GW25-e0846

Safety and Efficacy of Degradable vs. Permanent Polymer Drug-eluting stents A meta-analysis of 18, 395 Patients from randomized trials

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Objectives: Degradable polymer drug-eluting stents (DP-DES) represents a promising strategy to improve the delayed healing and hypersensitive reaction in the vessel. However, the efficacy and safety of DP-DES vs. permanent polymer drug-eluting stents (PP-DES) are less well defined. The aim of this meta-analysis was to compare the total, short (<30days), mid (30 days-1year) and long (>1 year) term outcomes of DP-DES vs. PP-DES.
Methods: PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for randomized clinical trials to compare any of approved DP- and PP-DES. Efficacy endpoints were target-lesion revascularization (TLR) and in-stent late loss (ISLL). Safety endpoints were death, myocardial infarction (MI), composite of definite and probable stent thrombosis (ST). The meta-analysis included 19 RCTs (n=18, 395) with interest results. As compared with DES, there was a significantly reduced very late ST (OR=0.42, 95% CI 0.24-0.77, P=0.852) and ISLL (OR=-0.07, 95% CI -0.12-0.02, P=0.000) in DP-DES patients. However, there were no difference for other safety and efficiency outcomes between DP-DES and PP-DES, except that the stratified analysis showed a significant decreased TLR with DP-DES as compared to paclitaxel-eluting stent (OR=0.41, 95% CI 0.20-0.81, P=0.457).
Results: DP-DES is more effective in reducing very late ST and ISLL, as well as comparable to PP-DES with regard to death, TLR and MI. Further large RCTs with long-term follow-up are warranted to better define the relative merits of DP-DES.
Conclusions: DP-DES is more effective in reducing very late ST and ISLL, as well as comparable to PP-DES with regard to death, TLR and MI. Further large RCTs with long-term follow-up are warranted to better define the relative merits of DP-DES.

GW25-e0847

Safety and Efficacy of Polymer Free vs. Based Drug-eluting Stents A Meta-Analysis of Randomized Trials

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Objectives: Polymer free drug-eluting stents (PF-DES) have recently been developed to improve the delayed healing and hypersensitive reaction in the vessel. However, Uncertainty exists regarding the relative performance of PF-DES versus polymer based-DES (PB-DES) in percutaneous coronary intervention. The aim of this study was to perform a meta-analysis of randomized controlled trials (RCTs) comparing the safety and efficacy profile of PF-DES vs. PB-DES.
Methods: PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for RCTs that compared PF-DES and PB-DES, enrolling at least 100 patients. Efficacy endpoints were target-lesion revascularization (TLR) and in-stent late loss (ISLL). Safety endpoints were cardiac death, death, myocardial infarction (MI), composite of definite and probable stent thrombosis (ST). The meta-analysis included 9 RCTs (n=6364) with a median follow-up of 26 months clinical outcomes and 7 RCTs (n=5027) with interest angiography results. The results showed that there was no difference between PF-DES and PB-DES with regard to cardiac death, death, ST, MI, ISLL or TLR.
Results: PF-DES is comparable as PB-DES with regard to cardiac death, death, ST, MI, ISLL and TLR. Further large RCTs with longer follow-up are warranted to better define the relative merits of these drug-eluting stents.
Conclusions: PF-DES is comparable as PB-DES with regard to cardiac death, death, ST, MI, ISLL and TLR. Further large RCTs with longer follow-up are warranted to better define the relative merits of these drug-eluting stents.

GW25-e0849

Up-regulation of caveolin-1 suppresses vascular smooth muscle cells proliferation and neointimal formation in balloon injured rat carotid artery

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Objectives: Caveolin-1 (cav-1) is the major coat protein responsible for caveolae assembly, regulating signaling via protein-protein interactions with resident caveolar proteins, but its biological mechanism in vascular smooth muscle cells (VSMCs) is still unclear. The aim of this study was to evaluate the role of cav-1 on VSMCs proliferation and the neointimal formation in balloon injured rat carotid artery.
Methods: Left common carotid arteries from Sprague - Dawley rats were injured by a balloon catheter, and the injured arteries were incubated with 30 μL solution of Ad-cav-1 adenoviral vectors, Ad-GFP adenoviral vectors or PBS for 30 min. The rats were euthanized for morphometric and immunohistochemical analysis, real-time PCR and western blot analysis at 2 weeks after balloon injury and gene transfer. The cultured rat VSMCs transduced with Ad-cav-1 or Ad-GFP adenoviral vectors were used for cell proliferation assay, real-time PCR and western blot analysis. The vascular or intracellular ROS level was also detected.
Results: Adenoviral vectors encoding cav-1 cDNA could increase cav-1 expression both in mRNA and protein levels in balloon injured artery walls and cultured rat VSMCs. Upregulation of cav-1 significantly suppressed VSMCs proliferation and intimal formation. Over-expression of cav-1 could reduce vascular or intracellular ROS level and decrease the phosphorylation of the ERK1/2 in balloon injured artery walls and cultured rat VSMCs.
Conclusions: Our study suggests that over-expression of cav-1 significantly suppresses VSMCs proliferation and progression of neointimal formation after vascular injury.

GW25-e1123

EPO prevents apoptosis via JAK2/STAT5 in experimental epilepsy

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Objectives: To investigate the protective effects of recombinant human erythropoietin (rhEPO) and carbamylated EPO (CEPO) against myocardial cell apoptosis in epilepsy and to explore potential mechanisms involved.
Methods: Rats were given an KA to induce epilepsy. Groups of rats were treated with rhEPO or CEPO before induction of epilepsy, while additional rats were given a caudal vein injection of AG490, a selective inhibitor of Janus kinase 2 (JAK2). At 0, 2, 6, 12 and 24 hours after onset of seizures, epileptic rats were killed for detection of myocardial cell apoptosis by TUNEL assay, the expression of JAK2 and STAT5 mRNAs by in situ hybridization, and the expression of caspase-3, JAK2, and STAT5 proteins by immunohistochemistry and Western blot.
Results: Induction of epilepsy significantly enhanced myocardial cell apoptosis and up-regulated the expression of caspase-3 and JAK2 and STAT5a at both the mRNA and protein levels. Pretreatment with either rhEPO or CEPO reduced the number of apoptotic cells, down-regulated caspase-3 expression in the myocardium of epileptic rats. The expression of JAK2 and STAT5a mRNAs and proteins in the myocardium of epileptic rats was up-regulated in response to rhEPO, but not to CEPO pretreatment. Moreover, AG490 treatment increased apoptotic rate, up-regulated caspase-3 protein expression in the myocardium of epileptic rats.
Conclusions: Myocardial cell apoptosis may contribute to myocardial injury in epilepsy. EPO protects myocardial cells from apoptosis via the JAK2/STAT5 pathway in rats with experimentally induced epilepsy, whereas CEPO exerts an anti-apoptotic action perhaps via a pathway independent of JAK2/STAT5 signaling.

GW25-e1524

SIRT1-Mediated Epigenetic Downregulation of Plasminogen Activator Inhibitor-1 Prevents Vascular Endothelial Replicative Senescence

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Objectives: The inactivation of plasminogen activator inhibitor-1 (PAI-1) has been shown to exert beneficial effects in age-related vascular diseases, such as atherosclerosis. Limited information is available on the molecular mechanisms regarding the negatively regulated expression of PAI-1 in the vascular system. SIRT1, a class III histone deacetylase, plays a critical role in the control of endothelium-dependent vascular tone and play a protective role in atherosclerotic vascular diseases. However, it remains unclear whether SIRT1 prevents replicative vascular senescence and by which SIRT1 facilitates the effects of anti-replicative senescence. Therefore, the purpose of this study is to determine whether SIRT1 exerts its protective role in replicative endothelial senescence via PAI-1 and elucidate the molecular mechanism underlying protective effects in atherosclerosis.
Methods: We first performed the correlation analysis between the expressions of SIRT1 and PAI-1 in human atherosclerotic plaques and aortas of old mice. Next, regulation of PAI-1 expression by SIRT1 was observed by adenovirus-mediated overexpression in senescent human umbilical vein endothelial cells (HUVECs) or RNAi in young HUVECs. Furthermore, manipulation on PAI-1 level by addition of exogenous PAI-1 protein or inhibition of PAI-1 via its inhibitor PAI-039 was introduced to determine whether the anti-senescent effect of SIRT1 was dependent on PAI-1. Finally chromatin immunoprecipitation (ChIP) was used to clarify the molecular mechanism of the regulation of PAI-1 by SIRT1.
Results: We observed an inverse correlation between SIRT1 and PAI-1 expression in human atherosclerotic plaques and the aortas of old mice, suggesting that internal negative regulation exists between SIRT1 and PAI-1. SIRT1 RNAi or inhibition by EX527 increased PAI-1 expression and SA-β-gal activity in young HUVECs, while adenovirus-mediated SIRT1 overexpression or activation by SRT1720 reversed the increased PAI-1 expression in senescent HUVECs and aortas of old mice, accompanied by decreased SA-β-gal activity in vitro, and improved endothelial function and reduced arterial stiffness in vivo. Moreover, addition of exogenous PAI-1 protein blocked the protective effect of SIRT1 in senescent HUVECs while inhibition of PAI-1 by PAI-039 ameliorated the senescence-promotional effect of SIRT1 RNAi in young HUVECs, suggesting SIRT1-mediated inhibition of PAI-1 expression contributes to the anti-aging effect of this protein in HUVECs. Furthermore, we demonstrated that SIRT1 is able to bind to the PAI-1 promoter, resulting in a decrease in the acetylation of histone H4 lysine 16 (H4K16) bound to the PAI-1 promoter region.
Conclusions: Taken together, our findings suggest that the SIRT1-mediated epigenetic inhibition of PAI-1 expression exerts a protective effect in vascular endothelial senescence and atherosclerosis.