

Nitrite and other NO donors for treatment of Subarachnoid Hemorrhage

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Following aneurysmal subarachnoid hemorrhage (aSAH), oxygenated, high-pressure blood forms a clot in the subarachnoid space increasing intracranial pressure (ICP), evoking early brain injury (EBI), ultra-early (<6hr) vasospasm and cortical and/or global cerebral ischemia. During the subsequent week(s), 70% of patients develop delayed vasospasm, and up to 50%-delayed cerebral ischemia (DCI) both portending poor outcome. The exact pathomechanism(s) responsible for those events remains debated. However, it is widely accepted that oxyhemoglobin and its degradation products being neurotoxic and NO scavengers, derail vasodilatory activity of endothelial and neuronal NO-synthases evoking endothelial dysfunction. Decreased NO - availability in the arterial wall endothelium coupled with depletion of brain NO storages by a transient ischemia increasing a local concentration of deoxy-hemoglobin affects conductive arteries and microcirculation, limits perfusion of the cortex, triggers local vasospasm as well as spreading depolarizations leading to spreading ischemia. In experimental and clinical settings an intravenous infusion and local administration of NO gas and different NO-donors demonstrated beneficial effect limiting brain damage, delayed cerebral infarctions, vasospasm and improving the outcome.

This presentation addresses historical data of NO-dependent relief of vasospasm, prevention of delayed brain infarctions, presents its impact on the outcome in the experimental and clinical setting after SAH, and suggests some future venues of NO-related research.

Speaker Biography

Ryszard M Pluta was born and educated in Warsaw, Poland where I obtained my medical, neurosurgical, doctoral degrees and postdoctoral award in the field of Neurosurgery from the Medical Research Center of Polish Academy of Sciences and the Jerzy and Krystyna Chorobski Foundation. In 1989 I joined the Surgical Neurology Branch at the National Institute of Neurological Disorders and Stroke of the National Institutes of Health, Bethesda, MD, USA, at first as the International Fogarty Fellow then as the Clinical Associate and Clinical Staff Researcher. In 2010 I joined JAMA Editorial Board as the Fishbein Fellow. In 2009 our patent "Nitrite for vascular diseases" got the "Deal of Distinction" Award. In 2013 I retired from the National Institute of Health. Over years of my clinical and research carrier, I presented over 120 lectures at national and international conferences, over 80 invited lectures and workshops at the universities and conferences and published over 130 articles in the leading medical and scientific journals. I am on the Editorial Board of several leading medical journals and the reviewer for numerous scientific and medical entities.

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