INTRODUCTION

One of the main goals of periodontal therapy is to re-establish anatomical and physiological conditions conducive to long term health and function of the periodontium.\(^{1}\)

Gingivectomy is used for the elimination or reduction of suprabony periodontal pockets. It may also be indicated to remove diseased tissue, for prosthetic reasons, to improve esthetics and/or establish normal gingival architecture.\(^{1}\)

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* Associate professor, Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of dentistry, Alexandria University, Egypt
** Lecturer, Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of dentistry, Alexandria University, Egypt
Wound healing process after gingivectomy is by secondary intention and takes about 5 weeks to re-establish normal gingival epithelialization. This finding tends to confirm the concept of a slow wound healing process. Studies have shown that the topical application of certain medicaments, antibiotics, or amino acids may result in improved healing of surgical wounds. Wound healing following gingivectomy is a complex, integrated series of biochemical, cellular, and physiologic processes. It is also considered as a dynamic process affected by reactive oxygen species.

Several antioxidants have been used to accelerate healing of gingival tissue after gingivectomy. One of them is the essential amino acid Taurine that has important physiologic roles, and has been shown to have osmo-regulatory, antioxidative, anti-apoptotic, anti-inflammatory, and anti lipid activities. Furthermore, the local application of Taurine-hydrated collagen membranes on human gingival wounds demonstrated histological evidence of rapid re-epithelization.

Vitrocure® is an antiseptic, anti-oxidant and anti-inflammatory oral gel that can improve and accelerate the healing of oral ulcers and stimulate epithelization. It is known in France by the trade name Aphtarine® healing gel and is commonly used for the treatment of aphthous ulcers and traumatic oral sores.

One of the gel’s main ingredients is Ribes nigrum (Blackcurrant berries) extract which is considered to be the first specific matrix metalloprotease (MMP) topical inhibitor that contains very high amounts of phenolic compounds. This fruit is sometimes called a “super fruit”, because of its antioxidant potential - related health benefits. Moreover, recent studies indicate that blackcurrant flavonoids exhibit anti-inflammatory properties. Lyall et al noted that blackcurrant extract concentrate in monocyte cell culture modulates inflammatory response with a decrease of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) production via an unknown mechanism. The other extract is from Bilberry (Vaccinium myrtillus), one of the richest sources of anthocyanins, known to have anti-ulcer, anti-cancer, wound healing and anti-allergic effects.

Another main component of Vitrocure® is honey. Studies indicate that the addition of a small quantity of honey, generates hydrogen peroxide ($H_2O_2$) bubbles which remove the smaller and snuggly lodged contaminants from tissues and substitutes for MMPs in their residue removal role.

For any dental surgeon, improving clinical practice by providing effective pain relief and improved patient comfort following surgery is a key objective. In view of the potent anti-inflammatory and antioxidant effect of Vitrocure® gel, it was interesting to verify the clinical effects of this gel, if any, on the healing of gingivectomy wounds.

Objectives of the study:

This study was performed to evaluate the effectiveness of Vitrocure® gel in promoting and accelerating healing and epithelization of gingival wounds, as well as controlling postoperative pain and discomfort following gingivectomy surgery.

MATERIALS AND METHODS

1-Study design:

The current study was a randomized, controlled, clinical trial, conducted on 20 patients (4 males and 16 females), with an age range from 20-45 years, mean age of 32 years. They were recruited from the Department of Oral medicine, Periodontology, Oral diagnosis and Radiology, Alexandria University, Egypt.

The study was approved by the institutional ethical committee on clinical trials involving humans.
CLINICAL EVALUATION OF RIBES NIGRUM AND VACCINIUM MYRTILLUS

(Faculty of Dentistry, Alexandria University) (IRB NO: 00010556 – IORG: 0008839) and conducted in accordance with the guidelines of the World Medical Association Declaration of Helsinki for the ethical principles of clinical trials involving human subjects.

The procedure and aim of the study were explained to the patients who signed an informed consent form. The patients were selected according to the following criteria:

**Inclusion criteria:**

All patients fulfilled the study’s inclusion criteria of the presence of an area of inflammatory gingival enlargement requiring surgical excision by gingivectomy. Tissues were firm, with no bleeding upon probing or any signs of inflammation. Furthermore, patients were required to maintain a modified O’Leary plaque index \( \leq 15\% \) after phase I therapy.

**Exclusion criteria:**

Patients who were smokers, indulged in habits, had any systemic disease or hormonal conditions that may impair normal soft tissue healing following the surgical procedure were excluded from the study. Similarly, those who were under treatment by any medication that may affect tissue response or healing were also not included.

After the completion of phase I therapy, allocation of cases to either group was conducted randomly using simple randomization procedures (computerized random numbers)

Group I (Test group): Consisted of 10 subjects managed by gingivectomy followed by the application of Vitrocure® gel and cyanoacrylate periodontal dressing.

Group II: (Control group): Consisted of 10 subjects managed by gingivectomy followed by the application of cyanoacrylate periodontal dressing only.

**2-Materials:**

Vitrocure® (Naturverda, Vitrobia ZAC de Lavaur, Issoire, France) is an osmotically active hypertonic solution which forms a film over the lesion and instantly attracts hypotonic liquid. It is composed mainly of Glycerol, Honey, Extracts of Ribes nigrum (Black Currant) and Vaccinium myrtillus (Grape) and Xanthan gum.

**3-Methods:**

Gingivectomy had been planned for each patient to excise the enlarged part of the gingiva according to each case.

**1-PreSurgical preparation:**

Phase I therapy including scaling and root planing, oral hygiene instructions, and minor occlusal adjustment, when needed, were undertaken. Using a periodontal probe with William’s markings ** (Hu-Friedy, Chicago, IL, USA) at pretreatment, initial probing depths were recorded for the mid-buccal, and mesial and distal interproximal surfaces of each tooth in the quadrant involved by gingival enlargement.

**2-Surgical phase:**

Gingivectomy according to standard technique described by Goldman was performed to remove the inflammatory enlargements. Excision of the soft tissue wall carried out to the base of the clinical pocket was performed to remove the enlarged tissue. After bleeding was controlled, the surgical sites in test group patients were covered with test gel and left for about ten minutes then cyanoacrylate periodontal dressing ( PeriAcryl®90**, GluStitch, Progress Way Delta, Canada) was applied while in the control group, the surgical sites were covered with cyanoacrylate periodontal dressing alone. (Figure- 1 )
3-Post surgical phase:

At the seventh day the cyanoacrylate dressings were removed, and photographs were taken at 7, and 14 days, post surgically. Pain was assessed using a numerical pain index \(^{20}\) by the patients themselves. The tissues were assessed by two periodontists, who were blinded to the procedures. They scored the tissue response applying the healing index of Landry \(^{21}\).

**Clinical parameters included:**

1-VAS scores (Huskisson, 1976) \(^{20}\):

Patients were given diaries and instructed to record the intensity of pain during the period of healing by giving the pain score of 10 when being maximum and score of 0 in case of absence of pain. The recordings were made just immediately after treatment and following recovery from local anesthesia and every day thereafter, for the first week postoperatively.

2-Healing index of Landry\(^{21}\):

This index is used to describe the extent of healing after periodontal surgery and is divided into the following scores:

**Healing Index 1: Very Poor**

Has 2 or more of the following:

- Tissue colour: ≥ 50% of gingiva red
- Response to palpation: bleeding
- Granulation tissue: present
- Incision margin: not epithelialized, with loss of epithelium beyond incision margin
- Suppuration present

**Healing Index 2: Poor**

- Tissue colour: ≥ 50% of gingiva red
- Response to palpation: bleeding
- Granulation tissue: present
- Incision margin: not epithelialized, with connective tissue exposed

**Healing Index 3: Good**

- Tissue colour: ≥ 25% and < 50% of gingiva red
- Response to palpation: no bleeding
- Granulation tissue: none
- Incision margin: no connective tissue exposed

**Healing Index 4: Very Good**

- Tissue colour: < 25% of gingiva red
- Response to palpation: no bleeding
- Granulation tissue: none
- Incision margin: no connective tissue exposed

**Healing Index 5: Excellent**

- Tissue colour: all tissues pink
- Response to palpation: no bleeding
- Granulation tissue: none
- Incision margin: no connective tissue exposed
Clinical evaluation of *Ribes nigrum* and *Vaccinium myrtillus*

**Test group case:**

- Fig. (1) Surgical site after gingivectomy
- Fig. (2) Vitrocure gel was applied and covered with cyanoacrylate pack
- Fig. (3) Follow up after 1 week

**Control group case:**

- Fig. (4) Post surgical picture showing gingival after excision
- Fig. (5) The surgical site covered with cyanoacrylate alone
- Fig. (6) Follow up after 1 week
RESULTS

A total of 20 patients having gingival enlargement (4 males and 16 females) were evaluated in the present study. They were divided into two groups: **Group 1 (test)** Comprised 10 patients, 8 females and 2 males, while **Group 2 (control)** Comprised 10 patients, 8 females and 2 males.

Concerning the Vitrocure® gel used in the present study, it was completely non-irritating and no adverse reactions were reported.

**Statistical analysis of the data**

Data were fed to the computer and analyzed using IBM SPSS Microsoft software package version 20.0. **Student t-test** was used to compare two groups for normally distributed quantitative variables. **Paired t-test** and **ANOVA** with repeated measures and Post Hoc test (LSD) was assessed for comparison between different periods. **Mann Whitney test** was used to compare between two groups for abnormally distributed quantitative variables. **Pearson coefficient** was used to correlate between quantitative variables. Significance of the obtained results was judged at the 5% level.

1-VAS scores:

There was a statistically significant reduction in VAS scores in relation to group 1, when compared to group 2 at first day has a potent analgesic action. Concerning the pain following the first day on comparing the 2 groups there were also statistically significant reduction in pain test group more than control group from the first day. (Table -1)

2-Healing index for Laundry:

There was a statistically significant improvement in healing according to healing index for Laundry in relation to group 1 when compared to group 2 at one and two weeks, postoperatively. However, there was no statistically significant difference between the 2 groups at the third week. Concerning D which means difference in healing improvement between first and third week there was a statistically significant improvement in healing in test group than control group. (Table -2).

**TABLE (1): Comparison between the studied groups with respect to pain index**

<table>
<thead>
<tr>
<th>Pain index</th>
<th>Group -1 (N=10)</th>
<th>Group-2 (N=10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>0.40±0.52</td>
<td>9.90±0.32</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Day 2</td>
<td>3.50±0.53*</td>
<td>7.40±1.35*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Day 3</td>
<td>2.40±0.52#</td>
<td>6.0±3.30#</td>
<td>0.007*</td>
</tr>
<tr>
<td>Day 4</td>
<td>0.0±0.0#</td>
<td>6.30±0.95#</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Day 5</td>
<td>0.0±0.0#</td>
<td>4.90±1.66#</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Day 6</td>
<td>0.0±0.0#</td>
<td>0.0±0.0#</td>
<td>-</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.0±0.0#</td>
<td>0.0±0.0#</td>
<td>-</td>
</tr>
<tr>
<td>Δ(Day 1 form Day 7)</td>
<td>0.40±0.52</td>
<td>9.90±0.32</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Normally quantitative data was expressed in mean ± SD
#: For comparing between Day 1 and each other period at p ≤0.05
P: p value for comparing between control and tablet
*: Statistically significant at p ≤ 0.05

**TABLE (2): Comparison between the studied groups according to healing index**

<table>
<thead>
<tr>
<th>Healing index</th>
<th>Group-1 (n=10)</th>
<th>Group-2 (n=10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Week</td>
<td>3.8±0.42</td>
<td>1.9±0.32</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>2nd Week</td>
<td>5.0±0.0#</td>
<td>4.1±0.32</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>3rd Week</td>
<td>4.90±0.32#</td>
<td>4.8±0.42#</td>
<td>0.556</td>
</tr>
<tr>
<td>Δ(1Week – 3Week)</td>
<td>1.10±0.32</td>
<td>2.90±0.32</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Normally quantitative data was expressed in mean ± SD
#: For comparing between 1st week and each other period at p ≤0.05
P: p value for comparing between control and tablet
*: Statistically significant at p ≤ 0.05
DISCUSSION

Surgical periodontal procedures are considered an integral component to the treatment of periodontal diseases. However, delayed wound healing and postsurgical patient perceptions of pain, which occur as a consequence of surgical trauma and release of pain mediators, are common postoperative sequela. \(^{(22-25)}\)

Therefore, the current study was focused on the acceleration of gingival healing and halting or decreasing post operative pain with the use of topical Vitrocure\(^{®}\) gel. The later proved to have a potent analgesic action that appeared clearly through the complete absence of pain in the first day following surgery in test group with absence of this advantage in control group.

Vitrocure \(^{®}\) contains glycerol, which is non-irritant, nearly 18 times more osmotically active than seawater. It is known to anyone who has ever entered the sea with a skin injury upon getting out of the water, the injury comes out cleaned, whitish, and appears to heal faster. This is attributable to the osmotic action of seawater. Although normal saline or seawater constitute a cleaning agent of choice, they are not often used because they prove too irritating, totally lack any filmogen action, have a short-lived or low efficacy, and cannot be patented. \(^{(26,27)}\)

Through its osmotic activity, glycerol induces instant exudation of hypotonic fluids across the injured surface, thus cleaning the lesion of free-floating protein-polymer conjugates, and all contaminants present, including bacteria, thus acting as an instant, mechanical antiseptic, natural antimicrobial, and hydrating device. \(^{(26,27)}\) Needless to say, the absence of infection and hydration contribute greatly to a decrease in pain and in the potentiation of the healing ability of the tissues. In addition, the enhanced retention properties of the film serve to protect the de-epithelized tissues and potentiate the action of the periodontal dressing.

Ribes nigrum (Blackcurrant berries) which is the main ingredient in Vitrocure\(^{®}\) contains high amounts of flavonoids with various health benefits as anti-inflammatory properties attributed to their antioxidant effect. \(^{14}\) This appeared clearly through our clinical results of healing assessment using the healing index for Laundry. A statistically significant improvement in gingival healing for group 1 was found when compared to group 2, specially at the first two weeks which proved that Vitrocure \(^{®}\) has the ability to promote and accelerate healing.

The results of the present study are in agreement with those obtained from another study that used a topical antioxidant in the form of Taurine-hydrated collagen membrane to accelerate healing and demonstrated the histological evidence of rapid re-epithelization in human gingival wounds. \(^{(28)}\)

Moreover, using photodynamic therapy (aPDT) with methylene blue (MB) in ethanol 20% was found to promote healing of periodontium due to its antioxidant effect. \(^{(29)}\) Furthermore, Xio et al (2017) \(^{(30)}\) demonstrated that hydrogen-rich water diminished physical injury-induced by reactive oxygen species (ROS) generation. The treatment promoted wound healing in human gingival fibroblasts (HGF) monolayer sheets via its antioxidant effects. The previous studies emphasized the importance of antioxidant properties which explains why Vitrocure gel, with these similar characteristics, promotes and accelerates the healing of gingival tissue wounds after gingivectomy.

CONCLUSION

To the best of our knowledge, this study is the first to demonstrate the effect of topical application of Vitrocure\(^{®}\) on gingival healing following gingivectomy in humans. Our evidence suggests that this gel may have a potential therapeutic effect to facilitate postoperative gingival wound healing and pain reduction through rapid re-epithelization by its anti-inflammatory and anti oxidant properties.
This conclusion is very close to that obtained from a recent study by Yıldırım et al. (2018) which concluded that topical hyaluronic acid (HA) exhibits a positive impact on postoperative pain and burning sensation. HA accelerated palatal wound healing in donor sites subsequent to free gingival graft (FGG) surgery, in terms of epithelization and color match due to its anti-inflammatory effect. Future studies with a larger number of patients are now needed to clarify the efficacy of topical Vitrocure® use in periodontal therapy.

REFERENCES


