Pharmaceutical Modulation of Scar Tissue Formation after Cleft Palate Surgery.

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Introduction

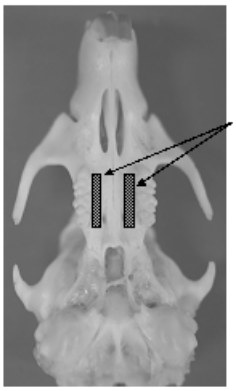
Push back palatoplasty is widely conducted in patients with cleft palate for the purpose of achieving good velopharyngeal function. However, this surgery is known to cause suppression of vertical and horizontal growth of the maxilla as well as narrowing of the maxillary dental arch.

In the present study, we focused on the effect of basic fibroblast growth factor (,,FGF) in modulating postsurgical scar tissue formation. A model of experimental scar tissue formation in the palate region was produced in rats. The effects of local administration of bFGF on scar tissue formation and maxillary growth were studied by histomorphometric and histopathological evaluations. We report our results.

Materials and Methods

One hundred fifty male 20-day-old Wistar rats were used in this study. All animals were kept under normal laboratory conditions and were fed standard rat chow and water ad libitum. The experiment was approved by the Board for Animal Experiments of the Fukuoka Dental College.

The animals were divided into three groups: a scar formation group, a bFGF group, and a control group. In the scar formation and bFGF groups, rectangular strips of the bilateral third of the hard palatal mucoperiosteum were excised under general anesthesia, induced by intraperitoneal injections of sodium pentobarbital (7mg/kg, Nembutal, Abbott Laboratories, Chicago, U.S.A.). The exposed bone surface was scraped with a cotton pellet for complete removal of the periosteum. The control animals underwent no operation (Fig. 1).



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The exposed bone surface was scraped with a cotton pellet for complete removal of the periosteum.

Fig. 1 The removed area of mucoperiosteal strips in the scar formation and bFGF groups.

Recombinant bFGF was provided by Kaken Pharmaceutical Co. (Tokyo, Japan). In the bFGF group, 10µl of bFGF solution (20µg/10µl) was injected into each side of the operated area one week after the excision.

At 2, 4, 6, 8 and 10 weeks after excision, 150 animals were anesthetized by intraperitoneal injections of sodium pentobarbital (7mg/kg, Nembutal) and perfused with physiological saline via the ascending aorta, followed by 10% neutral buffered formalin. The maxillae were dissected out, immersed in 10% formalin, decalcified in 10% EDTA solution, dehydrated in a graded series of ethanol, and embedded in paraffin. Serial frontal 7µm thick sections were stained with Hematoxilin–Eosin (H.E.) and observed under light microscopy.

In each of the three groups, molar inclination was measured by soft x-ray images between the 2nd and the 10th postoperative week. Statistically significant differences among the three groups were evaluated by a univariate variance analysis and a multivariate analysis by Scheffe's F.

After the perfusion, fixed by 1% glutaraldehyde. subsequently, 50ml of liquid acrylic resin with 2% hardner(Mercox CL-2R FDainippon-ink Chemical Co.Ltd., Tokyo,Japan) prepared according to the manufacturer's instructions was injected with manual pressure. They were then macerated in 5% sodium hypochlorite solution for 2 days.the vascular corrosion casts were rinsed in water,briefly rinsed in graded ethanol baths,dried and ion-sputter-coated with a layer of gold.

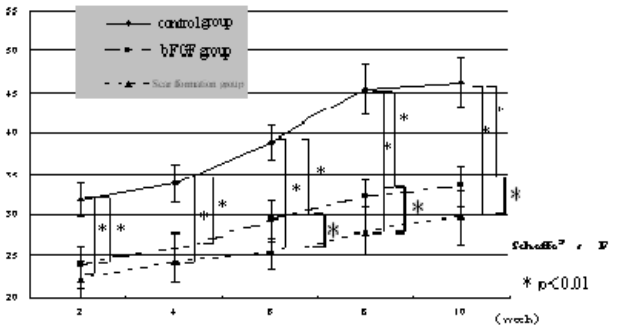

Fig.2 measurements of molar inclination

Results

1. The amount of lateral growth of the maxilla was significantly greater in the group administered bFGF compared to the scar formation control group.
2. More rapid disappearance of myofibroblasts was observed in the group administered bFGF compared to the scar formation control group (Fig. 2).

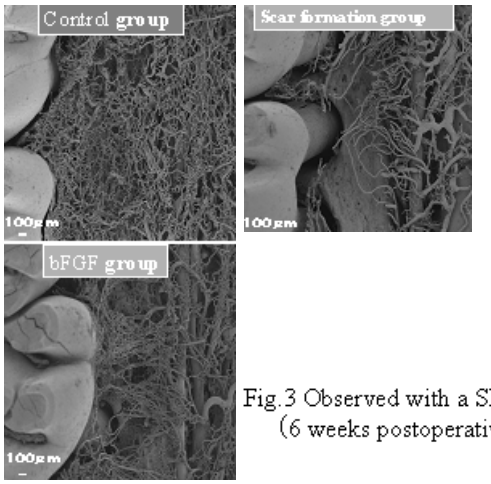

Fig.3 Observed with a SEM
(6 weeks postoperatively)

3. There were more vascular pores and capillaries in the group administered bFGF compared to the scar formation control group (Fig. 3).

Discussion and Conclusion

1. The present results confirmed that local administration of bFGF after excising the mucoperiosteum attenuates the suppression of lateral growth of dentition and vertical growth of maxilla caused by scar formation from 6 weeks after surgery.

2. This study also confirmed that by local administration of bFGF, myofibroblasts disappear early in the wound healing process and the degree of maturation of scar tissue is lowered, which probably attenuates the suppression of lateral growth of dentition by scar contraction.

3. By local administration of bFGF, regeneration of periosteum-like tissue occurs on the bone surface from which the mucoperiosteum had been removed and the numbers of arterioles and venules on the bone surface are maintained after surgery. These features may attenuate the bone growth suppressive effect due to a decrease in blood flow and nutrition supply to the bone as a result of scar formation.

4. Local administration of bFGF probably promotes vascularization from the middle of the palatal mucosa. On the other hand, since blood vessels were observed inside the arteriolovenular pores, it is possible that vascularization from the palatal bone may also be promoted.

The above findings suggest that administration of bFGF maintains arterioles and venules on the palatal bone surface and induces early disappearance of myofibroblasts to suppress scar formation, consequently attenuating the suppression of maxillary growth.