Efficacy of a new oral bandage for wound healing: comparative study using a rat model

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Abstract

Objectives Many trials have been conducted to establish the appropriate dental surgery method for wound repair and bone regeneration. The aim of this study was to evaluate the efficacy of a newly developed oral bandage for use in wound repair and bone regeneration following dental surgery.

Study Design Surgical defects were induced in the rat calvaria area, and the animals were randomly divided into three treatment groups. The new oral bandage was applied to the first group, the second group was treated with Reso-Pac® , and the third group, the control group, was left untreated. At 4 and 8 weeks after surgery, wound healing and bone formation in the calvaria area were histologically evaluated.

Results At 4 weeks after surgery, the animals treated with the new oral bandage demonstrated significant wound repair with thick connective tissue and new bone formation, while further bone regeneration was evident at 8 weeks following surgery. In the Reso-Pac® -treated group as well as in the control group, no new bone formation was observed until 8 weeks following surgery.

Conclusion The results demonstrate that the new oral bandage provides faster and better support for wound healing and bone regeneration in the calvaria than that provided by Reso-Pac® .

Introduction

Investigations have been conducted to determine the appropriate method for wound healing in the field of the dental and oral surgery.(1) A variety of topical preparations have been introduced for oral wound healing; however, so far no guideline or standardized method is available to treat patients with from oral diseases, such as oral cavities, periodontal disease, or stomatitis.(1) The preferred properties of topically applied agents are the ability to afford a smooth surface, prevent irritation, and to be flexible, as well as adhesive and dimensional stability. The most common topical preparations can be classified into three categories, namely, solid and non-soluble, soft and non-soluble, and soluble with soluble materials.(2) In Korea, there is a need to develop an efficient and convenient method to treat oral diseases in dental clinics.(3) Hence, a new oral bandage was developed by adapting a USA patented membrane. The new oral bandage which was introduced last year contains two more ingredients to improve the antibacterial effect and the stability of the bandage. The properties of the bandage, in terms of wound healing and bone regeneration, are yet to be determined. Therefore, the aim of the present study was to evaluate the efficacy of the newly developed oral bandage in a rat model and to compare the effects on wound healing and bone regeneration of the new oral bandage with those of a standard product in Korea.

Materials and Methods

Animals

Seventy-two male Sprague-Dawley rats (16 to 18 weeks old) were randomly divided into three groups of 24 animals each. The animals were housed in standard cages, kept in an experimental animal room and had access to a standard laboratory diet and water. This study was approved by the Committee for Animal Research of Chosun University Institutional.

Materials Preparation

New Oral Bandage

The new oral bandage is a soft film, which consists of a combination of polycarboxylic acids (Carbomer® Lubrizol Inc, Ohio USA) and hydroxyethylcellulose (Ashland Natrosol®, Seoul Korea) mixed in the compatible state or in a phase-separated state. In the compatible state, no adhesion occurred in a dry environment but strong adhesion upon water absorption and a high transparency were evident. When the bandage comes into contact with water, the polycarboxylic acid dissolves, out from the film in a phase-separated state, resulting in degradation of the bandage. Other components of the bandage include 0.1% tocopherol and 0.2% methyl paraben. Tocopherol is an anti-oxidant and free radical scavenger, while methyl paraben is added for its fungicidal properties.

Reso-Pac®

The Reso-Pac® preparation (Hager & Werken GmbH & Co. KG Postfach, Dulsburg Germany) is a hydrophilic paste that can be used without mixing. The product remains in place for 1~ up to 10 hours.

Procedure

The animals were divided to new oral bandage, Reso-Pac® , and control group. The rats were systemically anesthetized with 5% isoflurane and ketamine hydrochloride (Ketalar® , Yuhan Co., Seoul, Korea) and xylazine (Rumpun® , Bayer Korea Ltd., Seoul, Korea). The forehead was shaved, disinfected with tincture of iodine, and locally anesthetized with lidocaine (Lidocaine HCL, Huons, Seoul, Korea). Surgical defects (5 mm) were induced with a trephine bur in the area of the midsagittal suture preventing damage to the dura. The wound areas were then covered with the either the new oral bandage or the Reso-Pac® product according to the group allocation. The control group received no bandage. Half the animals of each treatment group was sacrificed at 4 weeks and the other half of the animals were sacrificed 8 weeks following surgery, using a fixative solution consisting of 0.1 mol/L phosphate-buffered 4% paraformaldehyde (pH 7.4).

Histological Evaluation

The block biopsy specimen included the membranes, the surrounding soft tissue, and the underlying calvarial bone. The thickness of the specimens was 7–10 μm. Slides were prepared and stained following drying with a Slide Warmer (Jisico, KOREA). The slides were finally evaluated with a microscope (Eclipse Ti, Nikon, JAPAN) under X4 and X10 magnification.

Result

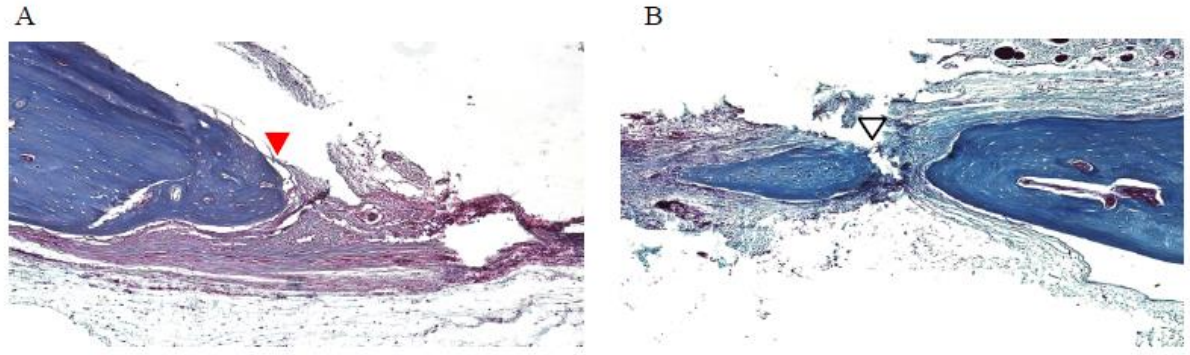
Histological Observations

At 4 weeks after surgery, we observed re-epithelialization in all groups. In the control group, initial wound closure was observed from the wound edge with the thin loose connective tissue. However, no new bone formation was detected at 4 weeks after surgery (Fig 1, A). Eight weeks following surgery, a thin tissue layer was formed around the wound and 0.85 mm length of new bone was observed close to the edge of the wound (Fig 1, B).

In the Reso-Pac® group, thin loose connective tissue covered the wound site 4 weeks after surgery, which appeared more stratified than the connective tissue in the control group. However, no new bone formation was evident in this group (Fig 2, A and C). Eight weeks following surgery, thicker connective tissue was observed to cover the wound area and new bone was detected under the wound edge (Fig 2, B and D).

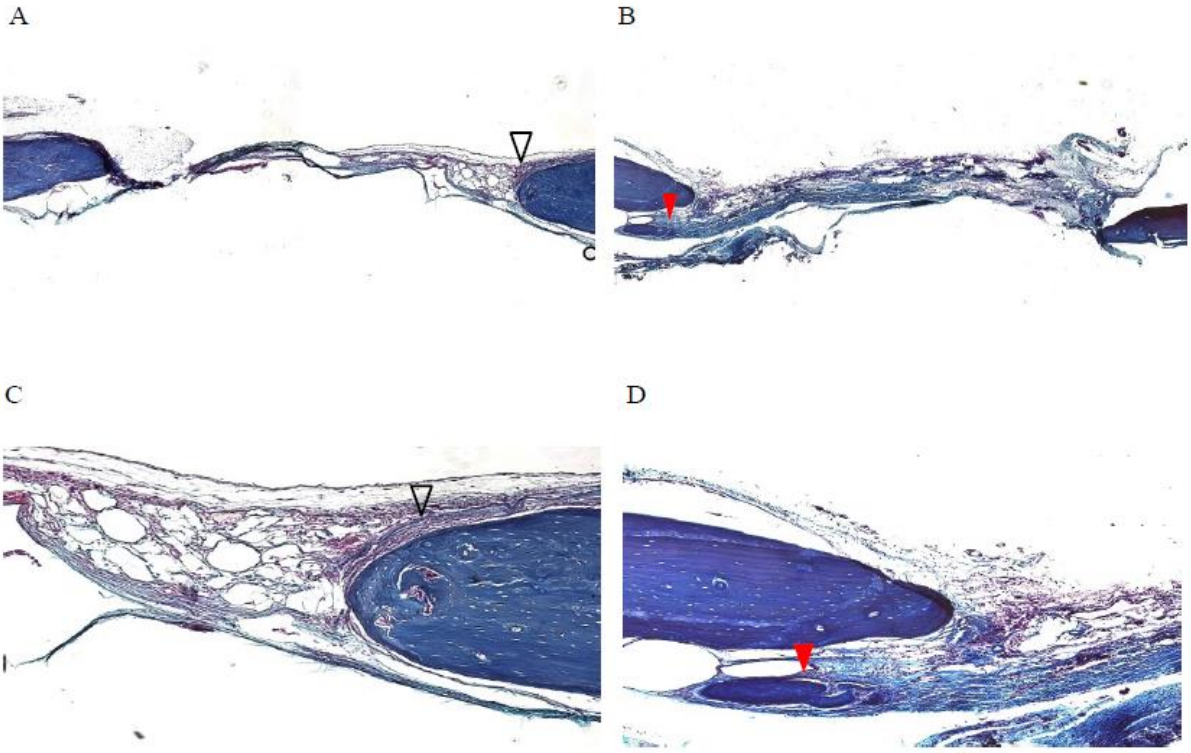
In rats using the new oral bandage, proper stratified and thick connective tissue was detected at the wound site 4 weeks after surgery. Additionally, 1.85 mm of new bone was evident 1.5 mm from the wound edge (Fig 3, A and C). At 8 weeks after surgery, further bone regeneration of > 2 mm was observed at the wound edge, while a thicker connective tissue covered the wound site (Fig 4, B and D).

Fig 1. Histological evaluation of the control group



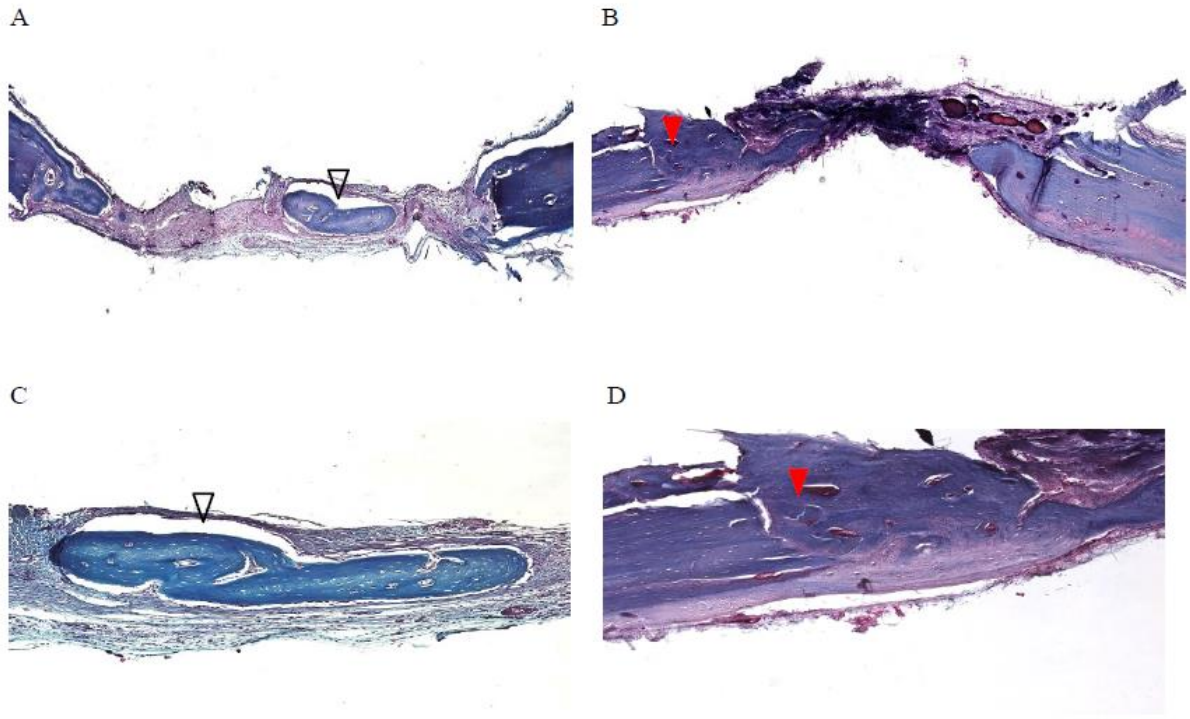
A. At 4 weeks after surgery (X10 magnification) initial wound closure is evident (red arrow).
B. At 8 weeks after surgery (X10 magnification) new bone formation is evident (white arrow).

Fig 2. Histological evaluation of the Reso-Pac group



A and C. At 4 weeks after surgery (X4 and X10 magnification, respectively) formation of thin tissue layer is evident (white arrow). B and D. At 8 weeks after surgery (X4 and X10 magnification, respectively) new bone formation is evident (red arrow).

Fig 3. Histological evaluation of the new oral bandage group



A and C. At 4 weeks after surgery (X4 and X10 magnification, respectively) new bone formation is evident (white arrow). B and D. At 8 weeks after surgery (X4 and X10 magnification, respectively) wound edge with new bone regeneration is evident (red arrow).

Discussion

The aim of the present study was to examine the efficacy of a newly developed topical wound protecting membrane to improve the healing process of wounds with large epithelial and connective tissue deficiency following surgical excisions. The calvarial defect procedure used in the current study is a recognized experimental model for poor blood supply and low mechanical stimulation preventing spontaneous healing.(4) Also, 5mm calvaria defect was demonstrated as the smallest intraosseous wound during the lifetime of animal.(4) The group treated using the new oral bandage showed more regenerated connective tissues than those shown by the control group and the Reso-Pac® -treated group, proving the efficacy of the new oral bandage for the wound healing in the dental surgery.(2) Wound healing involves complex processes including three overlapping stages, namely inflammation, re-epithelization, and granulation tissue formation and tissue remodeling, which is promoted mainly by wound protection and sufficient fixation.(5) The common methods of protecting wound areas are to use absorbable or non-absorbable membranes, which are convenient to use. The membranes maintain the shape until new tissue is formed by the end of treatment.(6) It has previously been demonstrated that non-absorbable membranes are superior to absorbable membrane.(4) Furthermore, it has been

suggested that a thicker membrane would afford reconstruction of more defect tissue(4); however, the new oral bandage is a soft film, with comparable benefit to that provided by absorbable membranes, which are more convenient to use.(7) The newly developed oral bandage, used in the present study, improved adherence to the buccal mucosa. Hence, it provided more protection in the wound area compared to that provided by Reso-Pac® and demonstrated enhanced connective tissue regeneration. Furthermore, the rats treated with the new oral bandage regenerated connective tissues more rapidly than the group treated with Reso-Pac® and the control group. This observation proves the efficacy of the new oral bandage in the wound healing following the dental surgery.

Interestingly, the present study demonstrated that application of the new oral bandage also lead to formation of new bone. When comparing to the Reso-Pac® product, which is predominantly used for implant surgery requiring bone regeneration, results demonstrated more new bone formation and bone regeneration with the new oral bandage. More bone regeneration involves more cell migration and therefore space is maintained.(8) Furthermore, results indicated that the new oral bandage produced new bone and bone regeneration already after 4 weeks of surgery compared to the Reso-Pac® product, which did not show any bone formation until 8 weeks after surgery. Therefore, the new bandage caused migration of more cells related to wound healing and had an additional effect on bone regeneration.

In conclusion, the results of the present study demonstrated the superior of the new oral bandage in terms of wound healing and bone regeneration. The limitation of the study was the lack of safety evaluation of the new oral bandage. However, this limitation should be addressed in a future study. Several studies have attempted to identify the most effective and convenient method for bone regeneration, which included various dental surgery procedures, however, no standardized techniques have been identified to cover both wound healing and bone regeneration.(9) Hence, there has been a need for a more efficient way to improve the recovery of wound sites following dental surgery. Accordingly, the new oral bandage has been demonstrated to be an efficient new application for wound healing and bone regeneration and is therefore a suitable treatment following dental surgery.

Conclusion

The new oral bandage afforded the recovery of more wound areas than did the standard Reso-Pac® product. Furthermore, rats in which the new oral bandage was used demonstrated new bone formation as well as bone regeneration earlier than that shown by the rats treated with the Reso-Pac® product or rats in the control group. Therefore, the results of the current study suggest that the new oral bandage is superior in wound repair and bone regeneration after dental surgery compared to the Reso-Pac® product.

Acknowledgements: This work was partly supported by the Small and Medium Business Administration (S2245446) and Kwangju Women University.

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