SILDENAFIL IN CONJUNCTION WITH ANGIOTENSIN-CONVERTING ENZYME INHIBITOR IS EFFECTIVE IN LIMITING INFARCT EXPANSION IN A PORCINE MODEL OF ANTERIOR MYOCARDIAL INFARCTION

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Background: Sildenafil, a selective inhibitor of phosphodiesterase type 5, induces cardioprotection against myocardial ischemia-reperfusion injury through activation of cGMP-dependent protein kinase. However, there are few reports on its effect in limiting infarct expansion after acute myocardial infarction (AMI). We investigated whether sildenafil could reduce myocardial infarct size (IS) in a porcine model of AMI, especially in combination with angiotensin converting enzyme inhibitor (ACEI).

Methods: 18 female pigs (20-25 kg) were randomized into group 1, ACEI (perindopril) 2 mg daily (n=6); group 2, sildenafil 50 mg (n=6); and group 3, combination of ACEI 2 mg and sildenafil 50 mg (n=6). The study medications were administered within 24 hours after induction of AMI by occlusion of the left anterior descending artery for 40 minutes. All subjects underwent multi-detector cardiac CT (MDCT) scan at 5 days and 35 days after the procedure. IS was determined as the ratio of the area showing delayed enhancement to the total left ventricular myocardial area and IS reduction as the change between the two MDCT measurements.

Results: Initial IS and left ventricular ejection fraction (LVEF) were 18.1±9.0%, 25.0±6.3%, and 29.3±3.7% (p=0.094) and 51.8±9.8%, 45.2±7.7%, and 48.6±6.0% (p=0.543) in groups 1, 2, and 3, respectively. Initial wall thickness at infarcted myocardium and reference normal myocardium were not different between the groups. IS and LVEF at follow-up were 10.4±5.1%, 11.2±5.4%, and 11.5±3.7% (p=0.935) and 52.2±10.7%, 46.4±6.6%, and 50.7±5.5% (p=0.502) in each group. IS measured by MDCT was well correlated with IS estimated by TTC staining. Changes in infarcted wall thickness and LVEF were similar between the groups. Quantitative assessment of temporal infarct expansion showed, however, marked differences between the groups (7.6±5.0, 13.8±8.1, 17.8±5.0, p=0.046), IS reduction being significantly greater in group 3, compared to group 1 (p=0.031).

Conclusion: The use of sildenafil after AMI, in conjunction with an ACEI, was effective in limiting infarct expansion and may be incorporated as a useful adjunct in post-MI management.