Methods to treat hypotension with NO inhibitors and pressor agents

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Technology description

This patent covers the idea of using nitric oxide blockers, including arginine derivatives, in conjunction with pressor drug therapeutics such as epinephrine, to raise the blood pressure of hypotensive patients.

Nitric oxide (NO) is an inter-and intra-cellular signaling molecule that mediates critical roles in key processes as diverse as the regulation of vascular tone and blood pressure, neuronal signaling, host-defense, and stimulation-secretion coupling.

Investigators at the Weill Cornell Medical College pioneered the cloning and study of NO synthases and the role of NO in the cardiovascular system. One of their clinical foci has been indications in which NO is toxically over-produced, leading to profound vasodilation, vascular collapse, and death.

Septic shock is a prime example. It is one of the leading cause of death in ICU's in the U.S., afflicting 250,000-350,000 people annually with mortality estimates ranging from 40%-60%. Our research has led to the concept that a key step in sepsis is the induction by LPS and cytokines of the gene encoding a specific isoform of NOS that produces unregulated and toxic quantities of NO.

Cornell has obtained a broad and deep portfolio of intellectual property around this work, most of which is directed to compositions and methods for administering analogs of arginine, its precursors, or metabolites to interfere with NO signalling.

While pressor drug therapy (i.e., adrenergic agonists) is a commonly employed method for attempting to restore blood pressure in septic patients, pressor agents are typically ineffective in these patients. Indeed, insensitivity to vasoconstrictors is a characteristic of septic shock and considered to be a major impediment to effective pharmacotherapy.

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