcumin gel significantly reduce the pain intensity.⁶ Another study by Deshmukh

et al. (2014) showed that turmeric act as anti-inflammation that relatively fast in reducing pain by hampering prostaglandin.¹ The prostaglandins are a group of fatty acids produced by many types of cells which are associated with the pain.¹⁴

CONCLUSION

Two percent turmeric extract gel has a good effect on minor RAS. The application of 2% turmeric extract gel for 3 days showed a significant reduction in erythematous halo, ulcer size, and pain intensity.

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