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How safe is the use of prosthetic materials in the repair of abdominal-wall defects in malnourished subjects?

Research Article

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Abstract: Incisional hernias and abdominal-wall defects consume large amounts of healthcare resources. Use of mesh is effective in treatment of these disorders and can decrease the rate of recurrence. This experimental study focused on the safety of mesh use in the setting of malnutrition, a condition that impairs wound healing. Rats were divided into two groups: normally fed and food-restricted. An abdominal-wall defect, 2 by 2 cm, was covered with polypropylene mesh, 2.5 by 2.5 cm. After sacrifice of the rats at the 21st and 60th days, tissue samples were sent for tensiometric and histopathological studies. No significant difference in infectious complications was observed between the two groups. Tensiometry revealed no significant differences between the groups. On histopathological examination, the only difference noted was in the vascularization scores of normally fed rats. For malnourished subjects that survived after surgery, the use of polypropylene mesh appeared safe in the closure of abdominal-wall defects, with no increase in infection rate and satisfactory wound healing.

Keywords: *Hernia repair • Mesh • Wound healing • Tensile strength • Malnutrition*

1. Introduction

Numerous patients around the world undergo repair of abdominal hernias every year. These repairs consume a large quantity of healthcare resources. Despite the advances in surgical techniques, the incidence of incisional hernia after midline laparotomy is still between 10% and 15%, [1] and the recurrence rates of the repair of those hernias with patients' own tissues can be as high as 50% [2]. However, lower recurrence rates have been achieved in the last two decades by tension-free repairs with the use of prosthetic materials [3,4]. Nevertheless, it may still be challenging to cope with an incisional hernia in cases where wound healing is affected by

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factors such as poor nutritional status. Furthermore, it is not clear whether the mesh itself improves or impairs the wound healing [5].

Wound healing is a dynamic process that is affected by several factors, including nutritional status. The relationship between nutritional status and wound healing has been investigated in a large number of studies [6-9]. Malnutrition is still a common problem in patients undergoing surgery, [10] and today it is well known that wound complications are observed more frequently in these patients; tensile strength is lowered, the infection rate increases, and wound disruption becomes a potential risk.

In this experimental study, we aimed to investigate the safety of prosthetic materials for the repair of the abdominal wall in subjects with malnutrition.

2. Material and Methods

Separate approval letters, one each from the local ethical committee of the Diskapi Teaching and Research Hospital where the surgical team work and Ankara University Veterinary Faculty where the experimental study was carried out, were obtained.

A total of 40 Wistar albino rats were used in the study. After resting for 1 week to avoid transport stress, all rats were located in separate cages to prevent cannibalism. After weighing the subjects and recording the base weights, they were divided evenly into two groups according to a 2-week feeding regimen:

- Group 1: Control subjects; normally nourished rats (52 kcal/day = 20 g/day)
- Group 2: Malnutrition model; rats fed with half of a normal diet (26 kcal/day = 10g/day)

At the end of the 2-week period, all subjects were weighed again. Blood samples were withdrawn from the tail vein for the evaluation of the immune response. Both groups were randomly divided in advance into early (E: 21-day) and late (L: 60-day) subgroups according to sacrifice dates.

G1-E : Control group; 3-week
G2-E : Malnutrition group; 3-week
G1-L : Control group; 2-month
G2-L : Malnutrition group; 2-month

2.1. Operative technique

After intraperitoneal injection of ketamine (90 mg/kg) and xylazine (10 mg/kg) for general anesthesia, the ventral abdominal wall was shaved and fully prepped with iodine solution. A 6-cm skin incision was made at the midline. A full segment of the abdominal wall, 2 by 2 cm, was excised. This defect was closed with a monofilament polypropylene mesh (Herniamesh, Turin, Italy), 2.5 by 2.5 cm. The mesh was secured with 12 separate 3/0 polypropylene sutures (Prolene, Ethicon, UK). Finally, the skin was approximated with the same suture material.

Each group received its preoperative feeding regimen until the sacrifice date. The subjects were sacrificed after their weights were obtained on day 21 and day 60 by a high-dose intraperitoneal xylazine injection (60 mg/kg). Intracardiac blood samples were obtained, and the ventral abdominal wall was fully excised for study.

The specimen was prepared for study by leaving free abdominal wall tissue, 1 cm, at the four sides of the mesh-tissue interaction line. Thus, the size of the specimen was set as 3.5 by 3.5 cm. It was divided vertically in half; one half was sent for histopathological study and the other for tensiometric study.

2.2. Tensiometric Study

All the fresh specimens were tested mechanically by the same person in the Middle East Technical University, Faculty of Chemistry, with the Lloyd LRX5K (Lloyd Instruments Limited, Fareham, Hampshire, UK) testing machine. All the sutures for mesh fixation were removed before the measurement, whereas the mesh was left in place. Tensile tests were performed at a strain rate of 10 mm per minute. Each tensile test ended when the specimen tore completely. The values were recorded as Newton (N).

2.3. Histopathological evaluation

The specimens were fixed in formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin as well as Masson trichrome. The variables (inflammation, vascularization, fibroblast activity, collagen fibers, and connective-tissue organization) were examined and evaluated by a single pathologist. Inflammation was studied semiquantitatively according to the intensity of inflammatory cells. To evaluate the vascularization, three separate “hot” fields (the field where vascularization structures are moct active) were identified and examined (magnification, 200 times). The vascular structures in these fields were counted, and the mean number was calculated. Vascularization was defined as + for 1-3 vessels, ++ for 4-6 vessels, +++ for 7-10 vessels, and ++++ for more than 10 vessels. A similar definition was accepted for fibroblast count. Collagen fibers and connective-tissue organization were evaluated semiquantitatively according to the intensity, homogeneity, parallelism to each other, and continuity with collagen fibers in peripheral tissue.

Table 1. The mean values for white-cell counts.

	Test date		White-cell counts (x10^3)	
	G1-E	G2-E	G1-L	G2-L
	3rd week	3rd week	2nd month	2nd month
Operation day	10.9	8.9*	10.9	9.9
Sacrification day	8.3§	4.3* §	8.7	8.2

** Significant difference within the same subgroup (p<0.05).*
§ Significant difference between two subgroups (p<0.01).

2.4. Statistical analysis

An SPSS 11.5 software program was used for the statistical analysis. Body weight changes, white-cell counts, histopathological scores, and tensiometric values of the groups were compared by use of the Mann-Whitney U test. Within each group, body weight, and changes in white-cell counts were tested with the Wilcoxon test. The p value was set at <0.05.

3. Results

3.1. Weight changes

The mean weights of the subjects in the two groups were similar at the beginning of the study. After the 2-week feeding period, the group receiving half the normal daily caloric count showed a statistically significant weight change compared with the control group; on average, in comparison to the base weights of the subjects in this group, there was a 12% loss in weight. The mean weight loss reached 18% at the third week and as high as 33% at the second month (p<0.01). In contrast, control subjects showed no statistically significant weight changes either at the third week or at the second month.

3.2. Wound complications

At week 3, both the G1-E and G2-E groups each had one mesh-related infection. At month 2, one incomplete skin-wound disruption was observed in each group. The results were completely similar.

3.3. White-cell counts

There was no difference in the mean white-cell counts of the groups on the day of surgery. A marked decrease was observed in the G2-E group on the day of sacrifice (21 days) compared with its mean basal value, whereas no significant change was observed in G1-E (Table 1). However, there were no differences between the subgroups sacrificed at 60 days.

Table 2. The mean tensile strength values of the groups (N).

	G1-E	G2-E	G1-L	G2-L
Tensile strength (N)	6.20*	6.58	8.91*	8.27
	(1.95)	(2.35)	(2.14)	(2.01)

Values in parenthesis display standard deviation.
G1-E vs. G2-E : p>0.05
G1-L vs. G2-L : p>0.05
*G1-E vs. G1-L : p=0.02**

Table 3. The means for histopathological scores.

	G1-E	G2-E	G1-L	G2-L
Inflammation	1.89	1.63	2.00	1.5
	(1-4)	(1-3)	(1-3)	(1-2)
Vascularization*	3.33	2.37	3.00	2.19
	(3-4)	(2-3)	(2-4)	(2-3)
Fibroblast	2.89	2.63	2.50	2.00
	(2-4)	(2-4)	(2-3)	(2-2)
Collagen	2.55	2.25	3.00	2.83
	(2-3)	(2-3)	(3-3)	(2-3)
Connective tissue org.	3.00	2.75	3.12	2.50
	(2-4)	(2-4)	(3-4)	(2-3)

Values in parenthesis display minimum and maximum scores.
** G1-E vs. G2-E : p<0.01*
** G1-L vs. G2-L : p=0.02*

3.4. Tensile strength measurements

All the tears took place at or just lateral to the tissue-mesh border, as expected. The mean tensiometric values of the two groups were similar at the third week. Both groups showed an increase at the second month, whereas the mean values of the two groups were still not different (Table 2). Nevertheless, the control group displayed a significant improvement in tensile strength from the third week to the second month (p=0.02), whereas the difference between the mean values of G2-E and G2-L was very close to, but did not reach, the level of significance (p=0.06).

3.5. Histopathological scores

The only significant difference between the groups was observed in the vascularization parameter. The mean scores of inflammation, fibroblast activity, collagen fibers, and connective-tissue organization for the groups were similar (Table 3).

4. Discussion

Because tissue repair requires energy and adequate nutritional intake, wound healing is impaired when the patient has a nutritional deficiency. Reducing caloric intake by 50% in rats decreases collagen synthesis and matrix protein deposition [11,12]. In humans, even modest protein-calorie malnutrition may impair fibroplasia [13]. It has been shown that patients with malnutrition are more susceptible to infection and wound complications and may have a higher mortality rate than those who are well nourished. Malnutrition is not uncommon in surgical patients. Some studies have reported malnutrition rates for patients undergoing abdominal surgery as high as 60% [11-13]. If adequate nutritional support cannot be achieved, malnutrition rates as high as 80% may be recorded at discharge after surgery [11].

Malnutrition can be diagnosed with several objective and subjective parameters and tools, commonly including serum albumin level and lymphocyte count. It is also possible to evaluate nutritional status in a clinical setting by use of the Nutritional Risk Index or Subjective Global Assessment. On the other hand, one of the easiest ways to recognize malnutrition is the occurrence of recent Unintentional weight loss in a patient's history. The definition of significant weight loss is a loss of 10% of body weight over a 6-month period [6]. A weight loss of about 15% is associated with an average 20% loss of body protein and significant alterations in physiologic functions [7]. Weight loss has also been found to be an independent factor for postoperative mortality after major abdominal surgery [14].

Collagen is the major protein in most tissues and constitutes 25% of the total protein mass in mammals [15]. Deficient collagen synthesis during the healing period directly affects the wound strength [5]. Spanheimer et al. showed that food restriction in rats causes a marked decrease in collagen production [16]. Malnutrition due to restrictive intake has also been suggested as prolonging the inflammatory phase of healing, reducing fibroblast proliferation, and neoangiogenesis [17-20]. However, in the present study, except for angiogenesis, subjects with malnutrition displayed somewhat lower but statistically similar histopathological scores of wound healing compared with normally fed rats.

Ideally, a mesh material should not excite an inflammatory response or foreign-body reaction in the host tissues [21]. In both groups, one gross foreign-body reaction was observed macroscopically, but microscopical examination revealed only mild inflammation scores, without an intense inflammatory response. Despite the widespread use of mesh, the short-term and long-term biological mechanism of its incorporation into the abdominal wall is not fully understood [5]. In terms of fibrous-collagenous response, polypropylene meshes can exhibit a proliferative picture, but this response may be disorganized [21]. The detailed time course and mechanism of fibroblast activation after the use of mesh have not been documented [5]. Besides, whether mesh use in subjects with malnutrition causes an improved or diminished fibroblast response is unknown to date. In the present study, although the malnutrition group had lower collagen and fibroblast scores, the differences between the groups did not reach the level of significance in the early or late phase. It is not possible to say that no synergistic negative effect took place when mesh was used in the presence of malnutrition.

When compared to abdominal-wall tissue, prosthetic meshes have much higher tensile-strength properties [22]. Tissue strength from the natural wound healing is negligible in comparison with the strength of the mesh itself. Therefore, if we choose to make the tensiometric study sample the exact size of the mesh, the result will not give us any information about the healing process beyond the mesh's mechanical strength. On the other hand, if the sample size overlaps the size of the mesh, it is possible to evaluate the healing at the border of tissue-mesh interaction. In this experiment, after such an evaluation, tensiometric studies did not show a difference between the groups at either week 3 or month 2. This does not agree with the findings obtained in previous studies. For example, Koback et al., using the bursting pressure of the abdominal wound in rats, showed a 3-day increase in the lag phase in protein-deficient animals [9]. It has also been shown that at day 21 there was a significant difference in the wound strength in malnourished animals [8,23]. In a more recent experimental study, Temple and colleagues found higher rates of mortality and wound complication within the first 2 weeks in rats with significant weight loss and poor nutritional intake [24]. However, in that study, malnourished animals surviving for 60 days had wound strength equal to that of the control rats as determined by the breaking strength of skin wounds. Thus, Temple et al. concluded that wounds in surviving malnourished subjects eventually gain sufficient strength for normal function.

It was previously observed that a high degree of integration of the polypropylene meshes into the wall was achieved after 2 months [25]. In our experimental study, the well nourished group displayed a significantly better healing determined by tensile strength between the third week and second month, but the wound strength in the two groups was similar at month 2. This finding supports the argument that if a malnourished subject can survive in the early postoperative period, it can show improved healing parameters afterwards.

In fact, this study design can address the safety of the use of polypropylene meshes in malnourished subjects in two ways. First, as a foreign body, does a prosthetic mesh produce an increased infection rate in the setting of malnutrition? The answer in rats is "no". The correct answer for human beings requires clinical trials. Second, given that malnutrition causes poor abdominal wound healing, would the use of mesh improve the healing process in malnourished patients? Neither tensiometric studies nor histopathological scores bear this out. On the other hand, it appears that the combined state of malnutrition and mesh use is either not detrimental to wound healing, or else mesh can compensate for the negative effects of malnutrition on wound healing.

In conclusion, the use of polypropylene mesh is safe in the closure of abdominal defects in malnourished subjects, with no increase in infection rate and satisfactory wound healing. The repair of abdominal defects and incisional hernias in major abdominal trauma or patients undergoing surgery seems possible but surely requires clinical research.

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