Memantine for the treatment of dementia: A review on its current and future applications

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Alzheimer’s disease (AD) is a neurodegenerative disorder characterized by the presence in the brain of extracellular amyloid-β protein (Aβ) and intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein. The N-Methyl-D-aspartate receptors (NMDAR), ionotropic glutamate receptor, are essential for processes like learning and memory. An excessive activation of NMDARs has been associated with neuronal loss. The discovery of extrasynaptic NMDARs provided a rational and physiological explanation between physiological and excitotoxic actions of glutamate. Memantine (MEM), an antagonist of extrasynaptic NMDAR, is currently used for the treatment of AD jointly with acetylcholinesterase inhibitors. It has been demonstrated that MEM preferentially prevents the excessive continuous extrasynaptic NMDAR disease activation and therefore prevents neuronal cell death induced by excitotoxicity without disrupting physiological
synaptic activity. The problem is that MEM has shown no clear positive effects in clinical applications while, in preclinical stages, had very promising results. The data in preclinical studies suggests that MEM has a positive impact on improving AD brain neuropathology, as well as in preventing Aβ production, aggregation, or downstream neurotoxic consequences, in part through the blockade of extrasynaptic NMDAR. Thus, the focus of this review is primarily to discuss the efficacy of MEM in preclinical models of AD, consider possible combinations of this drug with others, and then evaluate possible reasons for its lack of efficacy in clinical trials. Finally, applications in other pathologies are also considered. © 2018 - IOS Press and the authors. All rights reserved.

Alzheimer's disease
Amyloid-protein
Extrasynaptic N-Methyl-D-aspartate receptor
Memantine
Tau protein
amyloid
apoenzyme
brain derived neurotrophic factor
cyclin dependent kinase 5
memantine
n methyl dextro aspartic acid receptor
synapse receptor
memantine
neuroprotective agent
Alzheimer disease
clinical feature
clinical trial (topic)
dementia
diabetes mellitus
drug effect
drug efficacy
drug treatment failure
human
inflammation
insulin metabolism
modulation
multicenter study (topic)
neurofibrillary tangle
nonhuman
oxidative stress
pathology
pathophysiology
phase 3 clinical trial (topic)
preclinical study
priority journal
protein phosphorylation
randomized controlled trial (topic)
Review
Alzheimer disease
animal
metabolism
Alzheimer Disease
Animals
Humans
Memantine

Neuroprotective Agents