



175 Bloor Street East
Suite 700, North Tower
Toronto, Ontario M4W 3R8
Telephone: (416) 922-6065
Fax: (416) 922-7538
www.mssociety.ca

MEDICAL UPDATE MEMO
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**SMALL STUDY OF MINOCYCLINE SHOWS
PROMISE AS MS THERAPY**

SUMMARY

A small pilot study headed by Dr. Luanne Metz, associate professor of neurosciences at the University of Calgary and director of the MS Clinic at Foothills Hospital, has found that minocycline, an oral medication used to treat acne, decreased MS lesions in the brains of study participants. Study results were published in the May 2004 issue of the *Annals of Neurology*. The MRI portion of the study was headed by Dr. Ross Mitchell, associate professor at the University of Calgary. The findings offer the possibility of a new and safe treatment option for people with MS. The study grew out of basic laboratory research led by Dr. V. Wee Yong, professor of oncology and clinical neurosciences at the University of Calgary. The research found that minocycline decreased tissue damage and improved movement in mice with MS-like disease and spinal cord injury. The MS Society of Canada funded Dr. Yong's initial research while the current pilot study in MS patients was funded by an Interdisciplinary Health Research Team grant from the Canadian Institutes of Health Research. The potential use of minocycline as a treatment for MS will be studied further in a just announced clinical trial which will study the combined use of minocycline with Copaxone (glatiramer acetate).

DETAILS

A small pilot study headed by Dr. Luanne Metz, associate professor of neurosciences at the University of Calgary and director of the MS Clinic at Foothills Hospital, has found that minocycline, an oral medication used to treat acne, decreased MS lesions in the brains of study participants. Study results were published in the May 2004 issue of the *Annals of Neurology*. Ten people with relapsing-remitting MS took minocycline orally (by mouth) twice a day for six months. There was an initial three-month run-in period during which time participants did not receive active treatment but underwent MRI scans every four weeks. The MRI scans continued at four week intervals once treatment began. Dr. Ross Mitchell, professor of oncology and clinical neurosciences at the University of Calgary, directed the analyses of the MRI scans.

The primary outcome for the study was the change in the number of gadolinium-enhancing lesions in the brain in the treatment period compared to the three-month run-in period. (Gadolinium is a contrast agent which is sometimes injected into the veins of people with MS who are undergoing MRI scans. The gadolinium concentrates in areas where there is inflammation. If there is inflammation in the brain, the gadolinium shows up as a bright spot on the MRI scan.) At the end of the study, the researchers found the number of enhancing lesions was reduced after treatment began. During the untreated period the mean total of enhancing lesions was 1.38 per scan. During the treatment period the mean total of enhancing lesions was 0.22 per scan. This is a relative reduction of more than 84 percent. The study provides preliminary evidence that minocycline may be useful as an MS treatment and that it is safe.

The study grew out of basic laboratory research led by Dr. V. Wee Yong, professor of oncology and clinical neurosciences at the University of Calgary. The research found that minocycline decreased tissue damage and improved movement in mice with MS-like disease and spinal cord injury. Dr. Yong has been studying the role of enzymes called matrix metalloproteinases (MMP) in the disease process. He and his colleagues have found increasing evidence that MMPs are involved in MS activity. Certain MMPs may be responsible for allowing immune system cells to penetrate the central nervous system and to start the attack on the protective myelin covering of nerve fibres. Working with mice that have MS-like disease, Dr. Yong confirmed that minocycline inhibits MMPs and reduces the access of damaging immune system cells to the brain and spinal cord. There is also some evidence that minocycline may protect nerve cells.

Clinical Trial of Minocycline and Copaxone

The potential use of minocycline as a treatment for MS will be studied further in a just announced clinical trial. It will examine the combined use of minocycline with Copaxone (glatiramer acetate). A total of 50 people with relapsing-remitting MS will start Copaxone therapy (via daily injections) and at the same time will receive either oral minocycline or oral placebo tablets for nine months. This randomized, placebo-controlled study will compare Copaxone plus oral minocycline versus Copaxone plus an inactive oral placebo tablet. Earlier studies in animals through a research grant to Dr. Yong from Teva Neuroscience had determined that the combination of Copaxone and minocycline had enhanced benefits in reducing disease in mice with MS-like symptoms.

The primary outcome will be to evaluate MS lesions in the brain by various MRI measures. The study, which is funded by Teva Neuroscience, will take place at the

MS Clinics in Calgary, Vancouver and the University of Montreal MS Clinics and at Dr. Mary Lou Myles practice in Edmonton. All of the clinics mentioned and Dr Myles are enrolling people with relapsing-remitting who are currently not on any MS disease modifying therapy.

Commenting on the study, Dr. Metz pointed out: “The pilot study in people with MS shows great promise for minocycline but we do not have proof as yet that it works. The study sponsored by Teva Neuroscience allows us to further pursue the possible benefits of minocycline and it will also address whether the combination of Copaxone and minocycline will result in greater benefit for patients. The team approach at the University of Calgary has allowed us to rapidly translate bench research to clinical trials.”

The Multiple Sclerosis Society of Canada funded Dr. Yong’s initial research to explore the potential benefits of minocycline in mice with MS-like disease. The MS Society of Canada is funding Dr. Mitchell’s studies of MRI in MS.

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