Covering mucosal defect with PGA sheet and fibrin glue spray (CMPF method) for postoperative treatment after resection of oral cancer

Supervised by

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Introduction

CMPF method
Covering Mucosal defect with Polyglycolic acid sheet and spraying of Fibrin glue

While partial resection offers an extremely effective therapeutic option for oral cancer, it is associated with problems of possible postoperative hemorrhage and pain. Wound reefing is not applicable to extensive resection and may cause dysfunction. Covering with fibrin glue alone does not provide tight adhesion to a wound, resulting in early falling off of glue cover.

Recent reports in the field of respiratory surgery have suggested that fibrin glue combined with PGA (polyglycolic acid) sheet can reinforce adhesion to tissues. Here, we report that PGA sheet + fibrin glue applied to a wound after oral cancer resection exerts favorable hemostatic effect and produces marked improvement in pain.

Subjects/methods

Study population Sixty-three subjects who underwent CMPF in the period from November 2007 through June 2010.

<table>
<thead>
<tr>
<th>Sample size</th>
<th>63 subjects</th>
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<tbody>
<tr>
<td>Sex ratio</td>
<td>33 males to 30 females</td>
</tr>
<tr>
<td>Age</td>
<td>32 – 95 years (mean 57 years)</td>
</tr>
<tr>
<td>Disease name</td>
<td>malignancy in 58 subjects, others in 5 subjects</td>
</tr>
<tr>
<td>Site (with overlaps)</td>
<td>tongue 27 subjects, lower gingiva 13 subjects, buccal mucosa 10 subjects, upper gingiva 8 subjects, palate 5 subjects, floor of the oral cavity 3 subjects</td>
</tr>
<tr>
<td>Concomitant surgery</td>
<td>neck dissection 34 subjects, mandibulectomy/maxillectomy 18 subjects</td>
</tr>
</tbody>
</table>

CMPF application procedures

1. Rub the target site with 0.3 mL of fibrinogen solution (solution A).
2. Cover the target site with a dry PGA sheet.
3. Spray the PGA sheet with the remaining fibrinogen solution (solution A) + thrombin solution (solution B) so that the solutions are spread well over the PGA sheet.

Evaluation Evaluation items included postoperative hemorrhage, pain, and the number of days until the PGA sheet fell off.

1. Drop fibrinogen solution (solution A : 0.3 mL) to a target site.
2. Rub the tissue well with fibrinogen solution (solution A).
3. Apply a PGA sheet over the tissue rubbed with fibrinogen solution (solution A) so that it adheres well to the tissue.
4. Mix the remaining fibrinogen solution (solution A) with the same amount of thrombin solution (solution B) and spray the sheet with the AB mixedtured solution.
5. Allow to stand for 3 to 5 minutes.
6. Finish.
Results (n=63)

**Hemostatic and pain-relieving effects**

<table>
<thead>
<tr>
<th></th>
<th>With hemostatic effect</th>
<th>Without hemostatic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemostasis</td>
<td>57 subjects</td>
<td>6 subjects</td>
</tr>
<tr>
<td>PGA sheet falling off</td>
<td>2 subjects</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage from bone marrow, hemostasis achieved by compression</td>
<td>2 subjects</td>
<td></td>
</tr>
<tr>
<td>Arterial hemorrhage 12 days later</td>
<td>1 subject</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage after restart of an anticoagulant</td>
<td>1 subject</td>
<td></td>
</tr>
</tbody>
</table>

| Pain control             | 23 subjects            | 17 subjects               |
| No use of NSAID          | 23 subjects            | 17 subjects               |
| On-demand use of NSAID   | 23 subjects            | 17 subjects               |
| Regular need for an analgesic | 23 subjects | 17 subjects |
| Neck dissection          | 9 subjects             |                           |
| Ostectomy                | 5 subjects             |                           |
| Sheet falling off        | 3 subjects             |                           |

*No analgesic effect with NSAID except for 1 subject

These results confirmed the hemostatic effect and pain-relieving effect of CMPF method.

**Time of PGA sheet falling off**

<table>
<thead>
<tr>
<th>Days of final confirmation of PGA sheet remaining in place</th>
<th>0 – 57 days (mean 22.4 days, median 23 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA sheet early falling off (&lt; 1 week)</td>
<td>3 subjects</td>
</tr>
<tr>
<td>Reoperation: failure to adhere due to scar, leading to nylon thread suture</td>
<td>1 subject</td>
</tr>
<tr>
<td>Falling off at the start of oral intake</td>
<td>1 subject</td>
</tr>
<tr>
<td>Hemorrhage after restart of anticoagulant therapy, sheet removed for hemostasis</td>
<td>1 subject</td>
</tr>
</tbody>
</table>

**Conclusion**

1) The CMPF method was extremely useful for controlling hemorrhage/pain in defect after resection of oral cancer.
2) It was suggested that long-term PGA sheet attachment would be effective in preventing scar contracture.

**Actual experience (1) Tongue cancer: application of the CMPF method**

1) Pre-resection tongue cancer
2) After tongue cancer resection
3) After PGA sheet application
4) After fibrin glue application
Tips for application of PGA sheet + fibrin glue covering (CMPF method) after oral resection

1) **Single-sheet method**: Cases where post-resection wound is small/flat
   ① Rub the wound with a small amount of fibrinogen solution.
   ② Cut a PGA sheet to a size a little smaller than the wound, and apply to the wound.
   ③ Apply fibrin glue (fibrinogen solution + thrombin solution) over the PGA sheet.
   ④ Rapidly remove air from the space between the PGA sheet and the wound by pressing the sheet with fingers so that the sheet can firmly adhere to the wound.
   ⑤ Remove excess fibrin glue.

2) **Patchwork method**: Cases where post-resection wound is large/three-dimensional/associated with exposed bone or muscle
   ① Rub the wound with a small amount of fibrinogen solution.
   ② Cut a PGA sheet into small pieces of irregular shapes and sizes. Patch the wound with the PGA sheet pieces. Some overlapping or gaps are acceptable.
   ③ To prevent the sheet from falling off sequentially from one section to another, patch the wound separately for the muscle areas and bone areas so that the sheet does not spread over several areas.
   ④ Apply fibrin glue (fibrinogen solution + thrombin solution) over the PGA sheet.
   ⑤ Rapidly remove air from the space between the PGA sheet and the wound so that the sheet can firmly adhere to the wound.
   ⑥ Remove excess fibrin glue.

**Actual experience (2) Tongue cancer: Removal of excess fibrin glue**

Removal of excess fibrin glue
To prevent the wound cover from falling off sequentially from the wound part where fibrin glue runs off, be sure to cut away the excess fibrin glue running off the wound area. Fibrin glue, which does not adhere to the mucosa, can be easily removed.

**Actual experience (3) Mandibulectomy: Covering by the patchwork method**

① Lower gingiva of an 88-year-old female SCC T4aN0M0 tracheotomy + mandibular segmental resection + SÖHND

② After application of the patchwork method

③ 2 weeks postoperative, restart of oral intake + tracheal decannulation
Technical tips

1. Ensure that the PGA sheet adheres firmly to the wound.
   After application of fibrin glue, be sure to remove air from the space between the PGA sheet and the wound so that the sheet can adhere to the wound as thoroughly as possible.

2. Remove excess fibrin glue running off the wound area.
   To prevent the wound cover from falling off in succession, remove the fibrin glue running off the wound area.

3. Frequently trim any part of the PGA sheet that rolls up from the wound margin.
   As the wound heals, the PGA sheet rolls up from the wound margin. To prevent the wound center, which has not sufficiently healed, from being uncovered, trim the part of the PGA sheet that rolls up.

4. Keep the wound at rest.
   It is recommended to resume water and oral food intake almost 1 week and more than 1 week postoperative, respectively. Keeping the wound at rest facilitates assimilation of the PGA sheet and tissue, making PGA sheet unlikely to fall off. Furthermore, long-term persistent covering of the PGA sheet may suppress scar contracture.

Actual experience (4) Oral cavity cancer

1. Immediately after resection
2. After application of the CMPF method
3. 4 days postoperative

Actual experience (5) Upper gingival cancer

1. Pre-resection
2. Post-resection (muscle exposed)
3. After application of the CMPF method

Actual experience (6) Tongue/buccal mucosa resection

1. Tongue defect
2. Buccal mucosa hard palate defect
3. After application of the CMPF method
[Warning]

(1) Do not apply nor use in conditions where excessive tension and load act upon NEOVEIL; nor should it be used in cases where it presses the region by its own weight when used for reinforcement. (There are cases where NEOVEIL is torn or damaged)
(2) Do not apply to infected regions.

[Contraindication]
(1) Do not use NEOVEIL in patients with systemic complications.

[Prohibited]
(1) Do not reuse.
(2) Do not use in regions which take a long time to heal. Moreover, do not use NEOVEIL for the eternal purpose. (It might be unable to keep adequate fixation because of the characteristic of this product)
(3) Do not use on nerve system and cardiac vessels, since the safety and efficiency for these applications are not confirmed yet.
(4) Do not use to make up an epidural deficiency area.

[Care for usage]
Read contraindication, warning and the following lines before usage.

1. Usage note
(1) The use of NEOVEIL for the patients who have allergic should be considered from the characteristic of this product.
(2) Consider the possibility of using this product to weak patients and those wounds take a long time to heal.

2. Important basic cares
In case of postoperative infection, treat with debridemnet after removing this product.

3. Disadvantages and adverse reaction
No NEOVEIL related disadvantages or adverse reaction were reported. However, the following disadvantages may occur with the characteristic of this product.
As with any foreign body, prolonged coact of this product with the ureter or the biliary might result in calculus formation. Failure to support the region due to excessive tension Failure to support the region of elderly patients, weak patients or those whose wounds take a long period to heal Minimum acute tissue inflammation
In case of use in little blood stream regions or regions near the skin
*Inflammation or partial extrusion of material with late absorption or mechanical irritation
*Local pH decrease by accumulation of this dissolved unmetabolized material, and inflammation caused from pH decrease

4. Application of the elderly patients
The use of NEOVEIL for the elderly patients should be considered from the characteristic of this product.

5. Application of the pregnancy or the lactation
The use of NEOVEIL for pregnant women, lactated women or women suspected of being pregnant should be considered from the characteristic of this product.

6. Application of the child patients
Sufficient knowledge about using this product for child patients has not been obtained. Therefore the use of NEOVEIL for the child should be considered from the characteristic of this product.

[Result of clinical trial]
134 cases of clinical trials for reinforcing and preventing air leakage of the suturing part and hemostasis were conducted surgical procedure of respiratory organ and digestive organ from October 1989 to September 1990. Fibrin glue was used for hemostasis at the same time.
In general evaluation which based on the working easiness, the clinical efficacy and the side effect was that 68 cases were “very useful”, 62 cases were “useful” and 4 cases were “not deemed useful”.
602 case of PMS studied from March 1992 to April 2000. In any case, side effect, disadvantage and adverse reaction which caused by this product were not existent.

[Storage]
1. The available period is 3years from a manufacture day. The expiration time is defined on each package. Do not use the product past the term.
2. Handle and store carefully to avoid damaging the package.
3. Store this product in a clean place, and avoid high temperatures (over 40°C), direct rays of the sun and moisture.
4. Please use the product immediately after opened an aluminum bag. If the product exposed to the air, it may degrade due to moisture contained in the air.
5. When this product store, use in order of production days.

[Product Variation (sterilized by EOG)]

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<th>Code</th>
<th>Size and Color</th>
<th>Package</th>
</tr>
</thead>
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<td>1 sheet / box</td>
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<tr>
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