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Changes of pro- inflammatory and anti-inflammatory interleukins in cases of implantation of polypropylene meshes of different types in implant hernioplasty

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Abstract

The use of polypropylene meshes in the treatment of ventral and postoperative ventral hernias is uncontroversial. Their use is accompanied by a significant inflammatory response in the implantation area, contributes to the formation of a dense connective tissue capsule and, as a result, leads to shrinkage of the mesh. The issue of postoperative exudative complications that complicate the postoperative course much is topical.

Objective. The aim of the research was to conduct a comparative evaluation of the results of the use of ‘light’, ‘heavy’ polypropylene meshes, as well as the ‘light’ one in combination with the PRF membrane, based on the study of the state of systemic indices of cytokines in retro-muscular allohernioplasty in the patients with primary and postoperative ventral hernia.

Materials and methods. The research was based on the examination of 165 patients, who underwent surgery for primary and postoperative ventral hernia with the implantation of ‘light’, ‘heavy’ polypropylene meshes, as well as the ‘light’ one in combination with the PRF membrane. The study of systemic indices of cytokines in the serum of peripheral blood were conducted. The ratio of pro-inflammatory and anti-inflammatory interleukins TNF- α , IL-8 and IL-4 as well as the content of serum immunoglobulin (Ig) A was determined before the

surgery, on the first day after the surgery, and on the day of discharge from the hospital (7-9th day of the postoperative period), in order to evaluate the stage and course of the immune response to the implantation of different types of polypropylene meshes.

Results. On the day of discharge from the hospital, a decrease in the level of pro-inflammatory and anti-inflammatory cytokines in the main group was evidenced in the patients, who underwent implantation of the 'light' mesh as well as in those, who underwent implantation of the 'light' one in combination with the PRF membrane. In the patients, who underwent 'heavy' mesh implantation, a statistically significant increase in IL-8 and IL-4 levels was proved on the day of discharge from the hospital ($p < 0.05$). A decrease in the level of total and secretory IgA in the main group of patients, who underwent implantation of the 'light' mesh in combination with the PRF membrane, was evidenced, though in the patients, who underwent implantation of the 'light' mesh, the indices did not change compare to the 1st postoperative day. In the patients, who underwent implantation of the 'heavy' mesh, a statistically significant increase in both total and secretory IgA levels was proved on the day of discharge from the hospital ($p < 0.05$).

Conclusions. In the patients with primary and postoperative ventral hernia in cases of implantation of a 'heavy' polypropylene mesh, the immune response was characterized by a significant intensification of local and overall immune defense (according to the content of Ig A), and increase in pro-inflammatory and anti-inflammatory cytokines. When using the 'light' meshes in combination with the PRF membrane in the patients with primary and postoperative ventral hernia, the state of immune status was the best compared to the baseline data: the number of pro-inflammatory and anti-inflammatory interleukins decreased, local and overall immune defense reduced.

Key words: ventral hernia, postoperative ventral hernia, polypropylene mesh, cytokines.

Introduction

These days, the operation of choice in the surgical treatment of ventral and postoperative ventral hernias is alloplasty without a doubt. Although, the allohernioplasty does not always assure reliability of surgical intervention [2, 3]. A significant inflammatory response in the implantation area promotes formation of a dense connective tissue capsule and, as a result, leads to shrinkage of the polypropylene mesh [1]. The issue of postoperative exudative complications is topical [5]. The attempts to develop a lightweight mesh of polypropylene in combination with resolving materials proved to be inadequate due to the

increase in hernia relapses [4]. Therefore, the matter of choice of 'heavy' or 'light' meshes, taking into account the immunological reactivity of the body in each case, is urgent [7-11].

In our opinion, a comprehensive study of the combined use of a polypropylene mesh and a PRF membrane, which consists of platelet enriched fibrin, in the surgical treatment of postoperative ventral hernias, above all for the risk group patients, is promising. Biocompatible PRF membranes, rich in growth factors, have been already used in surgical dentistry, periodontology, implantology, bone plastic and maxillofacial surgery [6]. We have not found any information about their use in surgical treatment of hernias.

Objective

The aim of our research was to carry out a comparative evaluation of the use of 'heavy', 'light' polypropylene meshes as well as the 'light' one in combination with the PRF membrane based on the study of the state of system pro-inflammatory and anti-inflammatory interleukins in implant retro-muscular allohernioplasty in the patients with primary and post-operative ventral hernia.

Materials and methods

The research involved examination of 165 patients, who underwent surgery at the Clinic of Surgery of the Academic and Research Institute of Postgraduate Education of I. Horbachevsky Ternopil State Medical University at the premises of the Department of Surgery of Ternopil City Clinical Hospital No. 2 from 2014 to 2017. 55 (33.33%) patients underwent implantation of the 'heavy' polypropylene mesh. The 'light' polypropylene mesh was used for 56 (33.93%) patients; and in 54 (32.72%) patients the 'light' polypropylene mesh was implanted in combination with the PRF membrane. The control group consisted of 20 healthy respondents. The main group involved patients only with primary and postoperative ventral hernias of type M1-3, W1-2, R0-1 according to JP Chevrel, AM Rath classification (SWR-classification, 1999); the patients were implanted with the meshes of the same size in order to get statistically significant results.

The analysis of the content of cytokines was carried out by means of the enzyme analyser using the reagent kits produced by Diaclone (France). ELISA TNF- α , IL-4, IL-8 kits are designed for quantitative determination of the mentioned cytokines and human growth factor 'in vitro' in serum. CELISA enzyme-linked immunosorbent kits are based on the principle of 'sandwich'. The microtitration wells were covered with specific antibodies to TNF- α , IL-4, IL-8 respectively; the test samples and standards with known and unknown amounts of TNF- α , IL-4, IL-8 were added. During the first incubation, the antigens of the studied cytokines and the corresponding biotinol monoclonal antibodies were incubated

simultaneously. After washing, the streptavidinperoxidase enzyme was added. After incubation and washing the unlinked particles out of the sampling, a substrate solution was added, which reacted with the linked enzyme and resulted in coloration, the intensity of which after photometry was evaluated at 450 nm and 620 nm wavelengths by comparison. The intensity of the colour was directly proportional to the concentration of the studied cytokines and growth factor. The evaluation of the attained data was carried out in relation to that of the control group of young healthy people. The content of serum immunoglobulin (Ig) A was determined by the immunoassay (ELISA) using the reagents produced by Granum (Ukraine).

Results

The analysis of the attained results, which characterize the changes in systemic cytokines on the 1st day after surgical intervention in the patients with primary and postoperative ventral hernia of the main group, who underwent implantation of 'heavy' and 'light' meshes, proved a significant increase in the indices of pro-inflammatory and anti-inflammatory interleukins: IL-8 and IL-4. In particular, the level of pro-inflammatory IL-8 in the patients with implantation of 'heavy' and 'light' meshes on the 1st day of the postoperative period increased in 4.1 and 4.4 times in the main group compare to the preoperative indices ($p < 0.05$). Similar changes were evidenced regarding the concentration of anti-inflammatory IL-4. On the day of discharge from the hospital, a decrease in the level of pro-inflammatory and anti-inflammatory cytokines in the main group of patients, who underwent implantation of the 'light' mesh, as well as in the patients, who underwent implantation of the 'light' mesh in combination with the PRF membrane, was proved. In the patients, who underwent 'heavy' mesh implantation, a statistically significant increase in the levels of IL-8 and IL-4 was observed on the day of discharge from the hospital in two comparative groups ($p < 0.05$) (Table 1).

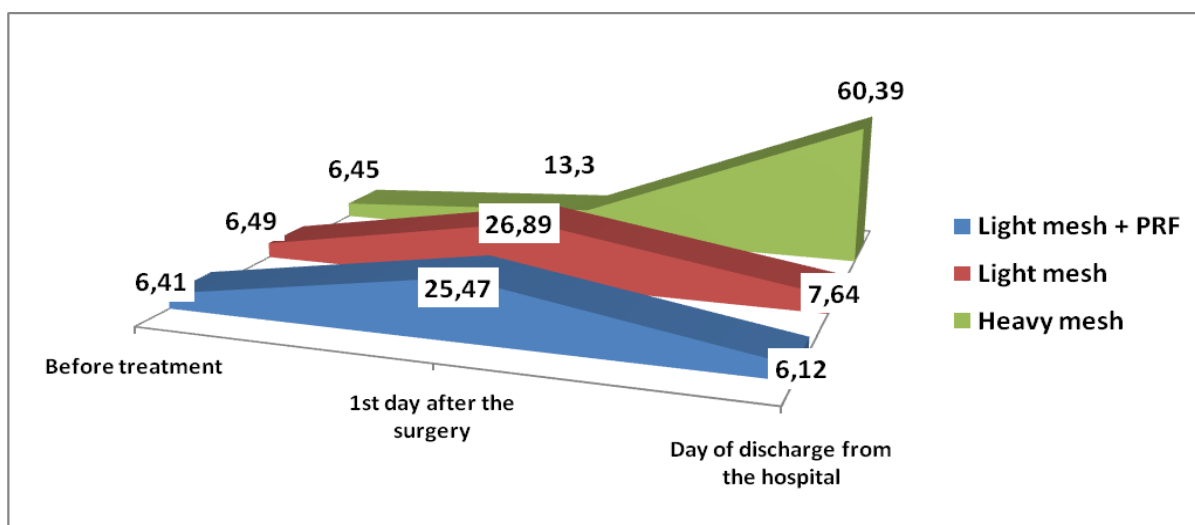
The analysis of the results of the level of TNF- α on the 1st day after the surgery in the patients with primary ventral hernia (PVH) and postoperative ventral hernia (POVH) of the main group, who underwent implantation of 'heavy' and 'light' meshes, proved its significant increase: the level of pro-inflammatory TNF- α in the patients, who underwent implantation of 'heavy' and 'light' meshes, on the 1st day of the postoperative period increased in 2.0 and 4.1 times in the main group and in 1.9 and 4.1 times in the comparative group compare to the preoperative indices ($p < 0.05$) (Fig. 1). In the patients, who underwent implantation of the 'light' mesh in combination with the PRF membrane, the level of TNF- α on the 1st day of the postoperative period was statistically significantly increased in 4.0 times compare to the baseline data ($p < 0.05$).

Table 1. Comparative characteristics of IL-4 and IL-8 content in the patients with postoperative ventral hernias in two comparative groups depending on the type of polypropylene mesh in combination with the PRF membrane (M±m)

| Index of the studied sample extinction; examination day | Main group | | | Control group (n=20) |
|---|---|--|---|----------------------|
| | 'Heavy' mesh (n=55) | 'Light' mesh (n=56) | 'Light' mesh+PRF (n=54) | |
| IL-4, pg/ml; before treatment | 3.20±0.04 #p<0.05 | 3.19±0.03 #p<0.05 | 3,26±0,03 #p<0,05 | 1.98±0.16 |
| 1 st day after treatment | 31.11±0.28 #p<0.05 *p<0.05 | 37.67±0.27 #p<0.05 *p<0.05 | 34.08±0.23 #p<0.05 *p<0.05 | |
| Day of discharge from the hospital | 77.27±0.32 #p<0.05 *p<0.05 *p<0.05 ##p<0.05 | 17.12±0.30 #p<0.05 *p<0.05 ##p<0.05 **p<0.05 | 3.73±0.06 #p<0.05 *p<0.05 **p<0.05 ***p<0.05 | |
| IL-8, pg/ml; before treatment | 14.32±0.32 #p<0.05 | 14.36±0.31 #p<0.05 | 14.39±0.30 #p<0.05 | 0.69±0.11 |
| 1 st day after treatment | 73.08±0.44 #p<0.05 *p<0.05 | 70.99±0.28 #p<0.05 *p<0.05 | 68.54±0.30 #p<0.05 *p<0.05 | |
| Day of discharge from the hospital | 82.70±0.36 #p<0.05 *p<0.05 *p<0.05 ##p<0.05 | 20.25±0.35 #p<0.05 *p<0.05 ##p<0.05 **p<0.05 | 13.65±0.09 #p<0.05 *p<0.05 **p<0.05 ***p<0.05 | |

Notes: # – statistically significant difference regarding that indices of the control group;
 * – statistically significant difference regarding that indices of the same group before treatment;
 ** – statistically significant difference regarding that indices in the patients with the heavyweight mesh;
 ## – statistically significant difference regarding that indices of the comparative group;
 *** – statistically significant difference regarding that indices in the patients with the lightweight mesh.

On the day of discharge from the hospital, the best positive changes were evidenced in the patients with PVH and POVH, who underwent implantation of the 'light' mesh in combination with the PRF membrane. The level of TNF-α in these patients decreased and reached the preoperative indices and was statistically significantly lower than that in the patients, who underwent implantation of the 'light' mesh only. Concerning the patients, who underwent 'heavy' mesh implantation, the concentration of TNF-α increased statistically significantly compare to the baseline data of the main group as well as the comparative one (p<0.05).



Note: # – statistically significant difference regarding that indices of the same group before treatment.

Fig. 1. Graphical comparison of the TNF- α level in the main group of patients with ventral and postoperative ventral hernia depending on the type of polypropylene mesh and the combination with the PRF membrane

Thus, the content of pro-inflammatory and anti-inflammatory cytokines in the patients with PVH and POVH proved the best state of immune response in the patients, whom the ‘light’ mesh in combination with the PRF membrane was used for.

The study of local immune resistance of mucous membrane of the patients with POVH in the presence of comorbidity revealed local immune responses that proved significant stress and instability of local immune resistance of those patients. The analysis of the results on the 1st day after the surgery in the patients of the main group, who underwent implantation of ‘heavy’ and ‘light’ meshes, evidenced the increase of total and secretory IgA indices (Table 2).

Table 2. Comparative characteristics of the content of total and secretory IgA in the patients with POVH in two comparative groups depending on the type of polypropylene mesh and the combination with the PRF membrane (M±m)

| Index of the studied sample extinction; examination day | Main group | | | Control group (n=20) |
|---|---|--|---|----------------------|
| | 'Heavy' mesh (n=55) | 'Light' mesh (n=56) | 'Light' mesh+PRF (n=54) | |
| Total IgA, pg/ml; before treatment | 2.87±0.05 #p<0.05 | 2.88±0.05 #p<0.05 | 2.87±0.05 #p<0.05 | 2.35±0.05 |
| 1 st day after treatment | 3.15±0.03 #p<0.05 *p<0.05 | 3.11±0.04 #p<0.05 *p<0.05 | 3.10±0.04 #p<0.05 *p<0.05 | |
| Day of discharge from the hospital | 3.83±0.03 #p<0.05 *p<0.05 *p<0.05 ##p>0.05 | 3.08±0.30 #p<0.05 *p<0.05 ##p<0.05 **p<0.05 | 2.59±0.04 #p<0.05 *p<0.05 **p<0.05 ***p<0.05 | |
| Secretory IgA, pg/ml; before treatment | 11.88±0.30 #p<0.05 | 11.94±0.26 #p<0.05 | 11.89±0.27 #p<0.05 | 10.25±0.12 |
| 1 st day after treatment | 13.71±0.11 #p<0.05 *p<0.05 | 13.67±0.12 #p<0.05 *p<0.05 | 13.71±0.13 #p<0.05 *p<0.05 | |
| Day of discharge from the hospital | 17.16±0.13 #p<0.05 *p<0.05 *p<0.05 ##p<0.05 | 13.59±0.14 #p<0.05 *p<0.05 ##p<0.05 **p<0.05 | 10.88±0.19 #p<0.05 *p<0.05 **p<0.05 ***p<0.05 | |

Notes: # – statistically significant difference regarding that indices of the control group;
* – statistically significant difference regarding that indices of the same group before treatment;
** – statistically significant difference regarding that indices in the patients with the heavyweight mesh;
– statistically significant difference regarding that indices of the comparative group;
*** – statistically significant difference regarding that indices in the patients with the lightweight mesh.

Discussion

The level of secretory IgA in the patients, who underwent implantation of 'heavy' and 'light' meshes, on the 1st day of the postoperative period increased by 15.4% and 14.49% in the main group and by 12.25% and 10.98% in the comparative one compared with the preoperative indices (p<0.05). Similar changes were evidenced regarding the concentration of total IgA. On the day of discharge from the hospital, a decrease in the level of total and secretory IgA in the main group of patients, who underwent implantation of the 'light' mesh

in combination with the PRF membrane, was proved, though in the patients, who underwent implantation of the 'light' mesh, the indices did not change compare to the 1st postoperative day. In the patients, who underwent implantation of the 'heavy' mesh, a statistically significant increase in the levels of IgA, both total and secretory, was observed on the day of discharge from the hospital in two comparative groups ($p < 0.05$).

Thus, the combination with the PRF membrane proved the most significant positive effect on the state of local immune response in the patients with PVH and POVH.

Conclusions

In the patients with primary and postoperative ventral hernia in implantation of the 'heavy' polypropylene net, the state of immune response was characterized by a significant intensification of local and overall immune defense (according to the content of Ig A), and increase in pro-inflammatory and anti-inflammatory cytokines; in cases of implantation of the 'light' mesh the intensification of immune status was less significant.

When using the 'light' meshes in combination with the PRF membrane in the patients with primary and postoperative ventral hernia, the state of immune status was the best compared to the baseline data: the number of pro-inflammatory and anti-inflammatory cytokines decreased, local and overall immune defense reduced.

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