A new injectable radiopaque chitosan-based sclerosing embolizing hydrogel for endovascular therapies

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Endovascular repair of abdominal aortic aneurysms with a stent graft is limited by the persistence or recurrence of endoleaks. These are believed to be related to the recanalization of the aneurysmal sac by endothelialized neochannels, which could lead to late type I and II endoleaks. Embolization has been proposed to treat or prevent endoleaks, but presently commercialized embolizing materials have several drawbacks and do not fully prevent endoleak recurrence. A novel chitosan hydrogel that is injectable, radiopaque and contains sodium tetradecyl sulfate (STS), a well-known sclerosing agent, was developed in order to combine blood flow occlusion and endothelium ablation properties. Chitosan/STS hydrogels were characterized and optimized using rheometry, scanning electron microscopy, swelling and ex vivo embolization assay. They were shown to exhibit rapid gelation and good mechanical properties, as well as sclerosing properties. Their potential for the embolization of aneurysms was subjected to preliminary in vivo evaluation in a bilateral iliac aneurysm model (three dogs) reproducing persistent type II endoleaks after endovascular aneurysm repair (EVAR). At 3 months no endoleak was detected in any of the three aneurysms treated with chitosan/STS hydrogels. In contrast, type I endoleaks were detected in two of the three aneurysms treated with chitosan hydrogels. Generally, chitosan/STS hydrogels have great potential as embolizing and sclerosing agents for EVAR and possibly other endovascular therapies.

1. Introduction

The development of minimally invasive procedures and tissue engineering strategies has led to a growing need for hydrogels. In particular, new embolizing agents are required to improve the clinical outcomes of endovascular aneurysm repair (EVAR). EVAR is an interesting alternative to conventional surgery to treat abdominal aortic aneurysm (AAA) and prevent rupture of the aorta. This procedure consists of inserting an implant, called a stent graft (SG), into the site of the aneurysm by fluoroscopic guidance through blood vessels, in order to exclude it from the blood flow. While EVAR has been shown to decrease short-term operating risks and reduce post-surgery recovery and hospitalization times, it is limited by the occurrence of blood flow perfusing the aneurysm outside the SG, termed endoleaks, which are frequently observed during imaging follow-up. Type I and III endoleaks, as well as persistent type II endoleaks, with documented aneurysm enlargement and cases of endotension (sac enlargement without documented endoleak) require re-intervention. Several attempts have recently been made to treat or prevent endoleaks using coils and/or polymeric embolizing agents (ethylene vinyl alcohol copolymer (Onyx), N-butyl cyanoacrylate (NBCA or Histoacryl), fibrin glue, and alginate) but frequent recurrence was seen in most studies. For type II endoleaks these agents were used to perform either trans-arterial embolization of collateral vessels or to fill the leak area in the aneurysm after direct puncture of the sac, the latter approach probably being more efficient when liquid embolic agents are used.

Recent reports suggest that combining embolization and destruction of the endothelium lining would decrease the risk of recurrence after embolization. This approach, based on sclerotherapy, consists of causing irreversible injury to the endothelial lining in the aneurysm to prevent recanalization and induce fibrosis. In a clinical setting this could be accomplished by injection of a sclerosing and embolic agent. To our knowledge, despite some preliminary research in this area, such a material does not presently exist commercially.