DESCRIPTION FOR THE GENERAL PUBLIC

Brain stroke is the third leading cause of death, after heart attack and cancer. This disease is also the most common cause of a long-term disability, among adults. In the majority of cases, the brain stroke is caused by the interruption of the blood flow in the brain. Unfortunately, the only available therapy for ischemic brain stroke is the administration of the tissue plasminogen activator (rTPA), which is a substance allowing the removal of a blood clot, that blocks the blood flow in the brain. Unfortunately, only a small number of patients qualify for this therapy, since this drug has to be administer within 4,5 hours following the blood flow interruption. Intensive investigation for a new therapeutic strategies have been conducted recently, since there is a high demand for new effective ischemic brain stroke therapies. Research results bring hopes for new therapeutic strategies in brain ischemia, showing intriguing phenomenon. Namely, it has been revealed, that the nervous tissue may develop tolerance to brain ischemia. This tolerance may be induced by several physical or chemical factors. Exposure of the brain to a harmful factor at low intensity i.e. short-term ischemia, low or high temperature, or administration of a specific compound at low dose, that is toxic to nervous tissue, cause induction of the brain tolerance to severe ischemia. So far, many different chemical compounds have shown the ability to induce development of brain tolerance to ischemia, i.e. some antibiotics. Recently, researchers, trying to find a cure for brain ischemia, have focused on hydrogen sulfide H_2S. This well-known gas, associated with protein food spoilage has turned out to also be an important signal transmitter in the brain. It has been proved, that in brain ischemia the H_2S level significantly drops. This phenomenon is accompanied by death of a great number of nervous cells in the brain. Supplementation of the H_2S, by administration of this gas to animals, before induction of brain ischemia, significantly decreased the paresis degree and the number of dead cells in the brain. The exact action of H_2S in the brain ischemia has not been revealed yet. Probably, H_2S increase the cellular survival through its antioxidants properties. This compound also inhibits decomposition of the internal cellular elements, by stabilization of the biological membranes, which form these elements. Also, H_2S blocks the generation of toxic compounds, produced by cells activated in brain ischemia. These encouraging scientific reports suggest, that H_2S has a potential to develop tolerance to brain ischemia as well as the possible therapeutic activity of this compound. However, it is difficult to image administration of H_2S in clinical practice, through inhalation of this gas. Several compounds have shown the ability to release H_2S, after administration to living organism. Many substances, such as sodium sulfides, that possess these properties are unstable and decompose in the blood. Thus, this makes them useless as brain stroke medications. Recently, attention of researchers has been focused on a new chemical H_2S donor - AP39. This compound advantages are its stability in the blood, ability to penetrate into the brain and to release there H_2S. The proposed scientific project involves evaluation of the AP39 activity, as a potential drug in the brain ischemia treatment. This compound will be administered to the experimental animals, before induction of the brain ischemia, in order to determine its ability to induce tolerance of the nervous tissue to ischemia. Additionally, we plan to check, whether administration of AP39, following induction of brain ischemia, limits nervous tissue damage. In particular, we plan to evaluate the mechanism of the AP39 action in this disease. The project involves examination of the nervous tissues, obtained from animals that will undergo brain ischemia. Specifically, we plan to investigate the blood vessel integrity, as well as features of cellular survival or death in the brain. Obtained results will allow for the better understanding of prophylactic and therapeutic potential of AP39 in brain ischemia, which may allow for introduction this compound as brain stroke therapy in the future.