The Benefits of Continued use vs. Discontinuation of Acetylcholinesterase Therapy in Moderate to Severe Alzheimer's Disease

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Abstract

Alzheimer's disease is a chronic progressive disease for which there is no cure. Pharmacotherapy used in treatment of the disease does not modifry the disease but instead provides symptomatic relief. These drugs are known to be effective in early stages of the disease but they are not without side effects. Drugs are often continued into moderate and severe stages of the disease. This literature review found that 5 studies indicated there was no significant change in MMSE scores in subjects who continued and discontinued acetylcholinesterase therapy in moderate and severe AD. The review of the literature found contradictory evidence on whether there was a difference in side effects and quality of life based off of treatment. The amount of contradictory evidence suggests it is worthwhile to consider discontinuing pharmacotherapy on a case by case basis in late disease

Introduction

AD is a chronic and ultimately fatal condition. It is a progressive and irreversible disease that is characterized by damage to brain cells. Damage takes place in the form of neurofibrillary tangles, , inflammation and amyloid plaques. AD impairs cognition, functional, and physical ability. There is no cure or disease modifying treatment for AD. However there is a typical regiment of drugs employed to treat AD symptoms. At early stages these rugs are effective however their efficacy decreases as the disease progresses. These medications have side effects and there is currently no standard of care recommendation for when these drugs should be discontinued. This review analyzes whether or not evidence suggests these drugs should continue to be utilized in late term disease.

Methods

A Literature search was performed using Pubmed and Google Scholar in November of 2019. A total of 5 articles that were all randomized controlled trials were selected based on the criteria of trial time, population type, date, and experimental variable type. The designs of these five studies in addition to their results and the quality of the design were then analyzed and compared

Results

The evidence collected from analyzing the studies was contradictory. The one finding that was not contradictory between studies was that there as not a significant change in MMSE score between groups that continued pharmacotherapy and groups that discontinued therapy or recieved a lower dose. The five studies had contradictory findings when they compared whether or not pharmacotherapy had a significant effect on the symptoms and effect of the illness at late disease stages and whether or not the side effects were significant compared to no treatment at all and treatment at lower doses.

Table 1. Comparison of Results

Appendix Comparison of acetylcholinesterase inhibitor to no treatment at all / treatment withdrawal **

Study	intolerance to side effects	Withdrawal from study	Increase in AE # compared to control	MMSE score change	Increase in disease effect based on MMSE score decline, BPMSE score decline, or decrease in time to nursing home placement
Adami M, Bruno G, Gaudio M, et al	n/a	S	n/a	NS	NS
Choi S, Hong Y, Jeong J, Park K, Choi S	n/a	S	n/a	n/a	S
Bibbiani F, Brand-Schieber F, Farlow M, et al	S	NS	S	n/a	n/a
Eryavec G, Herrmann N, Lanctot K, et al.	NS	n/a	n/a	NS	NS
Baldwin A, Barber R, Burns A. et al.	n/a	n/a	n/a	n/a	S

Discussion

In two of the five studies there was a significant difference in the effect of the disease between the treatment and control groups, however, in two of the five studies it was found that there was not a significant difference between the experimental and control groups. In addition, one of the studies found there was a significant impact of side effects on the quality o f life of the subject and another study found the side effect presence was not significantly different between the experimental and control group. Further study of this topic should be done to better determine the effects of the drug in late stages of Alzheimer's disease and whether or not these effects outweigh the side effects enough to justify continued use.

Conclusion

Acetylcholinesterase inhibitors are routinely used for the treatment of the symptoms of AD. Despite this, very few trials have effectively tested whether or not it is good standard of care to continue the use of these drugs in the late stages of the disease. The five studies found contradictory evidence reguarding thais question. While the evidence suggests it is worthwhile to re-examine the costs and benefits of such treatment in each patient to consider discontinuation as the disease progresses, more studies are needed before a definitive conclusion can be made.

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