Dynamics of degradation of new samples of membrane coating based on cellulose polymers

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ABSTRACT

Background: The use of polymeric coating implants is a promising way of preventing adhesion disease and its related complications in the peritoneum. In this paper, the dynamics of degradation of new samples were studied in an in vitro experiment. A sample was then chosen which is potentially suitable for further research in an in vivo experiment.

Methods: In the research, 7 different samples of polymeric coating were studied viz. No. 81 MN, No. 82. MN, No. 83 MN, No. 84 MN, No. 85 MN, No. 86 MN and No. 87 MN - developed by Lintex, LCC (St. Petersburg) together with the department of Operative Surgery and Topographical Anatomy named after A.D. Myasnekov of Kursk State Medical University. The samples were differentiated by subjecting them to different technological processing of temperature, and chemical agents etc.

Results: In the course of the experiment, it was discovered that the rate of degradation of the polymeric coating implants depended on their processing methods.

Conclusions: Membranes that quickly undergo degradation cannot be used for prophylaxis of complications caused by surgical interventions.

Keywords: Degradation; Polymer; Implantology; Membrane; Film; Adhesion formations

INTRODUCTION

Postoperative adhesive disease (PAD) is a globally widespread condition. This problem first arose when surgeons began operating on abdominal organs, yet there has been no effective solution to it till date. PAD reduces the quality of life of many patients and leads to acute adhesive intestinal obstruction (AIO). The occurrence of relapse of the condition is 60-70%; acute AIO is the most common form of intestinal obstruction.¹ ² ³

Annual discussions among specialists about this problem in conferences and congresses, constant publications in periodic scientific literature with suggestions on prophylaxis and treatment of abdominal adhesion tell about constant interest in this problem.

We consider that the use of agents, which possess a barrier action, is the most optimal and pathogenetically substantiated way of preventing peritoneal adhesions. The use of a temporal barrier of polymeric resorbable implants gives us the most prospect of preventing peritoneal adhesions. The presence of a barrier agent,
placed in an area, where surgical operation has been done provides not only the optimal conditions for regeneration of the injured tissues and organs of the abdominal cavity but also, with the aid of hydrofloation, creates an interposition between the injured or inflamed peritoneal surfaces.

The use of polymeric barrier agents, particularly, in the form of membranes, helps to achieve a sufficient long and effective action.

Suggested prophylactic solutions to Postoperative Adhesive Disease- polytetrafluoroethylene (Prelude and Gore-Tex Surgical Membrane, W.L Gore Corp) - an insoluble membrane produced from thin sheets (0.1 mm) of stretched polytetrafluoroethylene with pores averaging less than 2µm, which is, non-adhesive and requires fixation to tissues with the help of sutures or staples and removal at a later period.

Sodium hyaluronic acid - a transparent and absorbable coating, which within a period of 7 days, separates organs and tissues nearby but easily breaks down when manipulated. Unfortunately, an effective choice of treatment and prophylaxis of PAD does not exist. The use of polymeric coating implants (PCI), which creates a temporal barrier between injured tissues, gives hope in attaining a significant clinical anti-adhesion effect.

The duration of dissolution of the polymeric coating implant is key to the separation of injured surfaces, and the prevention of scars and adhesions; thus, polymeric coating implant with a sufficient duration of dissolution, will achieve a clinical anti-adhesion effect.

Considering the results of our previous experiments as well as the results of the scientific findings of our colleagues published in literature sources, together with Lintex, LLC we produced a series of membranes with the aim of increasing the duration of degradation, and consequently, increasing the anti-adhesion effect.

The aim of this research is to study the dynamics of degradation of new samples of polymeric coating implants in an in vitro experiment and to conclude which samples have the best parameters.

METHODS

In the research, 7 different samples of polymeric coating were studied viz. No. 81 MN, No 82. MN, No. 83 MN, No. 84 MN, No. 85 MN, No. 86 MN and No. 87 MN - developed by Lintex, LLC (St. Petersburg) together with the department of Operative Surgery and Topographical Anatomy named after A.D. Myasneecov of Kursk State Medical University. The samples were differentiated by subjecting them to different technological processing of temperature, and chemical agents etc.

For comparative analyses, 60 equal parts with a size of 2x1cm from each of the 7 samples of polymeric coating implants were used. These were placed in 420 test tubes, each containing 25 ml of 0.9% NaCl solution, which corresponds to the normal average amount of free fluid in the peritoneum. The test tubes were kept in a thermostat at a constant temperature of 37°C.

In the course of the experiment, the implants were removed from the thermostat in correspondence with the established time criteria (1 hour, 1 day, 3 days, 7 days, 14 days, 21 days, 30 days and 60 days), and changes in their form and state were observed. After the removal of the coating membranes from the test tubes, the degree of degradation of the coating membranes was evaluated; and the thickness and mass measured; and the volume and density of the samples calculated using formulas. By a score scale developed by the authors, the degree of degradation of the implants was evaluated, taking into consideration the most significant changes (softening, thickening, fragmentation, physical state). The scale for the scoring of the dynamic changes of the qualitative parameters of PCI is presented in Table 1.

A statistical processing was carried out with the help of a program (Biostat). For comparison, Mann-Whitney U test was used; the critical value of significance (p) was 0.05.

RESULTS

Table 2 was drawn based on the developed point scoring system for the changes in the qualitative characteristics of PCI.

From this, the properties of the membranes of samples 82 MN, 83 MN, 84 MN and 85 MN remained stable throughout the experiment; softening was not observed. Elasticity and flexibility of the membranes were the same as the initial sample. Softening was observed in coatings 81 MN and 86 MN from the 30th day and 14th day respectively during the experiment. For PCI 87 MN, softening was noticed on the 14th day; and on the 30th day of the experiment, it had dissolved completely.

In the course of the experiment, thickening of the membrane in all the samples was observed which caused difficulty in identifying the most optimum sample. In spite of that, during the experiment a decrease in the thickness of PCI 87 MN was discovered, and on the 30th day it dissolved completely.

The physical states of samples PCI 82 MN, 83 MN, 84 MN, 85 MN were constant (in their solid state) throughout the experiment. From day 30, samples 81 MN and 86 MN underwent softening and acquired a gelatinous consistency. Sample 87 MN completely dissolved in an isotonic solution on day 30.

During the experiment, fragmentation remained a stable parameter for all the PCI samples. For 82 MN, 83 MN,
84 MN, and 85 MN, fragmentation was absent. Marginal destruction of not more than 30% of the area of the membrane was observed in 81 MN and 86 MN from days 60 and 30 respectively. Complete degradation was observed in 87 MN on day 30.

### Table 1: Point scoring system for the changes in the qualitative characteristics of PCI.

| Qualitative characteristics | Points and their characteristics |
|-----------------------------|----------------------------------|
| Softening (S)               | 0 point (the elasticity and flexibility reduced more than twice) |
|                             | 1 point (the elasticity and flexibility was not reduced more than twice) |
|                             | 2 points (the elasticity and flexibility of the membrane remained intact) |
| Thickening (T)              | 0 point (the thickness of the membrane reduced) |
|                             | 1 point (the thickness of the membrane increased) |
|                             | 2 points (the thickness of the membrane remained unchanged) |
| Fragmentation (F)           | 0 point (destruction of the membrane by more than 30% of the area of the membrane) |
|                             | 1 point (destruction of the edges of the membrane was not more than 30% of its area) |
|                             | 2 points (absence of fragmentation) |
| Physical state (P)          | 0 point (the membrane is in a liquid state) |
|                             | 1 point (the membrane is in a gelatinous state) |
|                             | 2 points (the membrane is in a solid state) |

Figure 1: Change in mass of the samples (mg).

Figure 2: Change in thickness of the samples (mm).

Figure 3: Changes in volume of the samples (mm$^3$).

Figure 4: Changes in density of the samples (mg/mm).
The results of the research showed that all the samples possess pronounced hydrophilic properties. The mass of the studied implants remained relatively stable till the 21st day of the experiment. The mass of the coating of 83 MN was more in comparison to other samples. On the 30th day, after PCI 81 MN was placed in an isotonic solution, the sample unevenly increased in mass. The mass of 87 MN reduced significantly on the 21st day; and on the 30th day, it underwent degradation. On the 60th day of the experiment, it was impossible to distinguish samples 81 MN, 82 MN, 83 MN, 84 MN, 85 MN and 86 MN from each other, as per the results of the experiment, they turned out to be identical.

**Table 2: Point scoring system for the changes in the qualitative characteristics of PCI.**

| Samples | Parameter | 1 hour | 1 day | 3 days | 7 days | 14 days | 21 days | 30 days | 60 days |
|---------|-----------|--------|-------|--------|--------|---------|---------|---------|---------|
| 81 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 1       | 0       |
|         | Thickening | 1      | 0     | 1      | 0      | 1       | 1       | 1       | 1       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 1       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 1       | 1       |
| 82 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Thickening | 1      | 1     | 0      | 1      | 0       | 1       | 1       | 1       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 1       | 2       |
| 83 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Thickening | 1      | 1     | 0      | 1      | 0       | 1       | 1       | 1       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
| 84 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Thickening | 1      | 1     | 0      | 1      | 1       | 1       | 1       | 1       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
| 85 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Thickening | 1      | 1     | 1      | 0      | 1       | 1       | 1       | 1       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
| 86 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Thickening | 1      | 1     | 1      | 1      | 0       | 1       | 1       | 1       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
| 87 MN   | Softening | 2      | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Thickening | 0      | 1     | 1      | 0      | 0       | 0       | 0       | 0       |
|         | Fragmentation | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |
|         | Physical state | 2   | 2     | 2      | 2      | 2       | 2       | 2       | 2       |

**DISCUSSION**

During the experiment, the values of the thickness of the polymeric implants constantly changed. On the 7th day, a significant decrease in thickness was observed in 85 MN, after it was placed in an isotonic solution. The values of samples 81 MN, 82 MN and 83 MN were high during the whole research. In the course of the experiment, it was discovered on day 60 that the membranes of 84 MN and 86 MN had undergone a reduction in thickness. Sample 87 MN had undergone complete degradation.

During the experiment, it was discovered that the density of the given samples remained relatively stable. Significant increase in density was observed in membranes 85 MN and 87 MN on days 7 and 21 respectively. On day 60, PCI 81 MN possessed the greatest density and 87 MN underwent complete degradation. The rest of the membranes: 82 MN, 83 MN, 84 MN and 86 MN had similar values. That is why distinguishing them from each other per the given values was impossible.

In the results of the research, a significant decrease in volume in implant 85 MN was observed on day 7 whereas an increase in 86 MN and 83 MN was observed. On day 60, the greatest values were of membranes- 81 MN, 82 MN, 83 MN, and 85 MN and the least, of
membranes- 84 MN and 86 MN. PCI 87 MN completely dissolved in an isotonic solution of Sodium Chloride.

In the course of the experiment, it was discovered that the rate of degradation of the polymeric coating implants depended on their processing methods. Membranes that quickly undergo degradation cannot be used for prophylaxis of complications caused by surgical interventions. This is because their quick elimination from the abdominal cavity would not allow a sufficient continuous action for achieving a clinical effect.

Slowly degrading coatings on the contrary have prospects for further use. That is why subsequent research must be directly aimed at studying them. Sample 87 MN underwent degradation on the 30th day, which is an ample time, for the attainment of a clinical effect for prophylaxis against the formation of adhesions.

Also, in the future, it would be necessary to carry out the research in an in vivo experiment to ascertain the duration of dissolution of the coatings in an animal organism; since peristalsis of the intestines, peritoneal fluid and cells of the macrophage system will facilitate degradations; and will also lead to a change in the duration of reabsorption.

CONCLUSION

1. It was deduced from the result of the comparative analysis that the physical and manipulative property of the coating membrane, depend on the method (temperature, chemical agents, etc.) and the length of the processing.
2. In relating to the results of the conducted research; from the standpoint of time for degradation, it was concluded that sample MN 87 was the most suitable for an in vivo experiment. This is because the sample dissolved on the 30th day; thus, the time for regenerative process coincides with the time of biodegradation of membranes in an organism.
3. There needs to be a further research in an in vitro experiment, to determine the duration of degradation for the polymeric coating implants of: 81 MN, 82 MN, 83 MN, 84 MN, 85 MN, and 86 MN.

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