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mini-review

Topical hemostasis in laparoscopic surgery

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SUMMARY: **Topical hemostasis in laparoscopic surgery.**

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A major goal during any surgical intervention is minimization of blood loss, which reduces the need for blood transfusion.

In open surgery, the possibility for the surgeon to use the hands directly in contact with the bleeding tissues for hemostasis, makes mechanical methods, such as compression, ligatures or sutures, important to achieve proper hemostasis.

In laparoscopic surgery, where the intervention is performed by means of small incisions through which the surgeon's hand cannot directly achieve the tissues, the problem of hemostasis is critical and needs more attention.

Either in open or in laparoscopic surgery, significant bleeding during surgery is controlled through vessel ligation, suturing, and electrocautery. Topical hemostatic agents are useful adjuncts to surgical hemostasis for controlling non-specific bleeding. The introduction of different devices and topical agents has made possible to perform more complex interventions also in laparoscopy.

The Authors discuss about the type, the field of application, the side effects of the hemostatic devices and of the topical hemostatic agents.

KEY WORDS: Hemostasis - Laparoscopic surgery - Topical hemostatic devices.

Introduction

Control of hemostasis in surgery is a key target for the success of the surgical intervention and also for reducing either the complications or the risks due to possible adverse side effects of blood transfusions. In open surgery, the possibility for the surgeon to perform hemostasis using the hands directly in contact with the tissues, makes mechanical methods, such as compression of the tissues, ligatures or sutures, important to achieve proper hemostasis.

In laparoscopic surgery, where the intervention is performed by means of small incisions through which the camera and special instruments (but not the surgeon's hands) are introduced and manipulated from the outside, more attention has been put on the problem of hemostasis since control of the hemostasis is more challenging. Therefore, the introduction of different devices and topical agents has made possible to perform more complex interventions in laparoscopy.

Hemostatic devices and topical agents in laparoscopic surgery

Surgical approaches to hemostasis in the 21st century have evolved in response to increased recognition of transfusion's dangers, increased surgical complexity, and an expanded armamentarium of tools to stop blood loss.

Since the introduction of laparoscopic surgery in the late '90s, it soon became necessary to develop new systems of hemostasis, in order to overcome the lack of manual hemostasis.

The characteristics for hemostatic devices should be the efficacy, the clinical safety with minimal side effects, and a beneficial relationship between cost and benefit, with the potential to decrease transfusion- and bleeding-related complications.

Many of the aids introduced in the laparoscopic era have successively found wide application even in open surgery. Some of them are widely used and easily available in all operating rooms. Among these, Ultracision,

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laparoscopic staplers and Ligasure are the most common.

Mechanical techniques such as stapling, clipping, and electrocautery have been used for hemostasis for many years and are the mainstay of surgical hemostasis today.

Ultracision is a very useful tool for hemostasis that uses ultrasound to generate a locally hemostatic energy to control and seal medium/small size vessels. Ligasure is also a very useful tool and, compared to the older generation of Ultracision, allows hemostasis of larger size vessels. The new generation of Ultracision seals vessels up to 7 mm. Another very useful tool for the hemostatic control of large vessel in laparoscopy is the endoscopic stapler.

Biologic hemostatic adjuncts were first developed beginning around the 1940s and continue to be improved. These products, which can be also used in laparoscopic surgery, may be classified as topical hemostats, sealants and adhesives. Hemostats clot blood. Sealants create sealing barriers. Adhesives bond tissue together. Table 1 summarizes the topical hemostatic agents used in surgery.

Topical hemostats and sealants are indicated in surgery for improvement of hemostasis, to promote tissue sealing and for suture support when traditional methods (mechanical, thermal and chemical) are ineffective or not practicable. They can be divided according to the nature of the material (derived animal, human, vegetable and synthetic), the mechanism of action and the class of membership. Concerning the latter criterion, some belong to the class of drugs (Beriplast, Quixil, Tachosil, Tisseel, Tissucol), while others to the medical devices (Floseal, Syvek, Tabotamp, Curaspon, Coseal, Glubran, Dermabond, Histoacryl). The mechanism of action is different between drugs and medical devices. The first ones (consisting of human thrombin, factor XIII and fibrinogen, bovine aprotinin, fibronectin, and tranexamic acid) reproduce the last phase of coagulation, namely fibrinogen under the action of thrombin is transformed into fibrin monomers, which polymerizes into a fibrin clot by means of the action of factor XIII. The latter provide a mechanical barrier to bleeding.

The medical devices (consisting of matrix of collagen and bovine thrombin, polymers of cellulose backed with sponge, polymers and oxidized regenerated cellulose synthetic polymers, gelatin, synthetic polyethylene glycols, cyanoacrylates) instead act through a physical mechanism (so called "fibrin glue"). The clinical Literature highlights the use of "fibrin glues" for creating a stable network, for closure of fistulas, and for prevention of post-surgical adhesions (1). Fibrin glue is a sealant composed of a fibrinogen concentrate and thrombin solutions. Thrombin solutions are currently divided into two categories: commercial products and those created in the laboratory. Beriplast, BioGlue, Tachosil, Tissucol, Tisseel, Quixil are the most commonly used commercial products (2). Gelatin sponges are a protein mixture obtained from collagen (Spongostan or Surgifoam are diffuse products); the granules of gelatin, when saturated with blood, swell to form a mass which reduces physically bleeding. Oxidized celluloses are derived from cotton cellulose and are provided in sheets. In addition to the mechanical effects, the cellulosic acid facilitates hemostasis by denaturating blood proteins. The most commonly commercial agent used in this group is Surgicel (3).

Purified animal collagen, which was introduced in 1970, stimulates the local release of platelets and provides a mechanical interface for clotting. It has recently been incorporated with clotting factors like fibrinogen and thrombin in order to work with the body's natural clotting agents. Collagen is derived from bovine collagen; therefore, it contains a small amount of bovine serum protein, so it should not be used in patients who are allergic to this product. Collagen exists as sponges or in syringes. The most commonly used hemostatic collagens include Floseal, Syvek, Tabotamp e Curaspon. Others are also indicated for the sealing of tissue and the suture support (Beriplast, Quixil, Tachosil, Tisseel, Tissucol, Coseal and Glubran) (2).

Other devices include components such as sodium, silicon, aluminum, and magnesium oxides, which adsorb water from the blood, thus concentrating factors essential for clot formation.

Topical hemostats and sealants have become important tools of modern surgery due to their ability to significantly reduce bleeding complications. Key drivers

TABLE 1 - TOPICAL HEMOSTATIC AGENTS.

DRUGS	Reproducing the last phase of coagulation	Human thrombin, factor XIII, fibrinogen, bovine aprotinin, fibronectin, tranexamic acid	Beriplast, Quixil, Tachosil, Tisseel, Tissucol
MEDICAL DEVICES	Mechanical barrier to bleeding	Matrix of collagen and bovine thrombin, polymers of cellulose, polymers and oxidized regenerated cellulose synthetic polymers, gelatin, synthetic polyethylene glycols, cyanoacrylates	Floseal, Syvek, Tabotamp, Curaspon, Coseal, Glubran, Dermabond, Histoacryl

for new product developments derivate from the growing demand for minimally invasive procedures, the desire to reduce the number of transfusions and morbidity, and to optimize cost effectiveness.

Most topical absorbable hemostat products, such as fibrin sealants, are not very effective for severe bleeding, because the lack of sufficient adhesion strength allows forceful bleeding to throw the products away from the bleeding tissue when manual compression is released before achievement of full hemostasis. Therefore they are not indicated in such settings.

Alternatives in the form of hemostatic agents have been in use since the late 19th century and are, traditionally classified as solid preparations that mechanically stop bleeding by forming a seal, and liquid preparations that can facilitate the final stage of clotting by enhancing existing hemostatic mechanisms. More modern devices commonly integrate both approaches.

Currently available hemostatic pads are effective in treating oozing bleeds, but otherwise ineffective in more severe bleeding. The development of safe and effective hemostatic adjuncts is important to reduce the time required to achieve hemostasis, the bleeding intensities, and the incidence of bleeding-related complications. An ideal hemostatic adjunct has the potential to decrease the use of blood products in elective and emergency surgery, but must have the ability to manage hemorrhage from parenchymal, arterial, and venous structures. Such a product would require adhesive strength to prevent being carried away by flowing blood under pressure.

The combined use of topical absorbable hemostat products with standard hemostatic devices is more effective in brisk bleeding.

The use in laparoscopic surgery of some topical hemostatic devices, which are effective in traditional surgery, has recently been encouraged. An important and peculiar property that the topical hemostatic devices must have in laparoscopic surgery is its ease of use. However, their use in laparoscopic surgery is made difficult by the fact that the passage of the hemostatic patch through the trocar may result in its rupture, due to its fragility. In addition, when the hemostatic patch come prematurely into contact with blood or fluids, its subsequent manipulation in the bleeding site is altered. In fact, the patch must be applied carefully in the bleeding site and before being applied, must not come into contact with body fluids, otherwise its application is useless (3). To overcome the drawbacks of hemostatic patch's application in laparoscopic surgery, it is possible to roll up the patch on a clamp. It has recently been marketed a patch, the pre-rolled Tachosil, which has the advantage of an easy use, since the patch is already rolled up at the factory, ready to be inserted through the trocar. Tachosil is a development of TachoComb (NycomedLinz,Austria). TachoComb is made with equine collagen bovine thrombin, bovine aprotinin and human fibrinogen. TachoComb H contains human thrombin in place of bovine thrombin. Tachosil contains only human fibrinogen with equine collagen as a carrier. It does not contain aprotinin or any other component of bovine origin. It works by mimicking the final steps of the natural blood-clotting process, creating a fibrin clot at the surgical site to achieve hemostasis in 3-5 minutes. It consists of a collagen sponge coated on one side with fibrinogen and thrombin. The product is ready to use and do not need refrigeration or freezing, which represents an advantage when it has to be used quickly. This kind of product becomes active when the product comes into contact with bleeding or leaking tissue. Its use in laparoscopy has not become as popular as it is in open surgery, due to the exfoliation of the collagen compound during the passage via the laparoscopic cannula because of its fragility. When the product come into the abdominal cavity without its integrity, the fibrin-coated part is immediately activated and its manipulation becomes very difficult when it comes into contact with blood or fluid. The patch becomes unusable and another one should be inserted in the abdominal cavity (1).

Clinical applications in laparoscopic surgery

Ineffective local hemostasis is the major cause of bleeding during surgery.

Topical hemostatic agents are useful adjuncts to surgical hemostasis for controlling non-specific bleeding. The choice of the topical hemostatic agent depends upon the character, amount, and location of bleeding, the availability of a given agent, surgeon preference and cost considerations. For example, dry matrix agents are less useful when bleeding is brisk. Fibrin sealant and bovine albumin-glutaraldehyde tissue adhesive (eg, Bioglue) are appropriate choices when moderate bleeding does not respond to other measures.

Topical hemostatic devices find their specific use in case of bleeding from the peritoneal serosa, from parenchymatous organs'surfaces of section, from minimum bleeding next to important structures, such as, for example, the nerves, which are at risk of lesions by cauterization (1, 4).

In small districts, such as the pelvic cavity, in our experience the Ultracision is very useful. The ultrasound dissector can lead a bloodless section of the perirectal tissue and the mesorectum during laparoscopic left hemicolectomy. In our experience, the use of topical hemostatic devices, such as Tabotamp, is efficacious if oozing is present (5, 6).

As regards the control of hemostasis in laparoscopic hepatic resections, an extensive debate exists today in the Literature (7-9). It must be said that in the opinion of many surgeons, including us, the choice of topical hemostatic devices is conditioned by the intraoperative bleeding. The hemorrhagic circumstances can be divided into bleeding from large arteries, as part of the vascular surgery or in the event of accidental arterial injury, bleeding at the site of needle puncture, bleeding from section of parenchymal organs, or from parietal or visceral peritoneum lesions. In each of these circumstances, topical hemostatic devices find their application.

Clinical result supports the use of topical devices: patients operated on with major or minor hepatectomies with application of a carrier-bound collagen sponge on the raw surface of the liver, have a lower postoperative mortality, incidence and severity of postoperative surgical complications, and length of hospital stay. The duration stay, volume and content of the drainage are significantly shorter if the hemostasis is made by devices after liver resection (10). The fibrin sealant after liver resection is effective in decreasing drainage's volume, postoperative blood transfusion, complications and hospital stay (11). To facilitate the decrease of drainage output volume, a fibrin coat mimicking a Glisson surface on resected liver should be made by a fibrin sealant. As bile leaks are a frequent complication, Toti et al. have compared surgical complications in patients who had treated the cut surface of the donor liver with a patch, to those treated with fibrin glue. The results of the study showed that the fibrinogen collagen sponge patch may reduce bile leaks from the cut surface (12). Topical devices have also been used for life-threatening bleeding from a portal vein during open liver surgery. Toro et al. reported a case of massive hemorrhage in the area of the portal anastomosis, and hemostatic control was achieved by application of the fibrin sponge patch around the portal vein, with a slight finger pressure for several minutes. The patch should not be replaced or removed (1). We report the combined use of the main hemostatic devices during laparoscopic liver resections. Ultracision is the main instrument we use for parenchymal dissection, clips or hemlock are very useful to clamp major blood vessels or biliary vessels. Topical hemostatic devices with mechanical way of action stop the parenchymal oozing.

The fibrin pad demonstrated its safety and efficacy as an adjunctive hemostatic technique for mild-to-moderate bleeding in partial nephrectomy. Authors in the Literature also suggested that the product should not replace sutures or meticulous surgical techniques for the treatment of severe arterial hemorrhage (13, 14).

Benefits of devices application for spleen trauma or fragile damaged spleen or hematologic tumoral diseases and blood disorders have been reported in some studies (15-19). EndoGia is a very useful tool for the hemostatic vascular control of the splenic hilum. We use it during laparoscopic splenectomy, sometimes associated with a topical hemostatic device after having dissected the gastro-splenic, spleno-colic and spleno-diaphragmatic ligaments through Ultracision. In our series of more than 100 laparoscopic splenectomy performed also in thrombocytopenic patients, the control of the splenic hilum by stapler was optimal with insignificant postoperative bleeding (19).

Experimental clinical studies on sealing the colorectal anastomoses have been performed in order to reduce the rate of leakage, demonstrating good results using a fibrin glue-coated collagen patches in situations of adverse healing processes (such as peritonitis) (1, 20, 21). In our opinion, the use of topical sealing devices is efficacious in iatrogenic bowel lesions after suturing of the bowel wall.

Surgery for peptic ulcer perforation is common procedure today, with a high mortality risk (22). Omentoplasty by patch represents the treatment of choice. An experience on gastric wall repairing through a full thickness suture followed by collagen patch application and covered by the classic omental patch, has been reported in the Literature with good results (23).

Adverse effects and complications from topical hemostatic agents and tissue adhesives are generally uncommon. Complications related to thrombin-based agents, which are blood products, include the potential for transmission of blood-borne disease and anaphylaxis with the bovine-derived agents (1).

Therefore, we ask if there is an ideal hemostatic device, or rather the choice among different hemostatic devices has to be made on the basis of the type of bleeding, the tissue or organ involved, etc.

What matter the convenience and the quickness of use, especially in laparoscopic surgery? Is it more rational to have more topical hemostatic devices in the operating room or to have the best one, maybe more expensive, to use for all eventualities? The costs related to individual product would be in relation to effectiveness. Moreover, as regards the consumption of the individual product, an interesting observation comes from the comparison between the dosage units consumed and the cost per unit. The products with the highest cost per dosage unit usually have a lowest load, while those with lower cost have a greater consumption. In a context of growing expansion of the sector, it is crucial to have clinical information that will define both the profile of effectiveness and the cost of these products. This demand is stronger for products already approved as medical devices than drugs, because there are smaller clinical data and a high price. In conclusion, a product with optimal features but cheap is needed.

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