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Hydrogen Sulfide Releasing Ibuprofen Derivative Can Protect Heart After Ischemia-Reperfusion

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Abstract : Hydrogen sulfide (H_2S) is a toxic gas, but it is produced by certain tissues in a small quantity. According to earlier studies, ibuprofen and H_2S has a protective effect against damaging heart tissue caused by ischemia-reperfusion. Recently, we have been investigating the effect of a new water-soluble H_2S releasing ibuprofen molecule administered after artificially generated ischemia-reperfusion on isolated rat hearts. The H_2S releasing property of the new ibuprofen derivative was investigated in vitro in medium derived from heart endothelial cell isolation at two concentrations. The ex vivo examinations were carried out on rat hearts. Rats were anesthetized with an intraperitoneal injection of ketamine, xylazine, and heparin. After thoracotomy, hearts were excised and placed into ice-cold perfusion buffer. Perfusion of hearts was conducted in Langendorff mode via the cannulated aorta. In our experiments, we studied the dose-effect of the H_2S releasing molecule in Langendorff-perfused hearts with the application of gradually increasing concentration of the compound (0- 20 µM). The H_2S releasing ibuprofen derivative was applied before the ischemia for 10 minutes. H_2S concentration was measured with an H_2S detecting electrochemical sensor from the coronary effluent solution. The 10 µM concentration was chosen for further experiments when the treatment with this solution was occurred after the ischemia. The release of H_2S is occurred by the hydrolyzing enzymes that are present in the heart endothelial cells. The protective effect of the new H_2S releasing ibuprofen molecule can be confirmed by the infarct sizes of hearts using the Triphenyl-tetrazolium chloride (TTC) staining method. Furthermore, we aimed to define the effect of the H_2S releasing ibuprofen derivative on autophagic and apoptotic processes in damaged hearts after investigating the molecular markers of these events by western blotting and immunohistochemistry techniques. Our further studies will include the examination of LC3I/II, p62, Beclin1, caspase-3, and other apoptotic molecules. We hope that confirming the protective effect of new H_2S releasing ibuprofen molecule will open a new possibility for the development of more effective cardioprotective agents with exerting fewer side effects. Acknowledgment: This study was supported by the grants of NKFIH- K-124719 and the European Union and the State of Hungary co- financed by the European Social Fund in the framework of GINOP- 2.3.2-15-2016-00043.

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