

## The Effectivity of *Hyaluronic Acid* 0.1 % on the Healing Process of Traumatic Ulcer Caused by Fixed Orthodontic Appliance

Nada Ismah, Benny Mulyono Soegiharto, Hanna Silvia Debora  
Department of Orthodontics, Faculty of Dentistry, Universitas Indonesia  
Jakarta, Indonesia  
Phone : +6283892205887  
E-mail : green\_ivy1987@yahoo.com

---

### ABSTRACTS

**Introduction:** *Hyaluronic acid* is a substance of human connective tissues and is reported to have important role in wound healing process, facilitating the migration and cell differentiation during the development process of embryo, and the tissue repairing. **Objectives:** To study the effectiveness of *Hyaluronic Acid* 0.1 % on the healing process of traumatic ulcer caused by fixed orthodontic appliances based on the size, redness and pain perception of the ulcer. **Materials and Methods:** Thirty two subjects with fixed orthodontic appliance who had traumatic ulcer on buccal or labial mucosa due to the presence of fixed appliance on the examination day were included and divided into 2 groups. The first group (K1) was instructed to gargle with 10 ml *hyaluronic acid* 0,1 %-contained mouthwash for 2 minutes after tooth brushing, twice a day for 4 days in a row. The second group (K2) is given the same instruction but with placebo. The size and colour (redness) of the ulcer were measured before and after treatment using a caliper and customized redness measurement index. The Pain perception was measured after treatment using a questionnaire. **Results:** The percentage of changes (decline) in wound size and redness changes (decline) in K1 were more significant compared to K2 ( $p < 0.05$ ). The change of pain perception in K1 was not significant compared to K2 ( $p > 0.05$ ). **Conclusion:** *Hyaluronic acid* 0.1 %-contained mouthwash seemed to be effective in accelerating the wound healing, in size and colour of the ulcer, but might not be effective in reducing pain of the traumatic ulcer compared to placebo.

**Keywords :** Hyaluronic Acid 0.1 %, traumatic ulcer, fixed orthodontic appliance.

---

### **Author Corresponding Address :**

Department of Orthodontics, Faculty of Dentistry, Universitas Indonesia  
Phone : +6283892205887 E-mail: green\_ivy1987@yahoo.com



## INTRODUCTION

The interest in orthodontic treatment has increased along with the increase of people's awareness in oral and dental health importance.<sup>1</sup> The aim of orthodontic treatment is to correct malocclusion in order to improve the oral and dental health care, mastication, comfort, and aesthetics.<sup>2</sup>

During the treatment, a patient must be able to take care of his/her oral hygiene and do the routine call to the dentist. Various side effects which can be experienced by the patient during the treatment are caries, pulpitis, pulp devitalitation, root resorption, periodontitis and traumatic ulcer on oral mucosa.<sup>3</sup>

The trauma on oral mucosa due to orthodontic appliances is often experienced by many patients, and may cause discomfort and pain.<sup>4,5</sup> Kvam et al (1989) conducted a research in the University of Oslo to 79 fixed orthodontic patients where it showed that 94.9 % of the patients experienced the traumatic ulcer on their oral mucosa caused by the fixed orthodontic appliances. It also showed that 46.8% of the patients considered the traumatic ulcer as the most annoying aspect of orthodontic treatment.<sup>4</sup>

Traumatic ulcer in form of laceration can be caused by the friction of the oral mucosa to the components of the orthodontic appliance. It often happens on the first week when the oral mucosa is

adapting to the presence of the orthodontic appliance.<sup>6</sup>

The traumatic ulcer can occur from days to several weeks and often reappear in the same or different region, and may be acute or chronic. Although it can reappear and chronic, yet it will not cause any malignancy itself. This is because malignancy will not happen without the cancer risk factors such as smoking and alcohol consumption in long term.<sup>7</sup> Nevertheless, the discomfort and pain caused by the traumatic ulcer can disturb the patient's activity, especially during eating.<sup>4,5</sup>

One of the treatment usually chosen by patients, is to use mouthwash.<sup>8</sup> There are various active ingredients of the mouthwash which can be found in the market, one of them is *hyaluronic acid*.

*Hyaluronic acid*, also known as *hyaluronan* atau *hyaluronate*, is a substance of the human connective tissues. *Hyaluronic acid* is reported to have important role in wound healing process, facilitating the migration and cell differentiation during the development process of embryo, and the tissue repairing.<sup>9</sup> Recent studies reported that *hyaluronic acid* can accelerate the healing process in recurrent aphthous ulceration<sup>10</sup>, oral lichen planus<sup>11</sup> and gingivitis.<sup>12</sup>

This study is performed in order to evaluate the effectivity of *hyaluronic acid* 0.1% on the healing process of the traumatic ulcer caused by fixed orthodontic appliance.



## MATERIAL AND METHODS

This research design was clinical experimental which was carried out in Orthodontic clinic, RSGM-P FKG UI and Faculty of Dentistry, University of Indonesia on November 2009.

The research population were the patients in Orthodontic clinic, RSGM-P FKG UI and the students of the Faculty of Dentistry, Universitas Indonesia. Patients aged 10-40 years old with 3 - 10 mm diameter of traumatic ulcer on buccal/labial mucosa caused by the orthodontic appliances (bracket, cleat, band, hook, or sharp wire), wound lasted for maximum 3 days before the collection of the research data, not smoking, not consuming alcohol or drugs, and willing to participate in the research by signing the informed consent were included. Patients with systemic diseases, in menstruation period or pregnancy were not included in this research. The number of subjects was calculated by using Federer formula<sup>13</sup>:  $(t-1) \times (n-1) \geq 15$ ; where  $t$  is number of treatment and  $n$  is number of sample in each treatment group.

Based on the formula, the minimum 32 subjects (16 subjects in each group) were needed. The separation of the subjects into each group is decided by the researcher. Sample of this research was the traumatic ulcer caused by the fixed orthodontic appliance found on buccal/labial surface of mucosa. The samples were

collected through convenience sampling. Ethical clearance was approved by the ethical committee from Faculty of Dentistry, Universitas Indonesia and the patients were signing the inform consent.

The subjects in first group (K1) were instructed to gargle with *hyaluronic acid* 0.1 %-contained mouthwash (Sanorine<sup>®</sup>), while another group (K2) were instructed to gargle with placebo (sterile aquadest with mint essence). Both of them is instructed to gargle with the given mouthwash as much as 10 ml for 2 minutes after tooth brushing, twice a day for 4 days in a row.

The size of traumatic ulcer was measured using a caliper (Schezher<sup>®</sup>). The surface area of the traumatic ulcer was counted using the surface area formula of ellips: length x width x 0.785 (simple measurement technique)<sup>14</sup> in mm<sup>2</sup>. The colour (redness) of the traumatic ulcer was measured using customized redness measurement index which was a grading of red colour (R: 204, G: 81, B: 76) made using Adobe<sup>®</sup> Photoshop<sup>®</sup> CS2 Version 9.0, arranged by the color balance level, with interval of Cyan as much as 20 %. The measurement of traumatic ulcer size was done before and after the treatment, both in K1 and K2. In addition, the size of the traumatic ulcer (surface area, in mm<sup>2</sup>) after treatment was subtracted with the size of it before treatment and then multiplied by 100 to get the percentage of traumatic ulcer surface area



changes. The measurement of traumatic ulcer colour (redness) was done before and after treatment. The data taken is then scored. The measurement of pain perception was done after the treatment using a questionnaire consisted of 4 questions, the data taken is then calculated and scored.

In figure 1, the mean percentage of K1 traumatic ulcer surface area changes is 68.9 %, its minimum score is 40.48 % and its maximum score is 100 %. While, the mean percentage of K2 traumatic ulcer surface area changes is 47.34 %, its minimum score is 22.04 % and its maximum score is 85.24 %. To analyse the significant difference between them, the independent t test is used. The significance level shows  $p < 0.05$ , with  $p = 0.002$ . The conclusion from this test was the percentage of traumatic ulcer surface area changes (decline) between K1 and K2 is significantly different.

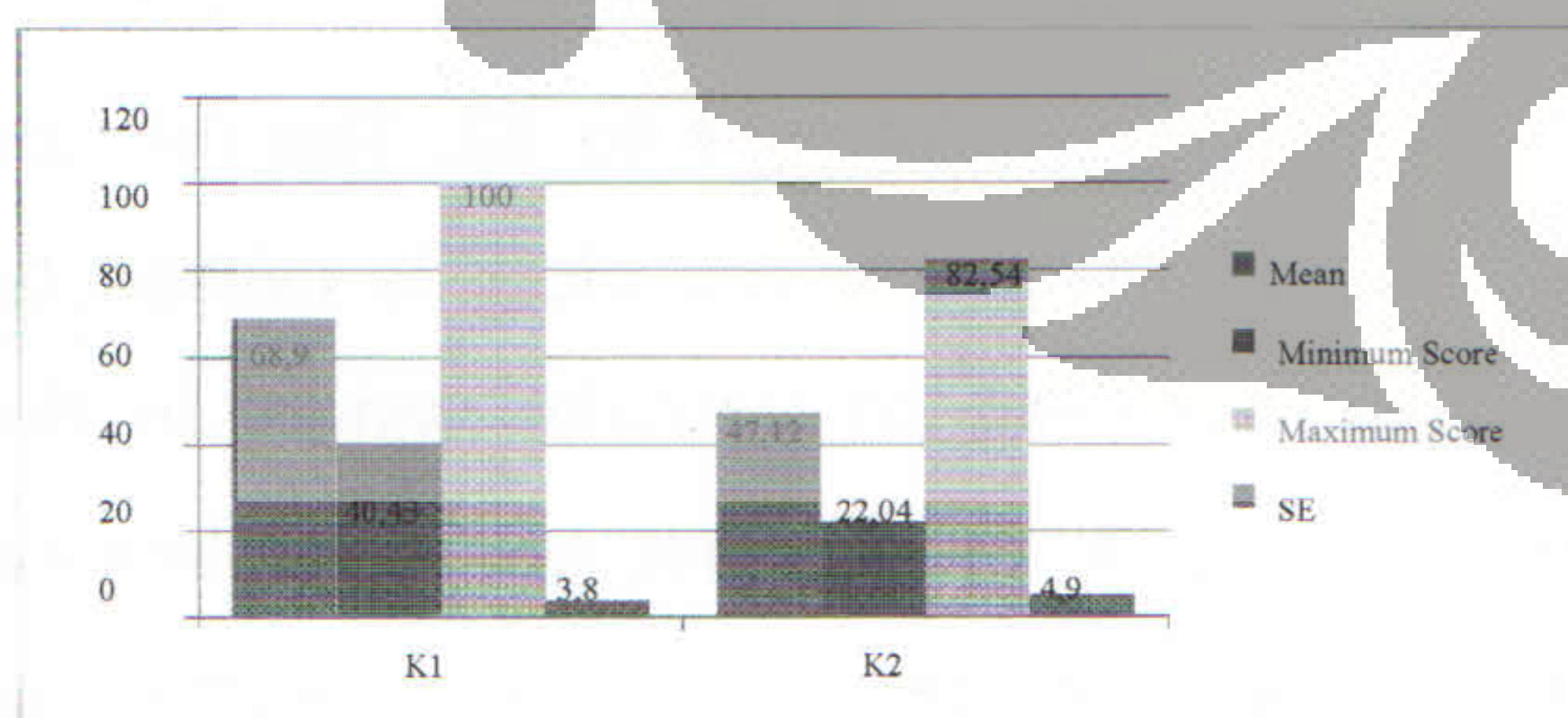


Fig. 1. The comparison of traumatic ulcer surface area changes in K 1 and K 2 (in%)

In figure 2, the colour of the traumatic ulcer after the treatment will be scored 0 if the redness of the ulcer is gone after the treatment (the colour of traumatic

ulcer is the same with the surrounding healthy mucosa), scored 1 if the redness of the traumatic ulcer is decreased but not has the same colour with surrounding healthy mucosa after the treatment, and scored 2 if the redness of the traumatic ulcer is still the same after the treatment. Mann Whitney U test is used in order to analyze the significance difference between the two groups. The significance level shows  $p < 0.05$ , with  $p = 0.008$ . Therefore, it can be concluded that the difference between K1 and K2 in traumatic ulcer redness changes is significantly different.

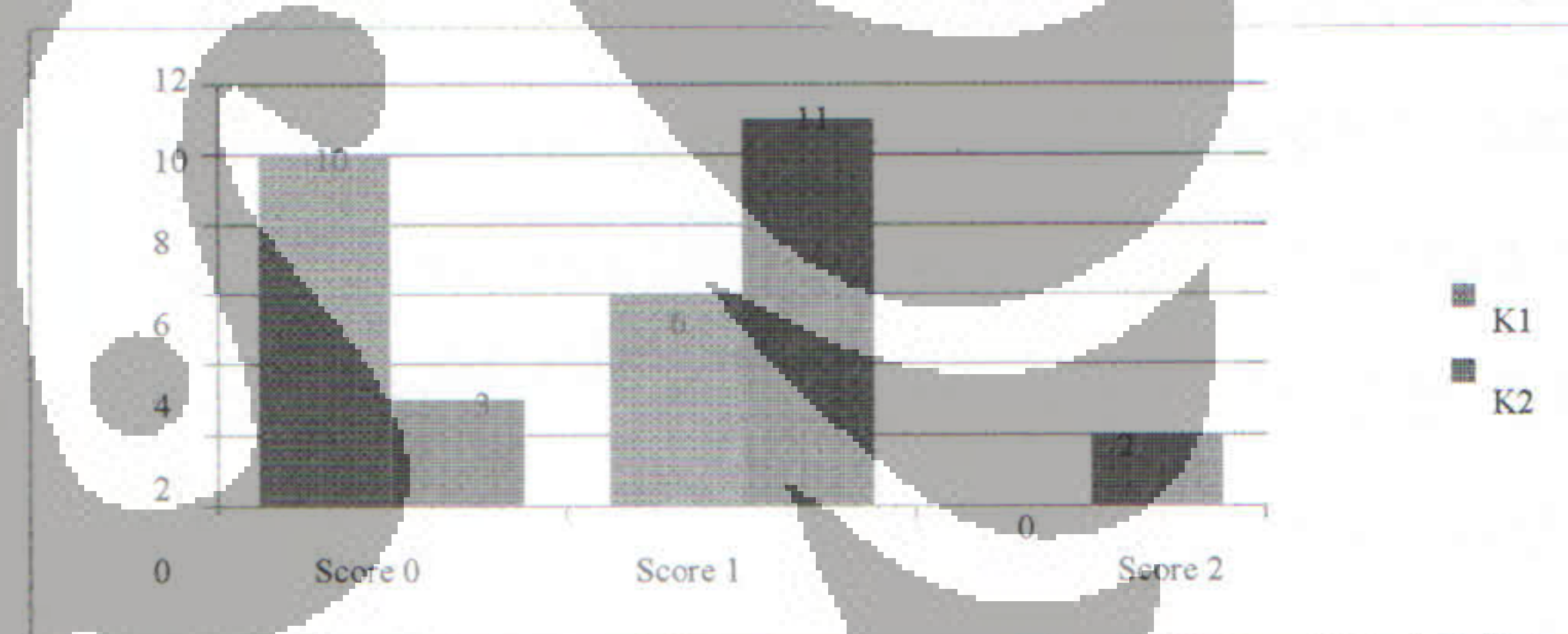


Fig. 2. The traumatic ulcer redness changes comparison between K1 and K2

In figure 3, the pain perception of the traumatic ulcer after the treatment is scored 1 if the pain is decreased after the treatment or scored 0 if the pain is still the same after the treatment. To analyze the significant difference between K1 and K2, Mann Whitney U test is used. The significance level shows  $p > 0.05$ , with  $p = 0.472$ . So it can be concluded that the pain perception between K1 and K2 is not significantly different.



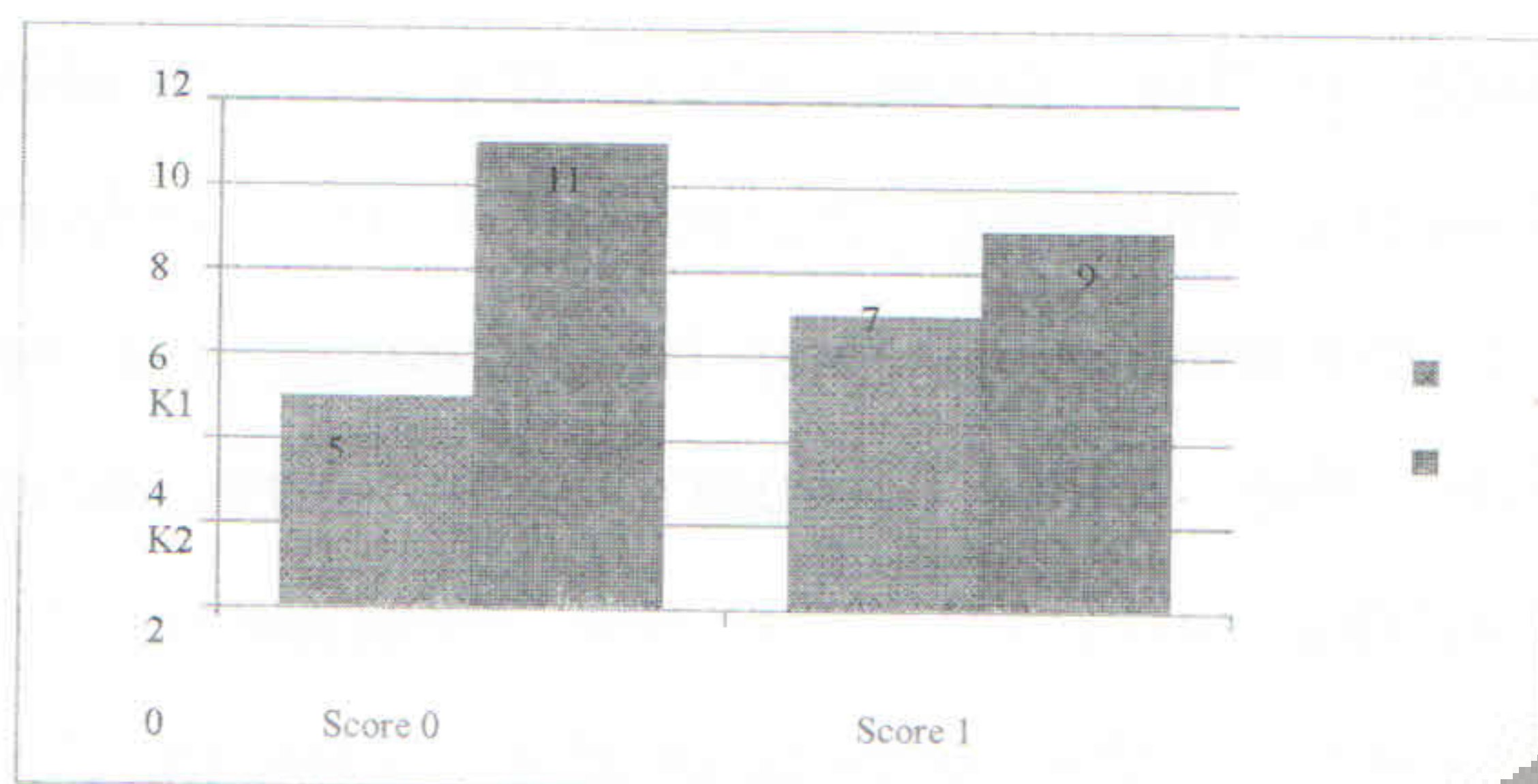


Fig. 3. The comparison of traumatic ulcer pain perception in K1 and K2

## DISCUSSION

The treatment was done for 4 days based on the literature stated that traumatic ulcer on mucosa would be healed in 7-10 days. The traumatic ulcer included in this research was aged maximum 3 days, so when the treatment was given for 4 days, the wound would show significant healing on the 4th day after the treatment.<sup>15,16</sup> Besides, the study done by Nofan et al shows that on the 4th day after treatment with *hyaluronic acid* the changes between control group and *hyaluronic acid* group already showed significant difference.<sup>10</sup>

The significance gained between K1 and K2 in percentage of wound area changes is showed that healing process in K1 (*hyaluronic acid* group) is more effective compared to K2 (placebo group). That result is supported with the study done by Liguori et al which found that *hyaluronic acid* accelerates the healing process because it roles in the phases of healing process. In inflammation phase, *hyaluronic acid* activates cells migration (fibroblast, lymphocyte and

neutrophil) to the site of injury. *Hyaluronic acid* also regulates the inflammation by producing proinflammation cytokines and stimulates angiogenesis. During maturation phase, *hyaluronic acid* also accelerates repair mechanism such as migration and proliferation of fibroblast, collagen synthases and proliferation of endothelium cells. The application of topical *hyaluronic acid* accelerates the wound healing process significantly.<sup>17</sup> Therefore, the changes (decline) of traumatic ulcer size occurred on K1 is more effective compared to K2. It is because the wound/ traumatic ulcer healing process in K1 is accelerated by *hyaluronic acid* which is given topically (by gargling) on the site of wound, while the wound/ traumatic ulcer healing process in K2 is occurred normally without any external help (physiologic reaction of body to the wound).

The significance gained in wound redness changes is showed that the declining in traumatic ulcer redness of K1 is more effective compared to K2. The redness of the wound/ traumatic ulcer is caused by the improvement of vascular system in the site of wound. In the last phase of healing process (maturation phase), the redness of the wound is decreased since the blood vessels start to do regression. The decline of the wound redness is happened as the wound start to heal and therefore shows the occurrence of wound healing process.<sup>18</sup> The decline of wound/ traumatic ulcer redness in



K1 shows that the redness (rubor) of the traumatic ulcer is decreased significantly compared to K2 as a result of the acceleration of wound/traumatic ulcer healing process done by *hyaluronic acid*.

The significance can not be gained in the wound pain perception. It shows that the pain perception in K1 is not more effective compared to K2. Based on the literature, the wound is more painful in the inflammation phase when the nerves is stimulated by the substance released by the mast cells due to the occurrence of wound compared to the active repair mechanism when the cells is started to be repaired and the inflammatory mediators is started to decline (in proliferation to maturation phase).<sup>19</sup> The changes in pain perception of K1 and K2 are not different significantly since the last examinations of the traumatic ulcer/wound (on the 4<sup>th</sup> day after the treatment) both in K1 and K2, were done when the traumatic ulcer/wound had passed the inflammation phase (which is ended on the 3<sup>rd</sup> day after the injury). This caused both K1 and K2 were experienced the declining in pain perception after the treatment.

In this research, there were 5 subjects in K1 and 6 subjects in K2 which did not feel any pain on the wound/traumatic ulcer, while others reported pain on the wound/traumatic ulcer which was decreased on the 4<sup>th</sup> day after the treatment (both in K1 and K2). The difference in pain perception

may be caused by the difference in pain threshold and pain tolerance in each individual. Pain threshold is a condition when an individual start to experience a pain, while pain tolerance is the duration or intensity of the pain which can be beared by an individual before he/she exerted a response to the pain. Thing that can cause pain on an individual might not cause the same thing to the others since the pain perception is subjective. The pain tolerance is different significantly in each individu, due to the difference of body ability in giving respons to different stimuli. It is also influenced by traditional perception, hopes, behaviour, mental and physical health of the individual.<sup>20</sup> Therefore, in this research there were some subjects which did not feel any pain although there were traumatic ulcers on their oral mucosa. Although the traumatic ulcer could be painless in some individual, it doesn't mean that the occurrence of it can be ignored. The traumatic ulcer on the oral mucosa of a person with fixed orthodontic appliance has a risk of infection. The infection of the wound (traumatic ulcer) will increase the pain on the wound (traumatic ulcer) and cause the healing process delayed.<sup>19</sup>

The result of this research supports the previous researches done which showed that *hyaluronic acid* can accelerates the healing process in acute wounds<sup>21</sup>, RAU<sup>10</sup>, OLP<sup>11</sup> and gingivitis<sup>12</sup>.



The result of this research showed that gargling with *hyaluronic acid* 0.1 %- contained mouthwash is effective in accelerating the healing process of the traumatic ulcer caused by fixed orthodontic appliance in wound size and redness changes (decline), but not effective in decreasing the pain perception compared to placebo.

Although *hyaluronic acid* 0.1 % did not show significant difference compared to placebo, it does not mean that *hyaluronic acid* 0.1 % is seemed to be not effective at all in decreasing pain perception. The measurement of pain perception in this research is the pain perception of the research subjects, which was quite subjective. Further research is needed to prove the effectiveness of *hyaluronic acid* 0.1 % in decreasing pain perception of the traumatic ulcer caused by fixed orthodontic appliance.

#### CONCLUSION

The result of this research was in agreement with previous research done which showed that *hyaluronic acid* can accelerates the healing process in acute wounds<sup>21</sup>, RAU<sup>10</sup>, OLP<sup>11</sup> and gingivitis<sup>12</sup>.

The result of this research showed that mouth rinsing with *hyaluronic acid* 0.1 %- contained mouthwash appeared to be more effective in accelerating the healing process of the traumatic ulcer caused by fixed orthodontic appliance in wound size and redness reduction, but not effective in

decreasing the pain perception compared to placebo. Although *hyaluonic acid* 0.1 % did not show significant difference compared to placebo, it does not mean that *hyaluronic acid* 0.1 % is seemed to be not effective at all in decreasing pain perception. The measurement of pain perception in this research is the pain perception of the research subjects, which was quite subjective. Further research is needed to prove the effectiveness of *hyaluronic acid* 0.1 % in decreasing pain perception of the traumatic ulcer caused by fixed otodontic appliance.

#### REFERENCES

1. Mitchell L. *An Introduction to Orthodontics*. Third Edition. London. Oxford University Press. 2007:1-6.
2. Lau PY, Wong RW. Risks and Complication in Orthodontic Treatment. *Hong Kong Dent J*. 2006; 3:15-22.
3. Travess H, Roberts-Harry D, Sandy J. Orthodontics. Part 6 : Risks in Orthodontic Treatment. *Br Dent J*. 2004; 196:74-5.
4. Kvam E, Bondevik O, Gjerdet NR. Traumatic Ulcers and Pain in Adults During Orthodontic Treatment. *Community Dent Oral Epidemiol*. 1989;17:154-7.
5. Kvam E, Bondevik O, Gjerdet NR. Traumatic Ulcers and Pain During Orthodontic Treatment. *Community Dent Oral Epidemiol*. 1987; 15:104-7.
6. Asher C, Shaw WC. Benzylamine Hydrochloride in the Treatment of Ulceration Associated with Recently Placed Fixed Orthodontic Appliances. *Eur J Orthod*. 1986; 10:61.
7. Perez M, Raimondi AR, Itoiz ME. An Experimental Model to Demonstrate the Carcinogenic Action of Oral Chronic Traumatic Ulcer. *J Oral Pathol Med*. 2005; 34:17-22.



8. Shaw WC, Addy M, Griffiths S, Price C. Chlorhexidine and Traumatic Ulcers in Orthodontic Patient. *Eur J Orthod.* 1984; 6:137.
9. Galli F, Zuffetti F, Capelli M, Fumagalli L, Parenti A, Testori T, Esposito M. Hyaluronic Acid to Improve Healing of Surgical Incisions in the Oral Cavity. *Eur J Oral Implantol.* 2008; 1: 199-206.
10. Nolan A, Baillie C, Badminton J, Rudralingham M, Seymour RA. The Efficacy of Topical Hyaluronic Acid in the Management of Recurrent Aphthous Ulceration. *J Oral Pathol Med.* 2006;35:461-5.
11. Nolan A, Badminton J, Maquire J, Seymour RA. The Efficacy of Topical Hyaluronic Acid in the Management of Oral Lichen Planus. *J Oral Pathol Med.* 2009; 4:299-303.
12. Pistorius A, Martin M, Willershausen B, Rockmann P. The Clinical Application of Hyaluronic Acid in Gingivitis Therapy. *Quintessence Int.* 2005; 36:531-8.
13. Federer WT. *Experimental Design: Theory and Application.* New Delhi. Oxford and IBH Publ. Co. 1955: 544
14. Fette AM. *A Clinimetric Analysis of Wound Measurement Tools.* <http://www.worldwidewounds.com/2006/january/Fette/Clinimetric-Analysis-Wound-Measurement-Tools.html>. Downloaded August 21, 2009. 23:00 WIB.
15. Sciubba JJ, Regeziv JA., Rogers III, Roy S. *PDQ Oral Disease: Diagnosis and Treatment.* London. BC Decker Inc. 2002:108-11.
16. Cawson RA, Odell WE. *Cawson's Essential of Oral Pathology and Oral Medicine.* 7<sup>th</sup> Edition. London. Churchill Livingstone. 2002:192.
17. Liguori V, Guillemin C, Pesce GF, Mirimanoff RO, Bernier J. Double-blind, randomized clinical study comparing hyaluronic acid cream to placebo in patients treated with radiotherapy. *Radiother Oncol.* 1997; 42 : 155-61.
18. Baxter, C. The Normal Healing Process. *New Directions in Wound Healing: Wound Care Manual.* New Jersey. Squibb & Sons, Inc. 1990
19. Lipincott. *Acute Wound Pain: Gaining a Better Understanding.* <http://www.nursingcenter.com/prodev/ce/article.asp?tid=928792>. Downloaded November 29, 2009. 21:18 WIB.
20. McCance KL, Huether SE. *Pathophysiology: The Biologic Basis for Disease in Adults and Children.* Fifth Edition. Missouri. Elsevier. 2006: 456.
21. Voinchet V, Vasseur P, Kern J. Efficacy and Safety of Hyaluronic Acid in the Management of Acute Wounds. *Am J Clin Dermatol.* 2006; 7:353-7