Application of Nanoparticles in Stent Technology

박정훈

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Abstract : Possessing unprecedented potential for early detection, accurate diagnosis, and personalized treatment of various disease, nanoparticles have been extensively studied over the last decade. Current therapeutic strategies are insufficient for suppressing stent-induced granulation tissue formation after metallic stent placement. The effects of photothermal (PT)-mediated local heating on suppressing stent-induced granulation tissue formation in the rate esophagus were investigated. Self-expandable metallic stents (SEMSs) were coated with branched gold nanoparticles (BGNP) to enable PT-mediated local heating. The effectiveness of local heating was assessed by comparing the results of histopathological examination. PT-mediated local heating suppresses granulation tissue formation after stent placement in the rat esophagus; moderate heating is a promising approach for preventing stent-related granulation tissue formation.

1. Introduction

Over the last decade, various nanoparticle-based agents with multifunctionality and high photothermal (PT)-converting efficiency have been investigated for biomedical applications to target diseases. Recently, Kim et al. reported a new type of branched GNP (BGNP) for highly efficient near infra-red (NIR) PT transducers. The synthesized BGNP showed distinct heating efficiency compared with conventional spherical GNPs. We hypothesized that BGNP-coated SEMS could be used for localized PT therapy (PTT) using NIR laser irradiation and that this therapeutic strategy may prevent granulation tissue formation after SEMS placement by thermal-induced apoptosis and cell cycle arrest. Therefore, the purpose of this study was to investigate the effect of PT-mediated local heating in suppressing stent-related granulation tissue formation in a rat esophageal model.

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2. Methods and Results

2.1. Fabrication of BGNP-coated SEMS

The cationic polymer was coated on the surface of SEMS through polydopamine (PDA) coating prior to deposition of BGNPs on the surface. Next, to coat the surface of the PDA-coated stent with a cationic polymer, the as-prepared PDA-coated stent was immersed in 15 mL of polyethyleneimine (PEI, 600 Da) solution (10 mg/mL) and stirred at room temperature for 12 h. Finally, the PEI-coated stent was washed with DW. The PEI-coated stent was immersed in 15 mL of 0.5 mM sodium cholate solution. Next, 90 µL of 50 mM $AgNO_3$, 3mL of 10mM $HAuCl_4$ solution, and 0.96 mL of 100mM ascorbic acid solution were sequentially added to the solution containing the PEI-coated stent.

2.2. NIR laser induced photothermal properties

Control, PDA-coated, and BGNP-coated SEMSs were irradiated with a 1-mm diameter fiber-coupled NIR (808 nm) diode-laser at 1.27 W/cm^2 to investigate PT characteristics *in vitro*. BGNP-coated SEMS was irradiated with four different laser powers (0.64, 1.27, 1.91, and 2.55 W/cm^2). The temperature increases and thermal images of the stent were examined by using an IR thermal camera. The surface characteristics of control, PDA-coated, and BGNP-coated SEMSs were examined by scanning electron microscopy with energy-dispersive X-ray spectroscopy.

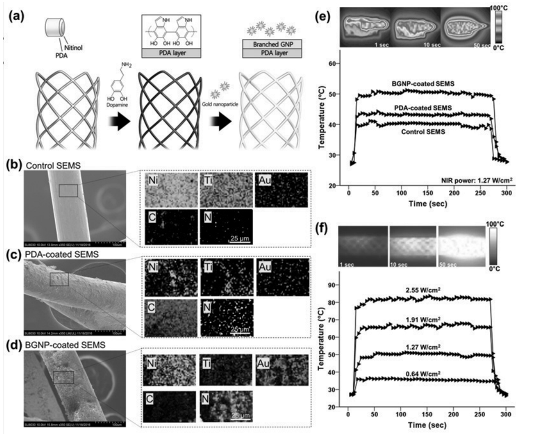

Fig 1. Schematic illustration of preparation precess for BGNP-coated SEMS.

2.3. Study design

A total of 52 Sprague-Dawley male rats weighing 300 - 350 g at 9 weeks of age were used for this study. Rats underwent BGNP-coated SEMS placement and were randomly divided into four groups using computer generated random numbers as follows: Group A (n = 13) received control treatment. Groups B (n = 13), C (n = 13), and D (n = 13) received local heating after stent placement at 50, 65, and 80 °C, respectively. The number of animals was calculated according to a previously published study. Ten rats from each group were sacrificed by administrating inhalable pure carbon dioxide at 4 weeks after stent placement for histopathological examination. Additionally, 3 rats from each group were sacrificed for western blot analysis at 3 days after local heating.

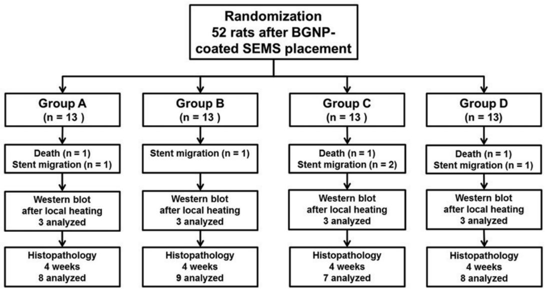

Fig. 1 Flow diagram and study design showing the randomization process and follow-up.

3. Conclusion

Localized PTT may be valuable for preventing granulation tissue formation and tumor ingrowth and/or overgrowth after SEMS placement in patients with malignant and benign esophageal strictures. The excellent stability of the BGNP-coated SEMS and its therapeutic strategy will provide opportunities for clinical application to prevent in-stent restenosis in the gastrointestinal tract. PT-mediated local heating suppresses granulation tissue formation after SEMS placement in the rat esophagus; moderate heating may represent a promising approach for preventing stent-related granulation-tissue formation. Further preclinical studies are needed to investigate the efficacy and safety of localized PTT using BGNP-coated SEMS under NIR irradiation.

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References

(1) Kim D.H., et. al., 2015, “Deoxycholate bile acid directed synthesis of branched Au nanostructures for near infrared photothermal ablation,” Biomaterials., pp. 154~164.