Review of Clinical Pharmacology and Pharmacokinetics

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INTERNATIONAL EDITION

VOLUME 22, 2008 ❁ No 2

Issue Devoted to Papers Presented at the

5th Panhellenic Congress of Pharmacology

Organized by the
Hellenic Society of Pharmacology

23-25 May, 2008
Athens, Greece

ISSN 1011-6583

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Επιθεώρηση Κλινικής Φαρμακολογίας και Φαρμακοκινητικής

Epitheorese Klinikes Farmakologias kai Farmakokinetikes

INTERNATIONAL EDITION

☸

Journal of Applied Pharmacology and Current Therapeutics Reviews, Review Articles on Drugs and Drugs Therapy, Original Papers and Practical Therapeutics Articles

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Published three times a year by PHARMAKON-Press
145 Michalakopoulou str., 115 27 Athens, GREECE
Phone-Fax (0030)2107784700 and (0030)2107700663
Email: stplessas@hotmail.com

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Τετραμηνιαία Ιατροφαρμακευτική Έκδοση
Εφηρμοσμένης Φαρμακολογίας, Φαρμακοκινητικής και Θεραπευτικής

Ιδιοκτήτης-Υπεύθυνος κατά το Νόμο: Ελένη Πλέσσα και ΣΙΑ Ε.Ε.
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GENERAL INFORMATIONS

REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS

publishes Applied Pharmacology and Current Therapeutics Reviews, Review Articles on Drugs and Drug Therapy, Original Papers and Practical Therapeutics Articles.

The *scientific standard* of the papers, which are accepted for publication, is controlled by the Editorial Board or by other Experts in the various fields of Pharmacology and Pharmacokinetics.

Manuscripts: These should mention, on the first page, the *Title*, *Author(s)* and the *Name of the Institution* at which the work was done. The complete *address* of the author, including Postal area code number, should be given under the rubric *Send reprint requests to*. Papers should follow the general form: *Introduction, Materials and Methods, Results, Discussion* and *References*. Drugs must be referred to by their generic or chemical name, but may be identified by trade name in parenthesis or o footnote. All papers should be submitted in duplicate.

Summary: A summary in English (maximum length 200 words) must accompany all manuscripts.

Key words: A list of key words should be submitted.

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Papers should be submitted to the Editors-in-Chief: Prof. S.T. Plessas or Dr C.T. Plessas.

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INVITED SPEAKERS

ORAL AND POSTERS PRESENTATIONS

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

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Chair of Hellenic Society of Pharmacology

REVIEW OF CLINICAL PHARMACOLOGY AND
PHARMACOKINETICS, INTERNATIONAL
EDITION 22: 176-177 (2008)

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

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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 Chalmer's 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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VOLUME 22, 2008 ❁ No 2

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