[gw22-e0470]

EFFECTS OF PIP TARGETING LOX-1 ELUTING STENTS ON IN-STENT RESTENOSIS AND RE-ENDOTHELIALISATION IN RAT ABDOMINAL AORTA STENTING MODELS

Lin Kaimin, Zhao Ziwen, Chen Lianglong₂ *Department Of Cardiology, Union Hospital, Fujian Medical University, Fujian, China*

10.1136/heartjnl-2011-300867.192

Background and Objectives Pyrrole-Imidazole polyamide (PIP) is a novel gene silencer that can be readily designed and synthesised to target any gene. Contrary to traditional gene-silencing agents, PIP is resistant to nucleases and can enter into the nuclei of target cells without any particular delivery system. Moreover, PIP has a low molecular weight, a high efficiency of cellular uptake and bioavailability, and is hydrophobic and lipophilic, making it pharmacokinetically suitable for loading onto the metal stent. The present study was designed to evaluate the potential effects of PIP on in-stent restenosis and re-endothelialisation in rat abdominal aorta stenting models.

Methods Rats were assigned to four groups (n=10 for each group): Control group, Bare-metal stent group, PIP-eluting stent group and Mismatch PIP-eluting stent group. In vitro pharmacological release kinetics was analysed by HPLC. The re-endothelialisation indices were determined by scanning electron microscopy (n=3). The expression of LOX-1, NADPH p22phox, NADPH p47phox will be determined by quantitative real-time PCR and Westernblot. The oxidative stress in

the aorta will be determined by measuring aortic MDA levels. Sections in methylmethacrylate will be cut into 5- μ m thickness and stained with hematoxylin-eosin. The area of neointimal hyperplasia (NIH), the rate of restenosis, and the injury and inflammation scores were measured.

Results In vitro pharmacological release kinetics showed that PIP eluting stents showed almost complete release of the PIP within 24h. In vivo pharmacological release kinetics demonstrated that trace amount of PIP was still remained in the local aorta tissues. Scanning electron microscopy showed that re-endothelialisation was nearly complete in all the three stents groups (n=3) at 14 days after stents implantation. The expression of LOX-1, NADPH p22phox, NADPH p47phox and the vascular MDA levels was significantly increased in BMS group compared with control group at 28 days after stents implantation ($p<0.05$). The increased LOX-1, NADPH p22phox, NADPH p47phox expression and vascular MDA levels was significantly inhibited in PIP eluting stent group compared to BMS group ($p<0.05$). However, the area of NIH and the rate of restenosis was significantly lower in PIP eluting stent group compared to BMS group ($p<0.05$). The area of NIH and the rate of restenosis was similar in mismatch PIP eluting stent group compared to BMS group ($p>0.05$).

Conclusions PIP targeting LOX-1 eluting stents could decrease in-stent restenosis (ISR) without impairing re-endothelialisation by silencing LOX-1 and lowering oxidative stress. These results indicated that PIP targeting LOX-1 is considered to be a feasible gene silencing agent using the next generation of DES for the prevention of in-stent restenosis of the coronary artery.