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Intestinal Adhesions and the Use of Dressings and Bio-Resorbable Membranes as Prevention and Treatment

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Abstract

After surgery, intra-abdominal intestinal adhesions present a big problem that is not solved yet. The formation of adhesions begins at the moment when the discontinuity of the peritoneal integrity occurs and the endocrine metabolic response is initiated at a cellular level to repair the defect caused in the peritoneum's surface. However, preventing adhesions from forming in the abdominal portion is considered to be a correlation, from the moment of the execution of the techniques to the total recovery of the patient. Containment measures and the best healing of the tissue can be applied, such as; the use of bio-resorbable membranes and specific dressings emphasized in this analysis. Ensuring stability and a lower probability of the development of the tissular adhesion.

Introduction

Intraperitoneal Adhesions constitute an important cause of postoperative complications in patients undergoing abdominopelvic surgery, including infertility, intestinal obstruction, and chronic pelvic pain, making explicit a high potential for morbimortality [1]. Directly correlated to the intestinal microbiota and the correlation between the human tissues of healing, the abundant production of a fibrous repair tissue can be harmful to the intestinal tract since it causes abdominal chronic pain, a recurrent intestinal obstruction that requires multiple hospitalizations, and infertility [2]. Moreover, it can become a chronic disease with significant mortality and minimum perspectives of a cure.

In a general context, defined as “adhesions”, they can be developed in many areas of the human body, possessing many nomenclatures such as; intrauterine adhesion, pericardial adhesion, epidural adhesion, and peritoneal adhesion, the latter being more emphasized in this study. The postoperative adhesions are pathological peritoneal tissues that connect adjacent structures. Then, the physical properties of these tissues can vary significantly from a thin membrane of connective tissue to a thick fibrous structure that can contain blood vessels and nerves. Still, avoiding its formation is of primordial importance [3].

From the start of the incision, it is necessary to respect the caution and care with which the tissue and the rupture of its cells are handled, that is, specific cutting techniques are theoretically utilized with precision. Even the prevention in the act of the surgical cut alone does not guarantee that the adhesions cannot be eventually and periodically developed. In this regard, current methodologies that make use of biomaterials as a theoretical and practical foundation are based on the possibility of avoiding the friction between the tissues and the exacerbated inflammation, as well as the coagulation cascade and the production of fibers [4]

The biomaterials are generally active biochemical compounds that prevent intestinal adhesions such as; biofilms, hyaluronic acids, bio-resorbable membranes, hydrogels, natural films, and resorbable biofilms. Each classification has specific physical properties, being used in specific cases of cellular regeneration. In short, they can avoid the consequences of adhesions [5].

Methodology

The present study has a descriptive-discursive character, emphasizing primarily the intestinal adhesion’s theme, as well as a possible form of prevention and treatment through the usage of membranes and bio-absorbable dressings applied in a perspective of proof of activity in the human body, besides emphasizing concepts in physiology, anatomy, and Pathophysiology in general.

In this way, objective research was performed in the following databases; PUBMED, SCIELO,

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and Google Scholar. This article's bibliographical research made use of these terms; "Intestinal adhesions", "biological dressings" and "bio-absorbable membranes", without exclusion criteria, however, greater attention was given to the most recent papers due to their greater applicability.

Results and Discussion

Adhesion formation process

The peritoneum is a membrane that covers the cavity of the abdomen and its internal organs, which is composed of two layers: a parietal layer that covers the abdominal wall and a visceral layer that covers the organs. Adhesions occur after peritoneal trauma from damage caused by surgical interventions, abdominopelvic inflammatory disease, or infections, and can take form between the intestinal loops, as well as among other abdominal structures such as the liver and diaphragm [6].

In the surgical process, the skin is injured by a local incision, the tissue injury initiates an inflammatory response and the subsequent healing process, which stimulates the formation of fibrous tissue. Systemic coagulation results in fibrin deposits, which are a matrix for the development of fibro-collagen tissue and the formation of the extracellular matrix [7]. The trauma of peritoneal tissue and other intra-abdominal tissues results in a substantial compound rich in proinflammatory cytokines: Fibronectin, hyaluronic acid, glycosaminoglycans and proteoglycans, and various cell types: Mesothelial, macrophages, neutrophils, lymphocytes, and fibroblasts. These, exhibit activation of the coagulation cascade, and a fibrin mesh forms, eventually reabsorbed or matured into an adhesive connection between surfaces [8]. The process of formation of intestinal adhesion is explained in Figure 1.

Thus, postoperative adhesions are a consequence of abnormal peritoneal healing: The lack of early postoperative fibrinolysis (in the first 48 h) allows cellular infiltration of the initial fibrinous matrix. Around the seventh day, the adhesions are composed of a collagenous extracellular matrix infiltrated by fibroblasts, smooth muscle cells, and neovascularization; this group is covered by a mesothelial covering [9].

Surgical treatments and techniques

Treatment can be challenging and often involves a multidisciplinary approach, including the use of medication, physical therapy, endoscopic interventions, and in some cases, surgery. In the case of intestinal obstructions caused by adhesions, initial treatment may include the use of medications to control pain and symptoms, as well as nasogastric tube feeding to reduce pressure on adhesions [10].

Removal surgeries can be a complex procedure, the adhesions often can be dense and deep, involving multiple layers and scar tissue formation. Delicate manipulation of the tissue should be fully performed using meticulous hemostasis, choice of sutures of small caliber, frequent irrigation of the dissection area to prevent the formation of fibrinous deposits, minimal use of monopolar electrocautery to prevent diffuse thermal injury, maximum resection of devitalized tissues, removal of fibrinous residues, and blood clots before peritoneal closure [11].

In this regard, techniques can be used at the last stages of the surgery to aid healing in the best way possible, such as containment barriers or tissues that allow better fixation between human tissues. An ideal barrier must possess certain properties: Biodegradability and biocompatibility properties, so a second surgical procedure is not required to recover it. Also, the area of the lesion must be accurately identified and covered completely, the barriers are difficult to apply due to the complex geometries of the abdominal cavity, however, the surgeon must apply the barriers manually and uniformly [12].

Biomaterials in general

Biomaterials, bio-membranes, and tissues are technologies that can be used as treatment and prevention of body adhesions; however,

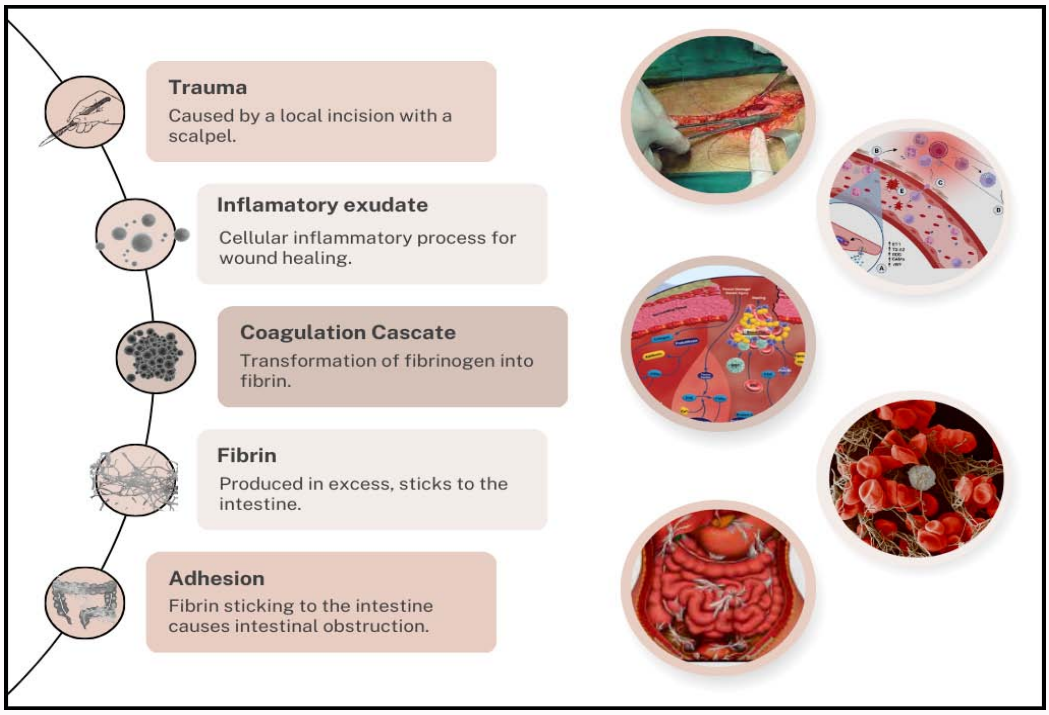

Figure 1: Process of formation of intestinal adhesions.

they have specific factors for distinct cases. Biomaterials have been studied as an option to prevent and treat intestinal adhesions. These materials can be used as a physical barrier to prevent the intestinal loops from joining during the postoperative healing process and improving intestinal function [13].

Hyaluronic acid and hydrogels

It is estimated that 93% of patients undergoing intra-abdominal surgery will develop some type of viscera-with-viscera or viscera-with-abdominal wall adhesions, the estimated risk being 60-90% in gynecological surgeries, thus consequently becoming one of the main causes of secondary infertility and chronic pelvic pain. Barrier intermediates that use hyaluronic acid and hydrogels are appointed as a method of prevention, avoiding the occurrence of adhesions. These barrier intermediates reduce the development of adhesions by disassociating the peritoneal areas injured during mesothelial restructuring, which is completed at around the eighth postoperative day [14].

Hyaluronic acid is a protein that is naturally present in the human body, with anti-inflammatory and antioxidant properties and its applications are on-site during the surgical procedure or in the gel after the closure of the incision. The most common formulas of pharmacological agents containing hyaluronic acid and hydrogels found in the pharmaceutical industry are Intergel, Hyalobarrier gel, ACP gel, Sepracoat, and Seprafilm, which is a promissory non-stick barrier that is formed by the biopolymer and carboxymethylcellulose [15].

An *in vivo* test performed in rabbits demonstrates the very high efficienc of the use of hyaluronic acid, effective in reducing the formation of intraperitoneal postoperative adhesions. It was demonstrated using a model of cecum abrasion with a defect in the side wall of a rabbit. This became particularly clear when comparing the prevalence of score 3 adhesions (firm and difficul to cut). In untreated rabbits, 8 out of 10 developed adherences, however, in rabbits treated with acid, only 2 in 8 developed adherences, confirming a high success rate and a possible treatment alternative [16].

In addition, Seprafilm (a chemically based on hyaluronic acid) demonstrates a remarkable reduction in the severity of adhesion formation after application in patients undergoing the Hartmann procedure. Particularly, in the case of planned relaparotomy, as in Hartmann's procedure, the application of Seprafilm can facilitate re-exploration and may reduce the risk of damage to the intestine during surgery. Therefore, the use of Seprafilm as a non-stick barrier is considerably effective [17]. As in the hydrogel of Hyaluronic Acid (HA), the application of HA gel reduces the number of organs involved in the formation of adhesions in an ischemic bud, moreover, the polarization of macrophages is associated with the formation of adhesions [18].

The using of several types of gels is a good option for preventing intestinal adhesions. Adhesive-capable hydrogel barriers can reach the physical isolation of the adjacent tissues and therefore are considered an ideal solution. Nevertheless, integrating the convenience of endoscopic delivery and viscoelastic hydrogel formation remains a major challenge [19]. The efficac of anti-adhesion in an *in vivo* model revealed that the hydrogel effectively separated itself from the wounds of the abdominal wall and cecum. In the seventh post-surgery, the wounds were completely covered by a new epithelial layer, while the wounds in the negative control group were glued [20].

Biofilm and resorbable bio-membran

Biofilms and resorbable biomembranes are a kind of covering and have been studied as an approach to reduce the risk of complications and susceptibility to long-term bacterial infections. These materials are made of biocompatible polymers and, are designed to be absorbed by the body after a certain period, they can also be programmed to release compounds that help reduce inflammation. These can be constituted of various biomaterials, such as collagen, cellulose, acids, and fibers among others [21].

A barrier membrane composed of hyaluronic acid can separate the peritoneal surfaces for about 7 days. The efficac of these membranes in reducing intra-abdominal adhesions after fibroid enucleation and colectomy has been investigated and verified in the scientific literature. A study conducted by Brüggmann et al. analyzed the use of the barrier membrane as the only preventive measure against occlusion related to small bowel adhesion after intestinal resection. They found that the membrane resulted in an absolute reduction of 1.6% and a relative reduction of 47% in the occurrence of this complication [22].

Another type of adhesion barrier, which can be applied as a spray, comprises a pair of polyethylene glycols in a two-component system. The barrier is sprayed on the injured serous surfaces and seals them for 7 to 14 days. Its effectiveness in an *in vivo* study reached 83% of effectiveness [23]

Using a resorbable collagen membrane, a prospective multicenter study points out that the removal of the gastric band without the use of a nonstick product was correlated with a higher rate of postoperative adhesions (90.3% including 29% of severe adhesions), while a highly significant reduction (89.9%) was observed in severe adhesions using the bio-membrane [24]. The effects of three electrospun fiber membranes on the formation of postoperative adhesions in surgical models of rats were studied, and submitted to laparoscopy, and the results were positive. The three electrospun submicrometric membranes were soft, flexible, easy to handle, and effectively reduced adhesion formation in rats [25].

Resorbable microbiological dressing

The microbiological dressing is a technology in development, in which its most recent studies include the use of beneficial microorganisms such as probiotics and lactic acid bacteria, assisting the rearrangement of the intestinal microbiota. Probiotics are living microorganisms that can be found in food or dietary supplements and that provide health benefits, especially for the digestive system. The lactic acid bacteria, for instance, are a type of beneficial microorganism that can be found in some types of food, such as yogurts and kefir, that promote resistance to colonization by pathogens. In this regard, microbiological techniques can be used as a method of prevention and postoperative care [26,27].

Bacterial cellulose within biomedical engineering is considered one of the ideal possibilities for its biocompatibility and possible applications within various prototypes of dressings such as nanocomposites, due to its properties of skin protection, blood coagulation, and healing. The use of implantable dressings to physically block surgical wounds is the main solution to prevent postoperative adhesions. Thus, the synergy between practicality and the high tissue recovery rate shows the method's effectiveness. As mentioned earlier, collagen and hyaluronic acid are great compounds that aid in the correct healing process of tissue. However, not only

bioactive can produce them, but specific bacteria can produce collagen and tissue activation properties [28].

The production of cellulose through bacteria is done by a metabolic process, directly correlated to cellular multiplication. Primarily, the metabolism is activated after the consumption of nutrients, usually, glucose and sucrose, which initiate the metabolic process in the pentose phosphate cycle and the Krebs cycle, resulting respectively in the oxidation of carbohydrates and oxidation of organic acids. In this regard, the synthesis of bacterial cellulose is the product of metabolic reactions of hexoses phosphate based directly by phosphorylation of exogenous hexoses and, indirectly, by the pentoses and gluconeogenesis pathway involving various biochemical reactions, which are regulated by a high number of enzymes and regulatory and catalytic protein complexes. Bacterial cellulose can be biosynthesized by several species of bacteria belonging to the genera: *Acetobacter*, *Achromobacter*, *Aerobacter*, *Agrobacterium*, *Alcaligenes*, *Azotobacter*, *Escherichia* and *Komagataeibacter* [29].

With the use of bacterial cellulose, with collagen properties, the dressing can be further enriched by vitamins and acids. Its effectiveness rate is usually higher than ordinary membranes, due to its high metabolism. However, its production is not yet fully feasible due to the complexity of the methods [30,31]. Also, the resorption of the dressing can be used in the final surgical moments, or be applied in a superior way to the skin with the addition of antimicrobial factors, which can also be applied to the dressing, ensuring that infections can hardly occur.

Conclusion

In summary, efficien methods to prevent and treat painful intestinal adhesions, such as dressings and bio-membranes, demonstrate full capacity on aiding in tissue regeneration. Moreover, active compounds such as hydrogel and hyaluronic acid can be great helpers. The combination of bioactive and membranes can be even more revolutionary. In general, new technologies can still be developed and fully applied, avoiding adhesions and promoting better postoperative quality.

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