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Review

Glue for superficial venous ablation

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ABSTRACT

Introduction: Varicose veins of the leg are a common clinical presentation. Management has progressed from open surgery to minimally invasive techniques. This paper reviews the introduction of minimally invasive cyanoacrylate ablation.
Methods: Medline and EMBASE were searched using combined search terms 'cyanoacrylates', 'varicose veins', 'varicosis', 'vein' and 'animal'.
Discussion: Cyanoacrylate is commonly used as an embolising agent in various anatomical locations. Its use is expanding and animal studies have demonstrated promising results for use in superficial venous ablation. Human studies are currently small but also demonstrate positive results with few complications or side effects.
Conclusion: Larger observational studies are required to demonstrate efficacy and future randomised controlled trials are required to directly compare venous treatment methods.

Contents

Introduction

Varicose veins of the legs are a common clinical presentation, with a reported prevalence as high as 56% in men and 60% in women [1]. The management of venous varicosities has progressed over the years and now includes a range of treatment options. Open surgery (high ligation and stripping of the long saphenous vein) is still frequently performed but minimally invasive techniques have become increasingly popular. Such techniques include ultrasound guided foam sclerotherapy and the endovascular treatment methods radiofrequency and laser ablation. Each has been shown to be clinically effective [2–6] but minimally invasive techniques have the additional benefit of avoiding general anaesthesia and a short duration of treatment.

This paper reviews the introduction of a new minimally invasive endovenous method for the treatment of varicose veins, the use of cyanoacrylate glue to achieve venous ablation.

Methods

Medline and EMBASE were searched using combinations of the search terms 'cyanoacrylates', 'varicose veins', 'varicosis', and

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Table 1
Summary of 30 and 60-day swine results.

	Swine 1		Swine 2	
	L SEV	R SEV	L SEV	R SEV
30 Day results	Dilated lumen with entrapped lytic erythrocytes. Tunica intima replaced with eosinophilic matrix, disrupted with histiocytes and multinucleated giant cells. Inflammation extends to tunica media and adventitia.		Histologically similar to swine 1. Narrowed lumen due to inflammation and fibrosis.	Similar histological changes to swine 1.
60 Day results	Complete vessel occlusion. Inflammatory cells and fibrous tissue. 1 Section: fibrotic projections that occluded nearly entire lumen. Segmentally thickened wall and dilated lumen with clear spaces containing debris, microphages and spindle cells. Spindle cells replaced tunica intima. Multinucleated giant cells present. Vessel wall disrupted by histiocytes and lymphocytes.	Analogous histological appearances to L SEV. 2-Side branches not injected with CA and remained patent.	Complete vessel occlusion. Similar histological changes to those found in swine 1. R SEV: 2 patent side branches.	

SEV = superficial epigastric vein; CA = cyanoacrylate; L = left; R = right.

'animal'. This returned 124 independent search results. Fifteen were appropriate for inclusion. References from accessed articles were included when of relevance to the review topic.

History of cyanoacrylate

The adhesive properties of cyanoacrylate polymers were first appreciated in 1951 during a search for tough, heat-resistant materials for use in jet plane canopies [7]. Since their discovery, cyanoacrylates (commonly known as 'superglue') have had diverse applications. Their use for medical therapy has gradually increased and they are now used to treat bleeding gastric varices [8] as well as an embolising agent for the treatment of arteriovenous malformations [9,10]. There is increasing evidence that cyanoacrylates may be a suitable medium for the treatment of peripheral varicose veins [11–14].

Histopathological behaviour

Cyanoacrylate compounds undergo polymerisation when in contact with ionic solutions or endothelium [15]. This causes an inflammatory reaction within vessel walls, which subsequently leads to vessel occlusion [10–12,16,17].

It is the process of polymerisation that gives cyanoacrylates their strength. The mechanics are incompletely understood. Kailasnath and Chaloupka [18] sought to further clarify the tensile properties of cyanoacrylates used for medical purposes. They found that polymerisation is a three-stage process. The first lasts no more than 10 s as is characterised by a linear increase in tensile forces. This is followed by a longer period of almost constant force, which lasts approximately 1 min before the third phase of complete polymerisation occurs, marked by an exponential rise in tensile forces. The rate of polymerisation can be prolonged with the addition of acetic acid [19,20] or ethiodised oil [11]. Modifying the polymerisation rate is essential for clinical use to ensure safe and accurate delivery of the cyanoacrylate medium to an area of required vessel occlusion [19,21].

Only a few studies have examined the histopathological behaviour of cyanoacrylate within veins [11,12,17,22]. Suga et al. [22] sought to establish the behaviour of n-butyl-cyanoacrylate within a varix. The results are limited, as only a small proportion of the experiments were conducted in animal vein. The initial experiment found that cyanoacrylate had similar adhesive properties in both canine vein and specially designed vinyl tubing of similar dimensions. For this reason, all subsequent investigations were conducted in vinyl tubes. Nevertheless, some important considerations are raised. They found that 0.7 mL of cyanoacrylate could occlude flowing blood in a vessel of up to 0.4 cm in diameter with a flow velocity of 20 cm/s. There was little benefit in slowly injecting the cyanoacrylate as this resulted in more fragmented polymer masses and a less complete occlusion.

Wang et al. [17] studied the histopathological vascular changes within arteries and veins injected with cyanoacrylate. They found similar changes in both vessel types with the exception of the arteries expressing hyperplasia and elastic fibril formation at 2 weeks, whereas the veins underwent tissue necrosis. Both vessel types were completely occluded and underwent an initial acute necrotising vasculitic reaction that progressed to chronic inflammation and tissue fibrosis. Histological analyses in other studies have shown that these changes are confined to the vessel lumen and do not extend to involve surrounding tissue and parenchyma [23,24].

Animal studies

To date, two studies have directly investigated the ability of cyanoacrylate adhesive to ablate truncal veins in an animal model. They report 30 [12,25] and 60-day [11] results following injection into swine vein.

The two studies used identical methods. The right and left superficial epigastric veins (SEV) were injected with a proprietary