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THE EFFECTS AND MECHANISM OF RESVERATROL ATTENUATING OXIDATIVE STRESS IN BALLOON INJURED RAT CAROTID ARTERY

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Objectives The neointimal hyperplasia is the common pathological basis of several vascular diseases, including atherosclerosis and restenosis. In recent years, a large number of studies have found that the oxidative stress after artery injury take a critical role in pathogenesis of intimal hyperplasia. Resveratrol as a polyphenols has showed significant antioxidant effect in a variety of diseases. However, it is unclear whether resveratrol participates in modulating vascular restenosis induced by oxidative injury after balloon injury.

Methods The male Sprague-Dawley rats were established with balloon-injury model in vivo, and vascular smooth muscle cells (VSMCs) isolated from thoracic artery were stimulated with angiotensin II (Ang II) in vitro.

Results Compared to model group, the neointimal/medial area (I/M) and the restenosis rate were both decreased significantly by 1mg/kg/d resveratrol intraperitoneal injection either 7 days or 14 days after surgery (I/M 7d:0.47±0.04 vs 0.13±0.02, $p<0.05$,14d:0.25±0.05 vs 1.06±0.08, $p<0.05$; Restenosis Rate 7d:0.08±0.03 vs 0.24±0.07,$p<0.05$,14d:0.09±0.03 vs 0.41±0.13, $p<0.05$).Moreover, the level of 8-iso-Prostaglandin F2a in serum were suppressed by 5.8 and 2.9 times after 7 days and 14 days respectively in resveratrol group compared to control group. The results of real-time PCR showed the MCP-1 and IL-6 mRNA expression in injured arteries were also inhibited by 4.27 and 3.06 times after 7 days and 14 days respectively with resveratrol. Interestingly, there was no significant difference of NF-κB p65 positive cell rate between resveratrol group and control group assayed by immunohistochemistry (7 d $p=0.54$; 14 d $p=0.82$).The CCK-8 test and transwell method suggested VSMCs pretreated with 200 μmol/l resveratrol represented a blunted response to proliferation and migration in the presence of 1 μmol/l Ang II($p<0.001$, $p<0.05$).Moreover, the intracellular ROS levels was decreased significantly in resveratrol pretreatment group ($p<0.001$).Meanwhile, the NADPH oxidase activity was significantly suppressed ($p<0.05$) and SOD activity was notably enhanced (58.99±0.38 vs. 37.09 ±1.29,$p<0.001$). Western blot results revealed that resveratrol could suppress the ERK phosphorylation and NF-κB transcriptional activity (both $p<0.001$),with no effects on NF-κB p65 translocation and IkB degradation (both $p>0.05$).

Conclusions Resveratrol could significantly suppressed neointimal hyperplasia after balloon injury though inhibition of oxidative stress and inflammation.