

Review of Clinical Pharmacology and Pharmacokinetics

ΕΡΙΤΗΘΕΟΡΕΣΕ ΚΛΙΝΙΚΕΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΕΤΙΚΕΣ
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Μιχαλακοπούλου 145, 11527 Αθήνα, Ελλάς
Τηλ.-Fax (0030)2107784700, 2107700663, 6932203802
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Letter from Guest Editor

The progress and contributions of 20th century pharmacology has been immense with over 20 pharmacologists to have received Nobel Prizes. This field of medical studies covers many areas; it is built upon and at the same time incorporates many disciplines such as biochemistry, biology physiology, pathology, anatomy, molecular biology, while the development of new analytical and experimental techniques and instruments has given a new boost in pharmacological research. Yet, although a remarkable progress has been made in developing new drugs and in understanding how they act, the challenges are endless. Integrating a depth of knowledge in many related scientific disciplines, pharmacologists offer a unique perspective to solving drug and chemical related problems which impinge on human health, with ultimate goal the treatment and prevention of major diseases.

The 5th Panhellenic Congress of Pharmacology focuses on four *hot* subjects: Regenerative Pharmacology, Herbal Medicines, Pharmacology of Abuse and Dependence, and Education in Pharmacology.

- *Regenerative Pharmacology* is one of the newest areas in Pharmacology, represents a groundbreaking field of research and has the potential to radically alter the treatment of diseases and disorders.

- *Herbal Medicines* have acquired an important percentage among the drug used; according to WHO 80% of people worldwide rely on herbal medicines for some aspect of their primary health care. This continuously increasing use of plant medicines imposes the need for establishing new regulations.

- *Pharmacology of Abuse and Dependence*, still not a well defined area, presents a lot of challenge for researchers and clinicians.

- *Education in Pharmacology* remains a hot subject in the Medical education, following the knowledge *explosion* of the last decades accompanied by a decreasing reliance on didactic teaching. The crucial question is: how and what should we teach?

We hope that the round table discussions along with the invited lectures, included in this abstract book, will raise new and intriguing ques-

tions that will further stimulate research, and will contribute to new therapeutic approaches and attitudes.

I would like to thank the Editorial Board of *Review of Clinical Pharmacology and Pharmacokinetics* in particular Journal Editors Prof. S.T. Plessas and Dr C.T. Plessas for invitation and for providing the suitable and high-standard forum through which new research findings will become available to the scientific community.

The Guest Editor

Charis Liapi

Assist. Professor in Pharmacology
Medical School, University of Athens
Chair of Hellenic Society of Pharmacology

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Cholinesterase Inhibitors and Memantine in Vascular Dementia: A Systematic Review of Randomized Controlled Trials

C. Kani¹, K. Papanikolaou², A. Pehlivanidis³, Z. Papadopoulou-Daifoti¹

¹Department of Pharmacology, Medical School, University of Athens, Athens, Greece

²Department of Child Psychiatry, University of Athens, *Agia Sophia*, Children's Hospital, Athens, Greece

³^{1st} Department of Psychiatry, University of Athens, *Eginition* Hospital, Athens, Greece

Key words: Vascular dementia; Cholinesterase Inhibitors; Memantine; Meta-analysis

S u m m a r y: *The purpose of the present review was to examine whether treatment with Cholinesterase Inhibitors (ChEIs) and memantine shows benefit in the treatment of vascular dementia (VaD). Data for cognition, functionality, global impression and dropouts were extracted. Overall the use of ChEIs and memantine provided modest benefits in VaD, with a significant dropout rate.*

INTRODUCTION

VaD is an heterogeneous disorder, emerging from various cerebrovascular diseases (CVD), which causes cognitive impairment. Cholinergic deficits and excitatory glutamate neurotoxicity, probably related to the damage due to ischemic stroke, have been observed in VaD. Therefore, drugs compensating cholinergic deficits or blocking glutamate excitatory actions may present a treatment option in VaD.

METHODS

Extensive literature search was performed to retrieve all relevant randomized, placebo-controlled trials on ChEIs and memantine in patients with VaD. Eligible studies were double blind, randomised, parallel group, placebo controlled trials (RCTs) of donepezil, rivastigmine, galantamine or memantine and participants included patients with VaD, diagnosed with the use of appropriate criteria. A random effects model was used to calculate combined estimates of all treatments effects. For continuous outcomes the Weighted

Mean Difference (WMD) was calculated. The Number-Needed-to-Treat (NNT) or Number-Needed-to-Harm (NNH) was calculated as the inverse of the meta-analytical Risk Difference (RD) for binary outcomes. The reporting quality was assessed using the Jadad scale and Chalmers modified checklist (1). Publication bias was assessed by a linear regression test (2) and adjustment, where applicable, was performed by the *Trim and Fill* method (3).

RESULTS

Six trials met the inclusion criteria for VaD (on donepezil, galantamine and memantine). All trials referred to the diagnosis of possible or probable VaD, except of one galantamine trial which included patients with a diagnosis of probable VaD or AD combined with cerebrovascular disease. Data on ADAS-cog scale (Alzheimer's Disease Assessment Scale Cognitive) measured as WMD suggest modest clinically significant effect of donepezil, galantamine and memantine in cognition deficits in VaD, while the NNT for global impression for patients stabilized or improved was rather high. Results for activities on daily living were available only for the donepezil trials. Dropouts due to any cause were higher in treatment arms (NNH 13). The reporting quality of included studies was moderate to very good as assessed by Jadad scale and Chalmers' modified checklist.

DISCUSSION

The use of ChEIs and memantine was associated with marginal clinical benefits in VaD, with a significant dropout rate. Generalization of the results should be done with caution, as the number of trials included in the present systematic review is small.

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