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TITLE: Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness

PRINCIPAL INVESTIGATOR: William J. Meggs, M.D., Ph.D.
Kori L. Brewer, Ph.D.
Allison Mainhart, B.S.

CONTRACTING ORGANIZATION: East Carolina University
Greenville, NC 27834

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William J. Meggs, M.D., Ph.D.
Kori L. Brewer, Ph.D., Allison Mainhart, B.S.

E-Mail: meggsw@ecu.edu

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East Carolina University
Greenville, NC 27834

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14. ABSTRACT

This research study aims to expand the field of knowledge of Gulf War Illness. The research may provide initial proof of the innovative hypothesis that Gulf War Illness is related to low grade neuron-inflammation, which can be down regulated, by Naltrexone and Dextromethorphan. This is untested but potentially ground breaking concept that could provide, both an enhanced understanding of, and beneficial treatment for, Gulf War Illnesses. Research at the National Institute of Environmental Health and other facilities has proven that naltrexone and dextromethorphan reduce inflammation in the brain. Clinical trials in humans with low dose naltrexone have established benefits in syndromes related to Gulf War Illness such as fibromyalgia. We have successfully enrolled 41 subjects in the study, and anticipate obtaining important data by the end of the coming year. A no cost extension has been obtained to complete the study.

15. SUBJECT TERMS
Gulf War Illness, naltrexone, dextromethorphan

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INTRODUCTION

Gulf war veterans' illnesses comprise distinct clusters of symptom-defined illnesses (1,2) for which there are neither diagnostic tests nor effective treatments. Gulf war veterans had variable exposures to a number of chemicals (3), including organophosphate insecticides, pyrethrum-related insecticides, DEET, Pyridostimine bromide, smoke from oil well fires, and Sarin gas. Gulf war veterans' illnesses may reflect an inflammatory cycle involving the brain which may be a common mechanism of many neurological conditions, whether initiated by toxic exposures, infection, or trauma. In this theory, central nervous system inflammation initiated by toxic exposures and sometimes exacerbated by subsequent exposures is a component of illness hypothesized to explain the neurological manifestations. Substance P release at sensory nerve endings is an explanation for the peripheral pain manifestations of illness.

This theory suggests that novel anti-inflammatory drugs may be of benefit in symptom-defined illnesses related to a cycle of inflammation. Dr. J. S. Hong's laboratory at the National Institute of Environmental Health Sciences has demonstrated that Morphine-related analogs, including Naltrexone and Dextromethorphan, have great potency in anti-inflammation and neuroprotective effects. Naltrexone is a safe and readily available generic medication. Dextromethorphan is also a safe and readily available generic medication that is available without a prescription as a cough medication. Results from several clinical trials showed that Naltrexone is effective in several inflammation-related diseases, such as neurogenic pain, movement disorders, etc. In addition, there were no obvious side effects in patients taking this drug for six months. This project is a randomized double-blinded studies for treating ill Gulf war veterans with Naltrexone and Dextromethorphan. Laboratory tests for markers of inflammation including neurogenic inflammation will be performed pre- and post-treatment, to see if these markers are elevated and if so, to see if treatment modulates these markers.

BODY

The major accomplishment of the past year was successfully recruiting and enrolling veterans with Gulf War Illness in the study. Compliance of those enrolled has been excellent.

A no cost extension has been obtained, so we can continued the study for a final year. We anticipate accomplishing study goals and objectives.

KEY RESEARCH ACCOMPLISHMENTS

The most significant accomplishment during the past year was successfully recruiting and enrolling significant numbers of veterans with Gulf War Illness in the clinical trials. Compliance with study protocols has been excellent. Data collection has been complete with no gaps on last data review.

Total Enrolled	41
Loss to follow-up	1
Completed combined naltrexone & dextromethorphan protocol	2
Completed naltrexone only protocol	1
Completed dextromethorphan only protocol	1
Currently enrolled in naltrexone protocol	27
Currently enrolled in dextromethorphan protocol	27
Discontinued naltrexone due to adverse reaction (subjective dizziness)	1
Discontinued dextromethorphan due to adverse reaction	0

In addition, we successfully obtained a no cost extension to continue the study for the coming year. We anticipate a successful outcome to the study at the end of this annual study period.

Our goal is to meet the study target of 60 patients enrolled. We have stepped up recruitment efforts.

REPORTABLE OUTCOMES

No data has been analyzed. There has been only one adverse event, with one subject reporting subjective dizziness while taking naltrexone. This was discontinued and he proceeded to the dextromethorphan arm.

CONCLUSIONS

Successful recruitment, enrollment, compliance, and data collection has been gratifying. We anticipate a successful outcome to the study aims and objectives.

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