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博士の専攻分野の名称	博士（医学）
学位記番号	第 19360 号
学位授与年月日	平成17年3月25日
学位授与の要件	学位規則第4条第1項該当 医学系研究科未来医療開発専攻
学位論文名	Embolic effects of superabsorbent polymer microspheres in rabbit renal model : comparison with tris-acryl gelatin microspheres and polyvinyl alcohol （家兎腎動脈モデルにおける高吸水性ポリマー微小球の塞栓効果：トリス・アクリル・ゼラチン微小球及びポリビニル・アルコール粒子との比較）
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論文内容の要旨

〔目的〕 **Purpose**

Polyvinyl alcohol (PVA) has been the most commonly used particulate embolic agent for transcatheter embolization. Although it has been associated with the clinical success, drawbacks have been reported with its use such as unpredictable proximal vessel occlusion and microcatheter blockage. Many different microspheres have been developed to overcome the drawbacks of PVA. Tris-acryl gelatin microspheres (EM) is the most commonly used microspheres in clinical applications.

We have developed a spherical embolic agent, superabsorbent polymer microsphere (SAP-MS), which is non-toxic solid microsphere composed of sodium acrylate and vinyl alcohol copolymer and has the property of absorbing fluids and swelling within several minutes. The swollen particle is soft and compressible with maintaining the spherical shape. The aim of this study to describe the radiologic and histologic characteristic of SAP-MS in comparison with PVA particles as a conventional agent and tris-acryl gelatin microsphere as a current spherical agent in rabbit renal model.

〔方法ならびに成績〕 **Matetials & Results**

Materials and Methods: The right kidney of nine rabbits were embolized with the given agents ; PVA (180-300 μm) (n=3), EM (100-300 μm) (n=3), and SAP-MS (106-150 μm) (n=3). Each embolic agent was injected slowly through a microcatheter placed into the renal artery until the blood flow cessation under fluoroscopy. The embolized kidneys were evaluated immediately after the embolization by angiography. One week later, the angiograms were performed followed by dissecting of the kidneys for the histological examinations with light microscope. Two stains were used ; Hematoxylin-eosin as a basic dye for cellular components and elastica-van

Gieson to outline the arterial elastic fibers. The distribution pattern, the shape and appearance, and the associated perivascular reaction for each embolic agent were evaluated. For microspheres, ten peripheral occlusion points were randomly selected for each kidney section to compare the particle size range of EM and SAP-MS in the vessel lumen using the short-axis diameter of the particles.

Angiographic results : All embolizations were successfully performed in all groups. Immediate angiograms showed opacified renal hilum with homogenous parenchymal staining in the kidneys embolized with PVA while faint patchy staining inhomogenous parenchymal staining were seen with both mirospheres EM and SAP-MS. All one-week follow-up angiograms showed complete occlusion of the main renal artery without recanalization or parenchymal visualization regardless of the embolic agents.

Histologic results : The renal artery occlusion and prominent coagulative necrosis was confirmed regardless of agents. PVA aggregated in the proximal vessels with tiny fragments migrated into glomeruli. Both EM and SAP-MS traveled distally up to interlobular artery level, and a single particle achieved the cross-sectional vessel occlusion. SAP-MS was markedly swollen, deformed, and conformed to the vessel lumen compared with constantly spherical EM. No perivascular reactions were seen around the microspheres in the cortex with complete infarction, while mild reaction was seen in the cortex with incomplete infarction for both microspheres. The internal elastic membrane was variably changed depending on the reaction towards the particles.

〔総括〕 Conclusion

SAP-MS resulted in targeted end-organ infarction in rabbit renal model as EM and PVA. Both EM and SAP-MS distributed homogenously in the distal vessels with mild perivascular reactions. SAP-MS is more deformable and conformable with vessel lumen than EM due to its different mechanical properties.

論文審査の結果の要旨

独自の球状塞栓物質・高吸水性ポリマー微小球（SAP）の塞栓効果に関して、家兎腎臓モデルを用いて、欧米で市販されている従来型ポリビニルアルコール粒子（PVA）及び新世代のトリスアクリルゼラチン微小球（EM）と比較検討が行われた。不整形状の PVA が粒子径によらず血管近位に凝集あるいは微小断片を作り糸球体レベルに到達するなど、塞栓レベルの制御が困難であるのに対して、完全球形の SAP 及び EM は、粒子径に応じて弓状から小葉間動脈レベルに正確に到達し均一に分布しており、標的塞栓に優れた材料であることが示された。EM が血管内で球状を保ち粒子間に隙間を認めたのに対して、SAP ではその吸水性により血管内で膨潤し血管腔を隙間なく完全に密閉しており、特に動静脈瘻など短絡性血管病変への臨床応用が期待された。また、SAP 粒子の異物反応は軽微で、市販材料と比べて生体適合性に問題はないことが示唆された。本邦では、球状塞栓物質の塞栓効果に関する基礎的検討の報告は乏しく、本論文は学位を授与する価値があると思われる。