Basic fibroblast growth factor loaded polypropylene meshes in repair of abdominal wall defects in rats

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Rezumat

Plasele de polipropilenã impregnate cu factor de creætere fibroblastic bazal în repararea defectelor peretelui abdominal la æoareci

Premize æi scop: hernia incizionalã dupã laparotomie æi hernierea recurentã sunt în continuare probleme de actualitate în ciuda perfecåionãrii plaselor. Mecanismul biologic descris poate fi legat de metabolismul colagenului. Recent, câåiva membri ai familiei factorilor de creætere au fost testaåi în prevenåia dezunirilor de plagã æi formãrii herniilor incizionale. Factorii de creætere pot iniåia proliferarea fibroblasticã æi depunerea de colagen. În acest studiu, am cãutat efectele factorului de creætere fibroblastic bazal (bFGF) într-un model de hernie incizionalã cu plasã pe æoareci.

Metodã:
un total de 80 de æoareci Wistar albino au fost împãråiåi randomizat în 5 grupuri. O procedurã chirurgicalã uniformã a fost utilizatã în toate grupurile: a fost fãcutã o incizie tegumentarã medianã de 5 cm æi a fost excizat în totalitate peretele abdominal pe o arie de 3/2 cm. Peretele abdominal a fost rapid închis cu catgut 3/0 resorbabil. Dupã aceastã procedurã standard, 5 procedee diferite au fost aplicate înainte de sutura tegumentarã cu polipropilenã monofilament 4.0. Grupul 1, de control, nu a mai suferit nici o procedurã suplimentarã. Plasa de polipropilenã a fost utilizatã cu plasã pe soareci.

Metodã: un total de 80 de soareci Wistar albino au fost împãråiåi randomizat în 5 gru puri. O procedurã chirurgicalã uniformã a fost utilizatã în toate grupurile: a fost fãcutã o incizie tegumentarã medianã de 5 cm æi a fost excizat în totalitate peretele abdominal pe o arie de 3/2 cm. Peretele abdominal a fost rapid închis cu catgut 3/0 resorbabil. Dupã aceastã procedurã standard, 5 procedee diferite au fost aplicate înainte de sutura tegumentarã cu polipropilenã monofilament 4.0. Grupul 1, de control, nu a mai suferit nici o procedurã suplimentarã. Plasa de polipropilenã a fost utilizatã în poziåia stabilã, fiind fixatã cu polipropilenã monofilament 4.0, fi re separate la celelalte 4 grupuri. O plasã standard, fãrã tratament chemic, a fost utilizatã în grupul 2. O plasã impregnatã cu gelatinã a fost utilizatã la grupul 3, în timp ce grupurile 4 æi 5 au primit plase impregnate cu bFGF în cantitate de 1 μg respectiv 5 μg. Toate grupurile au fost apoi divizate în sub-grupuri (n=8 fiecare) de prima lunã (precoce: P) æi de a doua lunã (tardiv: T), în funcåie de data sacrificãrii. S-a fãcut evaluare tensiometricã æi histopatologicã. Probele pentru histopatologie au fost recoltate de la interfaåa plasã organism æi colorate cu hematoxilinã-eozinã, respectiv tricrom Masson “în orb” de un singur anatomopatolog, urmãrind inflamaåia, vascularizaåia, activitatea fibroblasticã, fibrele colagenice æi organizarea åesutului conjunctiv. Metoda avidinã-biotinã-peroxidazã a fost efectuatã utilizând anticorpi monoclonali împotriva colagenului tip I æi III.

Rezultate: plasele impregnate cu bFGF au prezentat valori de rezistenåã tensionalã crescûtã în comparaåie cu plasele standard dupã 2 luni. Studiile histopatologice æi imunohistochimice au relevat, de asemenei, oarecare avantaje în favoarea plaselor impregnate cu bFGF faåã de plasele de polipropilenã standard. Aceste efecte limitate ale bFGF nu pot sã fie dependente de dozã.

Concluzii: folosirea plaselor impregnate cu bFGF în tratarea peretelui abdominal poate determina valori de rezistenåã tensiionalã mai mari în comparaåie cu plasele standard dupã 2 luni. Studiile histopatologice æi imunohistochimice au arãtat numai o vindecare puåin mai bunã în favoarea plaselor impregnate cu bFGF faåã de cele standard.

Cuvinte cheie: factor de creætere, fibroblast, FGF, vindecare plagã, perete abdominal, hernie incizionalã, cunã herniei, plasã
Abstract

Background and Aim: Incisional hernia following laparotomy and recurrent herniation after its repair are still common problems in spite of mesh augmentation. The underlying biological mechanism may be related to collagen metabolism. Recently, some members of growth factors family have been tested in the prevention of wound failure and incisonal hernia formation. Growth factors may promote fibroblast proliferation and collagen deposition. In the present study, we searched the effects of basic fibroblast growth factor (bFGF) loaded polypropylene meshes in an incisional hernia model in rats. Methods: A total of 80 Wistar albino rats were randomly divided into five groups. A uniform surgical procedure was employed in all groups: a 5 cm skin incision was made at the midline and a full segment of the abdominal wall sized 3 x 2 cm was excised. Abdominal wall was closed with rapidly absorbable 3/0 catgut. Following this standard surgery, five different procedures were applied to the groups before closing the skin with 4/0 monofilament polypropylene sutures. Control subjects (Group 1) received no extra procedure after abdominal wall suturing. Polypropylene meshes were used in onlay position by fixing 4/0 monofilament polypropylene interrupted sutures in other four groups. A standard mesh with no chemical treatment was used in Group 2. Gelatin coated meshes were used in Group 3, while Group 4 and 5 received bFGF loaded meshes with 1 microgram (μg) and 5 μg doses respectively. All the groups then divided into 1st month (early: E) and 2nd month (late: L) subgroups (n=8 each) according to sacrificed dates. Tensiometric and histopathological evaluations were done. The specimens for histopathology were obtained from the interface area of the meshes and stained with hematoxylin and eosin, and also Masson trichrome. The variables were examined and evaluated by a single blinded pathologist under light microscopy in respect of inflammation, vascularization, fibroblast activity, collagen fibers and connective tissue organization. The avidin-biotin-peroxidase method was performed using the primary monoclonal antibodies against collagen type I and collagen Type III. Results: bFGF loaded meshes showed higher tensile strength values in comparison with a standard polypropylene mesh after 2 months. Histopathological and immunohistochemistry studies also revealed somewhat better scores in favor of bFGF loaded mesh over a standard polypropylene mesh. These limited effects of bFGF did not seem to be dose dependent. Conclusions: The use of bFGF loaded polypropylene mesh in the abdominal wall healing may cause somewhat higher tensile strength values in comparison with a standard polypropylene. However, histopathological and immunohistochemistry studies revealed only a slightly better healing in favor of bFGF loaded mesh over a standard polypropylene mesh.

Key words: growth factor, fibroblast, FGF, wound healing, abdominal wall, incisional hernia, hernia repair, mesh

Introduction

Prospective studies revealed that up to 20% of the laparotomies are resulted in incisional hernias (1, 2). These hernias today are mostly repaired with prosthetic meshes with lower recurrence rates in comparison with suture repairs (3). However, surgeons still face with early and late recurrences in spite of mesh use (4).

The main cause of early incisional hernia development is technical failure. However, some hernias may appear even a proper wound closing is performed. Current concept in herniology says this kind of hernia formation is a collagen disorder (5). Deficiencies in collagen formation during wound healing may cause incisional hernia and recurrence after its repair. This suggests that a more comprehensive approach to incisional hernia repair than a mere mesh reinforcement is required. Recently, some members of growth factors family have been tested in the prevention of wound failure and incisonal hernia formation (6, 7). Several studies have shown that local application of growth factors might lower the incidence of incisional hernia. Nevertheless, a recent experimental study stated that local application of growth factors did not augment the strength of the abdominal wall (8).

Basic fibroblast growth factor (bFGF) is a potent mitogen and chemoattractant that stimulates growth of many cell types including fibroblasts (9-11). It is an angiogenic factor in-vivo and in-vitro. Exogenous bFGF has been shown to stimulate wound healing process and produce a lower risk of experimental incisional hernia (7).

In this experimental study, it was tried to combine the potential effects of bFGF with the benefits of polypropylene meshes in abdominal wound healing. The objective of the study was not only to measure the incidence of incisional hernia, but also observing the healing parameters by tensiometry and microscopy.

Materials and Methods

This experimental study was designed in Diskapi Teaching and Research Hospital, Department of Surgery, and completed in the Animal Laboratory of Ankara University School of Medicine after obtaining ethical committee approvals from both institutions.

Animals

A total of 80 Wistar albino rats were used in the study. All rats were located within the separate cages to prevent cannibalism after rested for 1 week to avoid transport stress. They were fed with regular rat Chow and tap water from drinking bottle.

Gelatin coating and FGF loading onto polypropylene meshes

Standard weight monofilament polypropylene mesh was used in the study (Herniamesh®, Italy). Gelatin was obtained from Difco, USA, and glutaraldehyde (50%) was purchased from BDH, UK. bFGF was purchased from Sigma®, Germany. Polypropylene meshes were cut into 20 mm x 20 mm pieces.
and placed into Petri dishes. 48 mesh pieces were first coated with gelatin, then, 32 pieces of them were loaded with bFGF.

Aqueous gelatin solution (10% w/v) with glutaraldehyde (0.1 M) was poured onto square mesh pieces and dried at room temperature. Finally, thin layer of gelatin coatings approximately 100 μm in thickness were obtained on PP meshes. On the other hand, bFGF was first dissolved in 50 μL heparin, and then diluted with phosphate buffered saline (PBS, pH 7.4). Aliquots of PBS containing 1 μg or 5 μg FGF were impregnated onto gelatin coated meshes. 100 μL of a FGF solution containing 1 μg or 5 μg FGF was impregnated onto each gelatin coated mesh.

Surgical procedures and grouping

The subjects were randomly divided into five groups. A uniform surgical procedure was employed in all groups: After setting intraperitoneal anesthesia by using 0.09 mg/g ketamine hydrochloride (Ketalar®, Pfizer) and 0.01 mg/g xylazin hydrochloride (Rompun®, Bayer), the ventral abdominal wall was shaved and fully prepped with iodine solution. A 5-cm skin incision was made at the midline and a full segment of the abdominal wall sized 3 x 2 cm, was excised. Abdominal wall was closed with rapidly absorbable 3/0 catgut (Atravmat®, Dogsan). Following this standard surgery, five different procedures were applied to the groups before closing the skin with 4/0 monofilament polypropylene sutures (Prolene®, Ethicon) (Table 1). Control subjects (Group 1) received no extra procedure after abdominal wall suturing. Polypropylene meshes were used in onlay position by fixing 4/0 monofilament polypropylene interrupted sutures in other four groups. A standard mesh with no chemical treatment was used in Group 2. Gelatin coated meshes were used in Group 3, while Group 4 and 5 received bFGF loaded meshes with 1 microgram (μg) and 5 μg doses respectively. All the groups then divided into 1st month (early: E) and 2nd month (late: L) subgroups (n=8 each) according to sacrifice dates. Sacrifications were done with intraperitoneal overdose anesthetic injections.

Tensiometric tests

Lloyd LRX 5 K® mechanical test device was used for the assessment of tensile strength (Lloyd Instruments Limited, Hampshire, UK) of mesh applied tissue samples. Tension force was applied with a strain rate and gage length of 20 mm/min and 20 ± 2 mm, respectively. Each tensile test ended when the specimen tore completely. The maximum strain values were recorded as Newton (N). For tensiometric tests, the specimens were excised by leaving free abdominal wall tissue, 1 cm, at the vertical two sides of the mesh-tissue interaction line. Thus, the final dimensions of tensile specimens were 4 cm x 2 cm.

Histopathological study

The specimens were obtained from the interface area of the meshes (12) and fixed in 10% formaldehyde, embedded in paraffin, sectioned, and stained with hematoxylin and eosin, and also Masson trichrome. The avidin-biotin-peroxidase method was performed using the primary monoclonal antibodies against collagen type I (1:100, Santa Cruz Biotechnology Inc, sc59772) and collagen Type III (1:100, Santa Cruz Biotechnology Inc, sc8781).

The variables were examined and evaluated by a single blinded pathologist under light microscopy in respect of inflammation, vascularization, fibroblast activity, collagen fibers and connective tissue organization. Inflammation was studied semiquantitatively according to the intensity of inflammatory cells. To evaluate the vascularization three separate hot fields were identified and examined by x 200 magnification. The vascular structures in these fields were counted and the mean number was calculated. Definition of vascularization was set as “++”: 1-3 vessels, “+++”: 4-6 vessels, “++++”: 7-10 vessels, and “+++++”>10 vessels. A similar definition was accepted for fibroblast count. Collagen fibers and connective tissue organization was evaluated semiquantitatively according to the intensity, homogeneity, parallelism to each other, and continuity with peripheral tissue collagen fibers (13).

The intensity and spread of collagen 1 and 3 was recorded by immunohistochemistry study. Areas for the analysis were selected under x10 magnification in a random manner for immunohistochemical scoring. The degree of positive staining was evaluated by semiquantitative scoring on a scale of 1 to 4 for intensity (I) such as inconspicuous (1), mild (2), moderate (3), and strong (4) and for distribution (D) such as perivascular or subepithelial (1), focal (2), patchy (3), and diffuse (4). Tissues with IxD less than or equal to 4 were considered weakly positive, and those with IxD greater than 4 were designated strongly positive (14).

Statistical analysis

SPSS for Windows version 11.5 software program was used for the statistical analysis. Histopathological scores and tensiometric values of 5 groups and each group’s early and late results were compared by using Mann-Whitney U test. The effects of bFGF applications and duration were analyzed by using 2-way ANOVA and subsequent post hoc test. A p value <0.05 was set as statistical difference.

<table>
<thead>
<tr>
<th>Table 1. Different surgical procedures used for 5 groups (10 subgroups)</th>
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<tbody>
<tr>
<td>Gr1E: Primary closure (control group), 1st month sacrifice</td>
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<tr>
<td>Gr1L: Primary closure (control group), 2nd month sacrifice</td>
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<tr>
<td>Gr2E: Primary closure + polypropylene mesh, 1st month sacrifice</td>
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<tr>
<td>Gr2L: Primary closure + polypropylene mesh, 2nd month sacrifice</td>
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<tr>
<td>Gr3E: Primary closure + gelatin coated mesh, 1st month sacrifice</td>
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<tr>
<td>Gr3L: Primary closure + gelatin coated mesh, 2nd month sacrifice</td>
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<tr>
<td>Gr4E: Primary closure + 1 μg b-FGF loaded gelatin coated mesh, 1st month sacrifice</td>
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<tr>
<td>Gr4L: Primary closure + 1 μg b-FGF loaded gelatin coated mesh, 2nd month sacrifice</td>
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<tr>
<td>Gr5E: Primary closure + 5 μg b-FGF loaded gelatin coated mesh, 1st month sacrifice</td>
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<tr>
<td>Gr5L: Primary closure + 5 μg b-FGF loaded gelatin coated mesh, 2nd month sacrifice</td>
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</tbody>
</table>
Results

As expected, control group displayed a 92.3% incisional hernia rate, while no herniation was observed in other 4 groups where meshes were used. The values of 5 groups in early and late sacrifice subgroups were compared. In addition, each group was evaluated by comparing its own early and late tensiometry and histopathology results.

Tensiometry results

All tears were observed at mesh/untreated tissue junction because of the mechanical strength of the mesh itself, except for the control group subjects. At the first month after surgery, there were no differences among five groups in respect of tensile strength measurements. However, at the end of the two months only Gr4L and Gr5L displayed significant improvements compared with their earlier values. Both groups also had significantly higher tensile strength values in comparison with Gr1L. In addition, Gr4L exhibited a significantly better mean tensiometric value in comparison with Gr2L (Table 2). However, neither the dose of bFGF and the duration had any effect on healing measured by tensiometry (p=0.79 and p=0.34).

Histopathologic examination

The histopathological findings and scoring in respect of inflammation, vascularization, fibroblast activity, collagen fibers and connective tissue organization were presented in Table 3. All these parameters were similar among early sacrifice groups except for a higher inflammation score in Gr4E in comparison with Gr1E and Gr2E. However, the later scores of the groups showed significant differences. Gr3L, Gr4L and Gr5L had higher vascularization scores than did Gr1L. Fibroblast scores were also better in mesh groups compared with the control subjects. Another striking finding was that only bFGF loaded mesh groups could improve their fibroblast scores between 1st and 2nd months. Lastly, Gr5L had a higher collagen fiber score than Gr2L.

Immunostaining for type I collagen displayed better intensity scores for bFGF loaded mesh groups in comparison with the control group both in the early and late phases of the study (Table 4). Type I collagen distribution was also similarly better in bFGF loaded mesh groups (Fig. 1 A,B). Other two mesh groups, where untreated and gelatin coated meshes were

<table>
<thead>
<tr>
<th>Gr</th>
<th>1st month [E]</th>
<th>2nd month [L]</th>
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<tbody>
<tr>
<td>Gr1</td>
<td>9.61 (1.59)</td>
<td>8.99 (1.85)</td>
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<tr>
<td>Gr2</td>
<td>9.82 (1.55)</td>
<td>9.41 (1.83)</td>
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<td>Gr3</td>
<td>10.54 (1.50)</td>
<td>10.24 (2.82)</td>
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<tr>
<td>Gr4</td>
<td>9.35 (0.94)</td>
<td>12.18 (1.85)</td>
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<tr>
<td>Gr5</td>
<td>8.90 (1.85)</td>
<td>11.43 (1.50)</td>
</tr>
</tbody>
</table>

Values in parenthesis display standard deviation

Gr1L vs Gr4L : p<0.05  Gr1L vs Gr5L : p<0.05  Gr4L vs Gr4L : p<0.05  Gr4L vs Gr5L : p<0.05  Gr2L vs Gr4L : p<0.05

Figure 1. Staining for type I collagen fibers after 2 months. (A). A subject received 5 μg bFGF loaded mesh in Gr5L; intensity:++++, distribution: ++++. (B) Another subject with untreated mesh in Gr2L; intensity: ++, distribution: ++. Immunoperoxidase staining, 100X magnification
Table 3. The mean histopathology scores of the groups

<table>
<thead>
<tr>
<th></th>
<th>Gr1E</th>
<th>Gr2E</th>
<th>Gr3E</th>
<th>Gr4E</th>
<th>Gr5E</th>
<th>Gr1L</th>
<th>Gr2L</th>
<th>Gr3L</th>
<th>Gr4L</th>
<th>Gr5L</th>
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<tr>
<td>Inflammation*</td>
<td>1.17 (0.41)</td>
<td>1.13 (0.35)</td>
<td>2.00 (1.00)</td>
<td>1.20 (0.44)</td>
<td>1.28 (0.48)</td>
<td>1.17 (0.41)</td>
<td>1.80 (0.83)</td>
<td>1.75 (0.71)</td>
<td>1.43 (0.53)</td>
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<td>[1-2 » 1.0]</td>
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<tr>
<td>Vascularization†</td>
<td>2.83 (0.98)</td>
<td>2.87 (0.99)</td>
<td>3.40 (0.54)</td>
<td>3.60 (0.81)</td>
<td>3.60 (0.00)</td>
<td>2.43 (0.78)</td>
<td>3.17 (0.41)</td>
<td>3.80 (0.44)</td>
<td>3.87 (0.35)</td>
<td>3.57 (0.53)</td>
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<tr>
<td>Fibroblast‡</td>
<td>2.50 (0.54)</td>
<td>2.62 (0.74)</td>
<td>3.00 (0.70)</td>
<td>3.00 (0.00)</td>
<td>2.20 (0.44)</td>
<td>2.28 (0.48)</td>
<td>3.40 (0.54)</td>
<td>3.20 (0.44)</td>
<td>3.75 (0.46)</td>
<td>3.43 (0.53)</td>
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<tr>
<td>Connec. tissue org.</td>
<td>3.16 (0.40)</td>
<td>2.37 (0.74)</td>
<td>3.00 (0.00)</td>
<td>2.80 (0.44)</td>
<td>2.60 (0.54)</td>
<td>2.80 (0.00)</td>
<td>2.80 (0.44)</td>
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<td>2.71 (0.48)</td>
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Values in parenthesis display standard deviations. Brackets show ranges and medians

* Gr1E vs Gr4E; p=0.030 Gr2E vs Gr4E; p=0.019
† Gr1L vs Gr3L; p=0.018 Gr1L vs Gr4L; p=0.006 Gr1L vs Gr5L; p=0.017 Gr3L vs Gr4L; p=0.029
‡ Gr1L vs Gr2L; p=0.008 Gr1L vs Gr3L; p=0.030 Gr1L vs Gr4L; p=0.001 Gr1L vs Gr5L; p=0.007
§ Gr2L vs Gr5L; p=0.035

Table 4. The mean collagen type I and III scores of the groups in immunohistochemical study

<table>
<thead>
<tr>
<th></th>
<th>Gr1E</th>
<th>Gr2E</th>
<th>Gr3E</th>
<th>Gr4E</th>
<th>Gr5E</th>
<th>Gr1L</th>
<th>Gr2L</th>
<th>Gr3L</th>
<th>Gr4L</th>
<th>Gr5L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen type I intensity*</td>
<td>2.00 (0.00)</td>
<td>2.37 (0.52)</td>
<td>2.80 (0.38)</td>
<td>3.60 (0.54)</td>
<td>3.20 (1.09)</td>
<td>2.00 (0.00)</td>
<td>3.00 (0.63)</td>
<td>2.80 (0.83)</td>
<td>3.62 (0.51)</td>
<td>3.29 (0.49)</td>
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<tr>
<td>distribution†</td>
<td>2.50 (0.54)</td>
<td>3.12 (0.35)</td>
<td>3.40 (0.54)</td>
<td>4.00 (0.00)</td>
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<td>2.57 (0.53)</td>
<td>4.00 (0.00)</td>
<td>4.00 (0.00)</td>
<td>3.75 (0.47)</td>
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<tr>
<td>Collagen type III intensity‡</td>
<td>2.33 (0.51)</td>
<td>2.25 (0.46)</td>
<td>3.20 (0.44)</td>
<td>3.20 (1.09)</td>
<td>2.80 (0.83)</td>
<td>2.14 (0.37)</td>
<td>2.66 (0.51)</td>
<td>2.60 (0.89)</td>
<td>2.75 (0.46)</td>
<td>3.14 (0.37)</td>
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<td>[2-3 » 2.0]</td>
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<tr>
<td>distribution§</td>
<td>2.50 (0.54)</td>
<td>3.12 (0.35)</td>
<td>3.40 (0.54)</td>
<td>3.40 (0.54)</td>
<td>3.60 (0.54)</td>
<td>2.57 (0.53)</td>
<td>3.33 (0.51)</td>
<td>3.40 (0.54)</td>
<td>3.25 (0.46)</td>
<td>3.71 (0.48)</td>
</tr>
<tr>
<td>[2-3 » 2.5]</td>
<td>[3-3 » 3.0]</td>
<td>[3-3 » 3.0]</td>
<td>[3-3 » 3.0]</td>
<td>[3-3 » 3.0]</td>
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</tr>
</tbody>
</table>

Values in parenthesis display standard deviations. Brackets show ranges and medians

* Gr1E vs Gr4E; p=0.024 Gr2E vs Gr4E; p=0.011 Gr1L vs Gr2L; p=0.008 Gr1L vs Gr4L; p=0.000 Gr1L vs Gr5L; p=0.001
† Gr1E vs Gr5E; p=0.030 Gr2E vs Gr4E; p=0.006 Gr1L vs Gr2L; p=0.001 Gr1L vs Gr5L; p=0.003 Gr1L vs Gr4L; p=0.004 Gr1L vs Gr5L; p=0.001 Gr1E vs Gr5L; p=0.001 Gr2E vs Gr2L; p=0.005
‡ Gr2E vs Gr3E; p=0.019 Gr1L vs Gr5L; p=0.004
§ Gr1E vs Gr5E; p=0.030 Gr1L vs Gr5L; p=0.007
used, also showed better distribution for type I collagen in the late phase in comparison with the control subjects. The difference between Gr2 and Gr4 at 1st month disappeared at 2nd month as Gr2 displayed a significant improvement by time. On the other hand, in respect the intensity and distribution of type III collagen, only Gr5 reflected better scores in comparison with Gr1. In 2-way ANOVA and post hoc test, bFGF application had a significant effect on inflammation score (p=0.026). Both bFGF and longer time affected fibroblast proliferation positively (p=0.029 and p=0.001). However, neither factor had ant effect on collagen deposition.

Discussion

Repair of primary abdominal wall hernias, incisional hernias or abdominal wall defects and the prevention of incisional hernias after laparotomies for major intraabdominal pathologies are two different aspects of the same common surgical problem. Apart from early postoperative herniation due to technical failure during wound closure a similar story may affect these processes. Meshes offer better results over traditional suture techniques in treatment of those conditions. However, a recent survey says that meshes do not reduce the risk of recurrence dramatically, but only delay its occurrence (4). Therefore, the researches to find novel methods for making repairs stronger and longer lasting are still going on.

Wound healing is a very complex process; abdominal wound healing is even more complicated because of the dynamics of the abdominal wall. Numerous endogenous substances are naturally involved in healing process, while some exogenous applications have been inserted in clinical or laboratory use. Incisional herniation may be associated with abnormalities in collagen metabolism (5). Therefore better long-term results may be obtained with biological interventions which can ameliorate these disorders in the early phase of the repairs.

The members of the growth factor family are derived primarily from tissue monocytes and macrophages, and promote chemotaxis, angiogenesis, fibroblast proliferation and collagen synthesis (9,15). They may have a potential to promote chemotaxis, angiogenesis, fibroblast proliferation and collagen synthesis. Therefore fibroblast proliferation and collagen synthesis. Therefore, the mechanism of a possible benefit in wound healing after bFGF treated mesh can be understood when we look at histological parameters of the inflammatory and healing. Especially fibroblast proliferation and collagen score is important. In the present study, the apparent findings in microscopy were that bFGF loaded meshes improved fibroblast scores between 1st and 2nd months, and 5 μg bFGF loaded meshes created a higher collagen fiber score than untreated meshes. Nevertheless, histopathological examination and immunohistochemistry for collagen hardly showed an obvious advantage in favor of bFGF application.

Those variable results coming from different studies about the effects of the exogenous growth factors on the abdominal incisional healing might be related to several reasons. In fact, despite a bunch of growth factors have been used in many
could keep the subjects alive. On the other way, collagen was mandatory contrary to serum measurement protocols that study were based on tissue evaluation, therefore sacrification however the subjects were not the same rats. The design of the groups received the same procedure in each arm of the study, meshes with built-in FGF may also be useful to cope with this the expression of angiogenic factor initially. Therefore, using (27). They speculated that polypropylene meshes might impair production following mesh repair immediately after surgery and colleagues revealed a decrease in serum level of bFGF found that mesh repair enhanced FGF expression and naturally indigenous elements of wound healing. Junge et al. found in the early wounds and body fluids. These factors are exhibit a dose-dependent effect in the present experiment, an acceptable cost/benefit ratio will be the key element prosthetic meshes in use for abdominal wall healing are not. these substances are quite expensive, while most of the doses of growth factor in this sort of experiments. However during the study planning. It is surely possible to use higher growth factors to obtain maximum benefit in wound healing are not definite for human being or animals. Furthermore, different doses may be required for healing of different tissues. Various doses from 1 ng to 200 μg have been used in bFGF studies on wound healing (23-26). Not only the application ways and doses but also the results are heterogenous. In addition, whether the effects are dose-dependent is not clear. Two different doses were used in the present study and both resulted in better healing. However, a dose-dependent effect did not appear. This was possibly due to either the short half-life of bFGF or a shorter release from the coated mesh than we had expected during the study planning. It is surely possible to use higher doses of growth factor in this sort of experiments. However these substances are quite expensive, while most of the prosthetic meshes in use for abdominal wall healing are not. An acceptable cost/benefit ratio will be the key element when a clinical use is considered. Although we did not exhibit a dose-dependent effect in the present experiment, it is always possible to test different doses in further studies. Basically, FGF and some other growth factors have been found in the early wounds and body fluids. These factors are naturally indigenous elements of wound healing. Junge et al. found that mesh repair enhanced FGF expression and fibroblast count more than suture repair (12). However, Di Vita and colleagues revealed a decrease in serum level of bFGF production following mesh repair immediately after surgery (27). They speculated that polypropylene meshes might impair the expression of angiogenic factor initially. Therefore, using meshes with built-in FGF may also be useful to cope with this early lack of FGF in the wound. Besides the lack of serum FGF measurements, the present study has some other shortcomings. The 1st and 2nd month groups received the same procedure in each arm of the study, however the subjects were not the same rats. The design of the study were based on tissue evaluation, therefore sacrifice was mandatory contrary to serum measurement protocols that could keep the subjects alive. On the other way, collagen studies were qualitative. A more precise result could be obtained if tissue hydroxyproline concentrations were obtained as in Fedakar-Senyucel and colleagues’ recent study that showed local and sustained release of FGF enhanced the healing of esophageal anastomoses (28). Lastly, unlike previous studies on the effects of growth factors in abdominal wound healing and incisional hernias, we used an unresorbable prosthetic material in the model. It was not possible to measure the strength of the abdominal wound itself because the mechanical strength of the mesh was already strong enough on the linea alba. We, instead, examined the mesh-tissue interference as others did before (12). In fact, most of late recurrences develop at the mesh-tissue interference (4). Therefore, the present model might produce a more reliable and predictive opinion about the duration of the repair. In conclusion, the use of bFGF loaded polypropylene mesh in the abdominal wall healing may cause somewhat higher tensile strength values in comparison with a standard polypropylene mesh after 2 months. However, histopathological and immunohistochemistry studies revealed only a slightly better healing in favor of bFGF loaded mesh over a standard polypropylene mesh. This potential effect did not seem to be dose dependent. The decision about the use of bFGF loaded polypropylene mesh in clinical setting seemed to need further investigations.

References


