SUMMARY

Entry

Alzheimer's disease (AD) accounts for 70% of dementias among the aging population. The pathogenesis of AD is associated with the accumulation of amyloid plaques in the extracellular space of the brain, resulting from the accumulation of insoluble amyloid β peptide (Aβ) and intracellular neurofibrillary tangles (NFTs), which primarily contain highly phosphorylated tau protein. The continuing upward trend in the number of patients in Poland and worldwide indicates a growing need for rapid diagnosis and treatment. Many studies indicate the important role of miRNA molecules in neurodegenerative processes. MiRNA levels can vary depending on the gene being regulated and the stage of the disease.

Aim of the study

The aim of the study was to examine changes in the expression of three selected miRNAs (miRNA-132-5p, miRNA-146a-5p, and miRNA-200a-3p) in relation to the stage of Alzheimer's disease and the relationship between miRNA expression and polymorphisms in the APOE and ACE genes. The association of selected miRNA expression with comorbidities and correlations with selected biochemical parameters (TC, HDL, LDL, TG, vitamin B12), proteins, and diagnostic markers isolated from CSF (Aβ1-42, Aβ1-40, p-Tau, t-Tau, Aβ1-42/Aβ1-40, p-Tau/Aβ1-42, h-Tau/Aβ1-42) were also analyzed.

Study Group

The study group consisted of 70 patients from the Provincial Clinical Hospital No. 2 in Rzeszów and 27 healthy individuals without dementia as controls. Molecular analysis was performed on 70 patients aged 59-92 years diagnosed with dementia ranging from mild cognitive impairment (MCI) through the three stages of Alzheimer's disease: AD I, AD II, and AD III. Classification was performed by the staff of the Neurology Clinic with the Stroke Treatment Unit.

Materials and Methods

The biological material used for the study was biobanked serum from which RNA was isolated according to the manufacturer's QIAGEN miRNeasy Serum/Plasma Advanced methodology. Analysis of selected miRNA expression was performed using qPCR. The miRCURY® LNA® SYBR® Green PCR Kit and specific primers from the miRCURY® LNA® miRNA PCR Assays kit were used for amplification, according to the manufacturer's recommendations.

Results and Conclusions

Molecular analysis demonstrated that as the disease progresses, there is a decline in the levels of both microRNA-132-3p expression and vitamin B12 concentration. Furthermore, a positive correlation was identified between the expression of microRNA-146a-5p and the values of diagnostic indicators in Alzheimer's disease (AD), specifically pTau/Aβ42 and hTau/Aβ42. Statistical analysis revealed a relationship between polymorphism in the *APOE* gene and reduced expression of miRNA-132-3p. Additionally, a relationship was observed between polymorphism in the *ACE* gene and the expression levels of miRNA-200a-3p, miRNA-132-3p, and miRNA-146a-5p. The presence of at least one insertion allele (I) in the ACE gene resulted in increased expression of microRNA-200a-3p and microRNA-132-3p, and decreased expression of microRNA-146a-5p.

Moreover, statistical analysis of the study group confirmed the influence of age on the stage of dementia. Older individuals tend to exhibit more severe stages of dementia, while younger individuals are more frequently diagnosed with mild cognitive impairment (MCI) or mild Alzheimer's disease impairment (ADI).