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Review Article

Surgical Glue: A Brief Overview

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Abstract

Wound closure is one of the cardinal steps of surgical procedure, and suturing is the most widely used method of wound closure. The process of suturing usually prolongs the length of surgery and increases the patient's risk of anesthesia awareness. It has several disadvantages, including iatrogenic trauma to the tissue, pain, increased risk of infection and inflammation, delayed healing, and inability to provide an immediate seal. Lately, there has been a growing interest in surgical glues as a substitute to suturing. However, surgical glues have their own unique disadvantages, which need to be addressed in designing "ideal" surgical glue.

Keywords: Surgical Glue; Hemostat; Sealant; Adhesive

Abbreviations

CSF: Cerebrospinal Fluid; CNS: Central Nervous System; FDA: Food and Drug Administration; PEG: Polyethylene Glycol; HLAA: Hydrophobic Light-Activated Adhesive; PGSA: Poly Glycerol Sebacate Acrylate

Introduction

Surgery (from Greek "hand work") is "the branch of medicine that relates to body injuries, deformities, and morbid conditions that require being remedied by operations or instruments" [1]. It typically involves cutting of tissues and closure of iatrogenic or traumatic wounds. The tissues that are closed can be static, such as skin, or dynamic, such as contracting myocardium. The environment can be dry, such as a bone, or wet, such as the lumen of a blood vessel. Traditionally, surgical wounds have been closed with a variety of sutures with different sizes, strengths, and compositions. Suturing typically achieves its intended goal of approximating the tissue at the wound site until the physiologic "seal" is accomplished, however it has disadvantages. The process of passing the needle can be traumatic and will cause additional pain. Often, it has to be removed and requires a second procedure. The suture tracts themselves can serve as conduit to secondary infections and necessitate antibiotic treatment, and the suture material can cause local tissue inflammation and delay healing. Although suturing is effective in approximating the edges of the tissue, it does not achieve immediate sealing of the wound and may be associated with prolonged bleeding [2]. Lastly, the process of suturing can be time-consuming and subject the patient to prolonged risk of anesthesia and increase the cost of healthcare. Therefore, with increasing popularity of minimally invasive surgery [3,4], which is not associated with large incisions, and advancement in chemical science, there is a growing need, application, and availability of surgical glues for different surgical subspecialties [5-10].

The currently available surgical glues, however, have shortcomings: they can be easily washed out under dynamic conditions; they can be toxic to the tissue; some are not strong enough; they can be difficult to reposition after initial application; and some can be destabilized by the presence of blood. There are a variety of surgical glues that have strong points (e.g. biodegradable, easy to handle, strength, suture-free, etc.), but there is no single ideal glue that addresses all shortcomings.

William D. Spotnitz provided a useful system of classifying surgical glues divided into groups and categories [11-14]. The groups are based on their purpose (hemostats, sealants, and adhesives) and categories based on their functional characteristics and mechanism of action.

The purpose of topical hemostats is to accelerate hemostasis by causing blood clot formation and it requires the presence of blood. The sealants stop leakage of fluid from tissue openings such as CSF from CNS, but the fluid does not have to be blood. The adhesives bond tissue together, such as a surgical incision wound.

It is notable that some agents can have multiple purposes, such as a fibrin sealant that can act as a hemostat, a sealant, and an adhesive. A significant number of surgical glues functionally depend on a physiologic coagulation cascade. Two of the essential components of the coagulation cascade are thrombin and fibrinogen. In the presence of calcium ions, thrombin cleaves the fibrinogen chains. The resulting fibrinogen monomers eventually polymerize and form a fibrin clot. These steps are independent of the coagulation pathway and can be reproduced artificially. The rate of the clot formation increases with thrombin concentration. The strength of the clot, on the other hand, depends on the concentration of fibrinogen.

Porcine gelatin, bovine collagen, oxidized regenerated cellulose, and polysaccharide spheres

These compounds work by creating a mechanical barrier and a surface to stop hemorrhage or accelerate blood clotting. Hence, they act as hemostats. They are relatively safe and easy to use. However, swelling and infection are drawbacks. Removal of the glue is recommended after achieving hemostasis to minimize side effects [6,15,16].

Bovine thrombin, pooled human thrombin, and recombinant thrombin

These compounds essentially provide concentrated levels of thrombin for rapid conversion of fibrinogen to a fibrin clot. They act as hemostats and can be effective in stopping both local and diffuse hemorrhage. They are relatively easy to use, but the side effects include

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Table 1: Summary of functions, strengths, and drawbacks of current surgical glues.

Glue #	Function	Strengths	Drawbacks
1	Act as hemostats	Safe and easy to use	Can cause swelling and infections
2	Performsimilar to hemostats	Safe and easy to apply	Antibody formation, plausible coagulopathy, and allergic reactions
3	Hemostat-like*via* fibrin clot	Easy to apply and more effective than 1 and 2	Similar to 1 and 2. Swelling, allergic reactions and infections
4	Hemostat, sealant, and adhesive	Very versatile, FDA approved, commercially available, and effective	Potential side effects are viral or prion disease, antibody formation, allergic reactions, and swelling
5	Moderately strong sealant	User friendly, low-cost, and biodegradable	Can cause significant swelling and not very effective on wet surfaces
6	Strong sealant and adhesive	User friendly and strong glue	Side effects are tissue necrosis and adhesive embolism
7	Strong adhesive	Readily available, easy to use, and instant bond	Limited to external use only and can cause foreign body reaction
8	Adhesive	Biodegradable, reduce dead space, and absorbed by the body	Increase surgical time for a few minutes. Not yet approved for sale or marketing in the USA.
9	Adhesive, used to seal defects in the heart and arteries	Strong and flexible, activated by UV light.	Promising adhesive. However, only animal models have been studied

antibody formation (bovine) that can lead to coagulopathy. Viral or prion disease may potentially be associated with pooled human plasma. Allergic reactions to hamster or snake protein are possible for recombinant products. More importantly, intravascular use of these products is counter-indicated [17,18].

Bovine or porcine gelatin with thrombin

These substances function both by creating a mechanical barrier and a surface to stop hemorrhage or accelerate blood clotting and by providing concentrated levels of thrombin for rapid conversion of fibrinogen to a fibrin clot. They act as hemostats. It appears that this combination is more effective than the individual categories. The advantages and the potential side effects are similar to those of individual ingredients discussed above [19].

Fibrin sealant

Fibrin sealant is the most versatile substance. It is approved by the FDA as a hemostat, sealant, and adhesive. The use of fibrin was first recognized in 1909 [20]. The first commercial fibrin sealant became available in Europe in 1972, and the FDA approved it in the United States in 1998 [21]. Human plasma-derived fibrin sealants are now commercially available.

Fibrin sealants are mainly comprised of fibrinogen and thrombin. They reproduce the cardinal steps of the physiologic coagulation cascade. Given that they supply both thrombin and fibrinogen, they do not depend on active bleeding for the source of fibrinogen [22,23]. The concentration of each component varies between different manufacturers. The fibrin sealants are most effective when applied to a dry surface. The potential side effects include viral or prion disease, antibody formation, allergic reaction, and swelling. The fibrin sealants are dependent on an intact coagulation system.

Polyethylene glycol (peg) polymer

This is a synthetic material and can be used as a moderately strong sealant. It is user-friendly and is most effective when applied to a dry surface. Polymerization takes approximately one minute. A major disadvantage is significant swelling [24].

Albumin and glutaraldehyde

This is a bovine serum albumin cross-linked with glutaraldehyde. It can be used both as a strong sealant and as an adhesive. It is user friendly, but there are several possible side effects, including tissue necrosis and adhesive embolism [25,26].

Cyanoacrylate

This is a synthetic product and is used as a strong adhesive. It is limited to external use only. Therefore, it should not be applied to deeper skin layers and has a limited value as a sole method of closing the skin. This product is readily available and is user friendly. The individual products in this category have varying viscosity that can be helpful to the surgeon. However, great care should be taken to avoid an inadvertent application of this adhesive to an unintended area. Cyanoacrylate can be associated with foreign body reaction and a sensation of warmth [27,28].

Lysine-derived urethane adhesive

This adhesive acts to bond together tissue layers, thereby reducing dead space. This is particularly relevant after certain surgical procedures such as abdominoplasty. A recent study demonstrated a decreased rate of seroma formation and fluid drainage following abdominoplasty when the adhesive is utilized. This adhesive is biodegradable and over time is absorbed by the body through hydrolysis [29].

Hydrophobic light-activated adhesive (HLAA)

This adhesive is based on polyglycerol sebacate acrylate (PGSA). It is a thick gel that is applied to a tissue and then cross-linked within seconds by ultraviolet light. The resulting bond is strong but flexible. Hence, it sustains under high pressure and flowing blood. It can potentially be used to seal defects in the heart and arteries, but so far, the testing has been limited to animal models [30].

Discussion

With an increased awareness of benefits of fast post-operative recovery and cost-effectiveness of surgical procedures, the role of surgical glue becomes increasingly more relevant. Presently, there are a myriad of surgical glues. However, they have limitations to their safety and usability. An ideal surgical glue must be safe, functional under dynamic or wet conditions, biodegradable, self-sufficient, flexible, fast drying, user-friendly, resist high pressures, and inexpensive.

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