Review Front Aging Neurosci. 2020 Aug 13;12:255. doi: 10.3389/fnagi.2020.00255. eCollection 2020.

Nicotinamide, a Poly [ADP-Ribose] Polymerase 1 (PARP-1) Inhibitor, as an Adjunctive Therapy for the Treatment of Alzheimer's Disease

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PMID: 32903806 PMCID: PMC7438969 DOI: 10.3389/fnagi.2020.00255
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Abstract

Nicotinamide (vitamin B3) is a key component in the cellular production of Nicotinamide Adenine Dinucleotide (NAD) and has long been associated with neuronal development, survival and death. Numerous data suggest that nicotinamide may offer therapeutic benefits in neurodegenerative disorders, including Alzheimer's Disease (AD). Beyond its effect in NAD^+ stores, nicotinamide is an inhibitor of Poly [ADP-ribose] polymerase 1 (PARP-1), an enzyme with multiple cellular functions, including regulation of cell death, energy/metabolism and inflammatory response. PARP-1 functions as a DNA repair enzyme but under intense DNA damage depletes the cell of NAD^+ and ATP and leads to a non-apoptotic type of cell death called Parthanatos, which has been associated with the pathogenesis of neurodegenerative diseases. Moreover, NAD^+ availability might potentially improve mitochondrial function, which is severely impaired in AD. PARP-1 inhibition may also exert a protective effect against neurodegeneration by its action to diminish neuroinflammation and microglial activation which are also implicated in the pathogenesis of AD. Here we discuss the evidence supporting the use of nicotinamide as adjunctive therapy for the treatment of early stages of

AD based on the inhibitory effect of nicotinamide on PARP-1 activity. The data support evaluating nicotinamide as an adjunctive treatment for AD at early stages of the disease not only to increase NAD^+ stores but as a PARP-1 inhibitor, raising the hypothesis that other PARP-1 inhibitors - drugs that are already approved for breast cancer treatment - might be explored for the treatment of AD.

Keywords: Alzheimer's disease therapy; PARP-1 inhibitors; lymphocytes; nicotinamide; oxidative death; parthanatos.

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