Anesthetic Management Of Patients With Alzheimer's Disease

Essay

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Ola Ahmed Yashin

Contents

List of Abbreviations

ABCA7	**:**	ATP-binding cassette subfamily A member 7
ACC/AHA	**:**	American College of Cardiology and the American Heart Association
ACE	**:**	Angiotensin converting enzyme
AD	**:**	Alzheimer's disease
ADDLs	**:**	Amyloid-derived diffusible ligands
ADL/IADL	**:**	Activities of Daily Living/Instrumental Activities of Daily Living
AKI	**:**	Acute kidney injury
APACHE	**:**	Acute Physiology and Chronic Health Evaluation
APOE4	**:**	Apolipoprotein E4
APOJ	**:**	Apolipoprotein J
APP	**:**	Amyloid precursor protein
ARB	**:**	Angiotensin receptor blockers
ASA	**:**	American Society of anesthesiologists
Aβ	**:**	Amyloid beta protein
BBB	**:**	The blood–brain barrier
BIS	**:**	Bispectral index
BOLD-fMRI	**:**	Blood-oxygen-level dependent Functional MRI

CAM	**:**	Confusion assessment method
CDK5	**:**	Cyclin-dependent kinase 5
ChEIs	**:**	Cholinesterase inhibitors
COX-1	**:**	Cyclooxygenase-1
CSF	**:**	Cerebrospinal fluid
CT	**:**	Computed tomography
DR6	**:**	Death receptor 6
EEG	**:**	Electroencephalogram
EOAD	**:**	Early onset Alzheimer's disease
FIO2	**:**	Fractional inspired oxygen
fMRI	**:**	Functional MRI
GABA	**:**	Gamma-Aminobutyric acid
ICU	**:**	Intensive care unit
IDE	**:**	Insulin-degrading enzyme
IQCODE	**:**	Informant Questionnaire on Cognitive Decline in the Elderly
IV	**:**	Intravenous
LOAD	**:**	Late onset Alzheimer's disease
LVH	**:**	Left ventricular hypertrophy
MAC	**:**	Minimum alveolar anesthetic concentration
MAP	**:**	Microtubule-associated protein

MMSE	**:**	Mini mental state examination
MRI	**:**	Magnetic resonance imaging
nAChR	**:**	Nicotinic acetylcholine receptors
NINCDS-ADRDA	**:**	National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association
NINCDSA DRDA criteria	**:**	The National Institute of Neurologic, Communicative Disorders and Stroke–AD and related Disorders Association Work Group
NMDA	**:**	N-methyl-D-aspartate
NPO	**:**	Nil per os (nothing by mouth)
NSAIDs	**:**	Non-steroidal anti-inflammatory drugs
PACU	**:**	Post-anesthesia care unit
PAINAD	**:**	Pain Assessment in Advanced Dementia
PaO2	**:**	Arterial oxygen partial pressure
PET	**:**	Positron emission tomography
PHFs	**:**	Paired helical filaments
POCD	**:**	Post-operative cognitive dysfunction
POISE	**:**	Perioperative ischemic Evaluation
POSSUM	**:**	Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity

PS-1	**:**	Presenilin 1
PS-2	**:**	Presenilin 2
RAAS	**:**	Renin-angiotensin-aldosterone-system
SIGN	**:**	The scottish intercollegiate guidelines network
SORL1	**:**	Sortilin-related receptor
SPECT	**:**	Single photon emission computed tomography
T2D	**:**	Type 2 diabetes
TEE	**:**	Transesophageal echocardiography

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Introduction

Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder in elderly people; it afflicts an estimated 26.6 million people worldwide, and without a major therapeutic breakthrough, the prevalence of AD is expected to increase to more than 100 million by 2050. This disease is the most common form of dementia and the prevalence rates at ages 65, 75, and 85 years are 0.9, 4.2, and 14.7%, respectively. ***(Brookmeyer et al., 2007)***

Scientists believe that for most people, Alzheimer's disease is caused by a combination of genetic, lifestyle and environmental factors that affect the brain over time. Only a small proportion of AD is due to genetic variants, the large majority of cases (over 99%) are late onset and sporadic in origin. ***(Blennow et al., 2006)*** The cause of sporadic AD is likely to be multifactorial, with external factors interacting with biological or genetic susceptibility to accelerate the manifestation of the disease. The main risk factor for AD is age, and persons over age 85 have a six-fold increase of getting the disease. ***(Bufill et al., 2009)***

So, surgical patients with Alzheimer's disease often require a special level of care during the perioperative period. They are prone to developing postoperative

complications, functional decline, loss of independence, and other untoward outcomes. In order to provide optimal care for the older surgical patient, a thorough assessment of the individual's health status is essential.

Alzheimer's Disease

Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder in elderly people. It afflicts an estimated 26. 6 million people worldwide, and without a major therapeutic breakthrough, the prevalence of AD is expected to increase to more than 100 million by 2050. This disease is the most common form of dementia and the prevalence rates at ages 65, 75, and 85 years are 0. 9, 4. 2 and 14. 7% respectively. ***(Brookmeyer et al., 2007)***

The cause of AD is not yet well known. Only a small proportion of AD is due to genetic variants. The large majority of cases (over 99%) are late onset and sporadic in origin. The cause of sporadic AD is likely to be multifactorial, with external factors interacting with biological or genetic susceptibility to accelerate the manifestation of the disease. The main risk factor for AD is age, and persons over age 85 have a six-fold increase of getting the disease. ***(Bufill et al., 2009)***

Hypothesis of Alzheimer's disease:-

- **Genetic hypothesis:-**

The genetic heritability of Alzheimer's based on reviews of twin and family studies shows that around 0. 1%

of the cases are familial forms of autosomal dominant inheritance, which have an onset before age 65. This form of the disease is known as early onset familial Alzheimer's disease. Most cases of Alzheimer's disease are termed sporadic AD, in which environmental and genetic differences may act as risk factors. ***(Wilson et al., 2011)***

Four genes that cause or predispose to Alzheimer's disease have been identified to date (amyloid precursor protein [APP], apolipoprotein E4 [APOE4], presenilin 1 [PS-1], and presenilin 2 [PS-2]). Mutations or polymorphisms in these genes cause excessive cerebral accumulation of the amyloid protein and subsequent neuronal and glial pathology in brain regions important for memory and cognition (cerebral cortex and hippocampus). ***(Dennis et al., 2002)***

- **Cholinergic hypothesis:-**

One of the most consistent changes in AD is a reduction of the activity of both choline acetyltransferase and acetylcholinesterase enzymes in the cerebral cortex and hippocampus contributing significantly to the deterioration in cognitive function seen in patients with AD. Reductions also occur in the corticotropin-releasing factor and somatostatin, both of which have been identified within

degenerating neuritis of the neuritic plaque. Glutaminergic neurons are also involved, which account for many of the large neurons lost in the cerebral cortex and hippocampus in AD. ***(Francis et al., 1999)***

- **Amyloid hypothesis:-**

It was found that that extracellular amyloid beta (Aβ) deposits are the fundamental cause of AD. The location of the gene for the amyloid precursor protein (APP) is on chromosome 21. Amyloid proteins are degraded by apolipoproteins. As some isoforms are not very effective at this task (such as APOE4), this leads to excess amyloid buildup in the brain. ***(Mudher and Lovestone, 2002)***

Amyloid-derived diffusible ligands (ADDLs), non-plaque Aβ oligomers are suspected to be the primary pathogenic form of Aβ. They bind to a surface receptor on neurons and change the structure of the synapse, thereby disrupting neuronal communication. ***(Lacor et al., 2007)***

In 2009, a protein called N_APP (which is a derivative of amyloid precursor protein (APP)) was found to trigger the self-destruct pathway by binding to a neuronal receptor called death receptor 6 (DR6) which is highly expressed in the human brain regions most affected by AD. ***(Nikolaev et al., 2009)***