Study on the application of embolization materials of collagen

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Abstract. The embolization mechanism, advantages and disadvantages as well as clinical application of collagen embolization materials were retrospectively analyzed, and the correlation between their application fields and the selection of embolization materials was discussed, so as to provide references for clinical treatment. Relevant literatures in Pubmed and Web of Science databases were searched, and the literature on clinical application and experimental research of emboli c materials was systematically evaluated. Embolic materials should be biodegradable and biocompatible. Embolic materials for clinical use include absorbable gelatin sponge, polyvinyl alcohol particle embolization agent, micro-spring coil and liquid embolization materials. Gelatin embolization materials have the advantages of non-antigenicity, histocompatibility, convenient preparation, excellent compressibility and expansion in water. Endovascular embolization materials have been produced and applied in clinical practice, but new problems and new requirements have been rising. All kinds of embolic materials have advantages and disadvantages, and none of them can be suitable for all diseases. Therefore, it is very important to select suitable embolic materials for safe and effective treatment.

1. Introduction

In recent years, with the promotion of endovascular embolization technology, embolic materials play an important role in the application of endovascular embolization [1, 2]. However, all kinds of materials have their own advantages and disadvantages. With the development of biological materials, how to choose suitable embolic materials is the focus of the current research, which is very important for safe and effective treatment.

The properties and applications of various bioembolic materials will be reviewed. Endovascular embolism has the characteristics of small trauma, strong repeatability, accurate positioning, high efficacy, quick response, low complications, and the combined application of various technologies. Vascular repair through endovascular embolization is the best cure [3, 4]. Instruments used during embolization include catheters and guidewires. Catheters include angiographic catheter, microcatheter, such as microcatheter for intracranial artery, microcatheter for peripheral artery interventional therapy, etc. Guidewires used to guide the catheters insist in selective or super-selective intubation, which can effectively protect the vessel wall and catheter head from damage. In embolization therapy, guide wire is often used to guide the catheter to the target vessels for corresponding treatment. In order to achieve transcatheter injection and vascular embolization, appropriate micro catheter is needed to complete the
embolization. In addition, the good characters of the material, killed operation of the doctor, video monitoring equipment are all factors affecting recanalization. However, embolism materials can be absorbed, but it also can cause serious damage to target if vascular embolization materials are not suitable. The choice of embolic materials is an important factor in embolization therapy [5].

2. Absorbable embolic material gelatin sponge

2.1. Advantages
The absorbable embolic material gelatin sponge is a biodegradable intermediate embolic material in vivo, which is not only a kind of collagen, but also a kind of macromolecular biological material [6]. Gelatin sponge is a spongy solid preparation made of gelatin liquid after foaming, curing, freeze-drying and sterilization. It has good histocompatibility, blood compatibility, biodegradability, weak antigenicity and biological safety requirements, making it an excellent embolization material [7]. It can be cut into small pieces according to the size of the target blood vessels, small strips or 1.0-2.0mm particles into 2-5 mL syringe, its characteristics are compressibility, reexpansible, non-toxic no antigen, low price, simple preparation, easy to inject, reliable embolization, generally 1-3 weeks absorption. Collagen is the most abundant and widely distributed protein in animals. Collagen has unique triple helix structure, low antigenicity, non-toxicity, good biocompatibility and biodegradability, etc. [8-10]. Cellulose oxide ACTS like a gelatin sponge [11].

2.2. Disadvantages
At present, the collagen used in China mainly comes from the skin and Achilles tendon of pigs and cows. The preparation of gelatin sponge from the residual system of rana chensinensis can promote the comprehensive utilization of rana chensinensis and increase the added value of rana chensinensis [12]. Fish scales and skin about more than 40, ten thousand tons of waste of aquatic products, such as the waste of aquatic products are rich in collagen protein, its amino acid composition and terrestrial mammal collagen there was no significant difference, and it does not exist zoonotic infectious disease, development and utilization of great value, develop skin and other aquatic products waste using new approaches, not only can improve the added value of aquatic products processing, and can reduce the pollution of the environment, has the good economic and social benefits. Angiography was performed before the use of gelfoam to understand whether the blood supply artery and intubation route of the lesion have relevant collateral circulation [13].

3. How to select the suitable materials
Superselective intubation was performed according to the standard technique, and the position of catheter insertion should be as close as possible to the treatment site to prevent embolization of normal vessels. Particles of appropriate size are selected according to the condition of the lesion, and improper selection of particle size may lead to particles entering the blood supply artery of the normal tissue or entering the outflow vein of the lesion [14]. Appropriate amount of low concentration contrast agent (usually 30%-40%), ionic type such as dimeglutamine or non-ionic type such as iopromide, triiodotriamide hexanol benzene mixed with gelatin sponge particles make a uniform suspension with appropriate concentration, there shall be no foam. The suspension is inhaled into the syringe with appropriate concentration and fine particle suspension. If the suspension is too thick, the catheter can be blocked and it should be avoided.

3.1. Possible interactions with other materials or drugs
Under angiographic fluoroscopy, gelatin sponge particle suspension was injected through the catheter at an appropriate rate without reflux, otherwise it might enter the non-embolic artery and cause ectopic embolism, thus leading to tissue and organ necrosis [15]. The gelatin sponge particles were continuously injected until the results were satisfactory. Gelatin sponge is one of the most widely used embolization materials at present, which is suitable for embolization treatment of various hemorrhagic
tumors and certain vascular malformations due to its safety, non-toxicity, easy sampling and convenient use [16]. However, as biomedical materials, aquaculture collagen and terrestrial mammal collagen have common disadvantages, such as fast degradation in vivo and poor flexibility, which limit its application.

3.2. Programmed preparation
Glutaraldehyde as a crosslinking agent can also increase the mechanical strength of collagen medical materials and slow down its degradation rate in vivo. Chitosan was added to gelatin to make a sponge preparation that can stop bleeding, promote the growth of granulation tissue and accelerate wound healing [17]. However, it has its own disadvantages.

It is non-permanent occlusion, and usually begins to be absorbed within 14-19 days after vascular embolism. It may be completely absorbed after 3 months, and it is easy to form recanalization. In addition, gelfoam should not be used in patients with difficulty in super-selective intubation, small arterial particles, larger arteriovenous fistula than particles, and patients requiring permanent embolization, etc. [18].

Stent implantation is a common way to treat patients with cardiovascular diseases, which are serious threats to human health. Conventional metal stents are mostly used in the past, and there are some hidden dangers for the metal stents that remain in the blood vessels when they are effectively treated [19]. The blood vessels will contract and relax regularly. If the blood vessels are always supported by the scaffold, the blood vessels will become stiff and lose elasticity, leading to various adverse reactions. For example, the vessel at the stent site lost its elasticity, vascular restenosis, thrombosis, etc., and affected the patient's subsequent surgical bypass [20]. In recent years, new stent has been developed. The advantage of the new scaffolds is that they are fully biodegradable and are mainly made of naturally biodegradable materials. After the implantation of blood vessels into the human body, after the treated blood vessels have healed and no longer need the support of the scaffold, the scaffold can be continuously degraded over time and eventually disappear completely. Magnesium and its alloys have excellent mechanical properties and biocompatibility [21]. The scaffold has the unique advantages of strength of metal scaffold and bioabsorbability of degradable polymer scaffold. Due to the special microenvironment inside the blood vessels, the stent should have good corrosion resistance.

4. Conclusions
The first generation of blood compatibility materials has experienced a history of more than half a century, and so far it has not been able to truly meet the clinical requirements. A variety of factors affect the blood compatibility, because of the complex changes of coagulation mechanism, material surface characteristics. How to modify the material become an important way to improve the blood compatibility. Currently, there are still some problems in the existing evaluation system. How to select effective materials and how to quantify the evaluation results have become important directions for improving blood compatibility.

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