My prog-MS ezine

For people with progressive MS and those interested in it

Free Issue 16, November/December 2017

Welcome to issue 16 of my ezine about progressive MS and MS progression. My name is Ian Cook. I'm a secondary progressive MSer from Birmingham, UK.

In this issue are five pages of news plus a feature about an antihistamine drug used to treat common allergies and available from high street pharmacies which has the potential to repair myelin, according to research published in the Lancet. These much more too, just look inside.

If there is any story you would like me to follow then I'm at iancookjournalist@yahoo.co.uk

IN THIS ISSUE

Further evidence that new drug siponimod slows progression of SPMS

A new experimental drug called siponimod led to a dramatic drop in the number of inflammation patches in the brains and spinal cords of secondary progressive multiple sclerosis (SPMS) patients, according to a Phase 3 clinical trial.

Robert Fox of the Cleveland Clinic's Mellen Center for Treatment and Research in Multiple Sclerosis presented the findings at the 7th Joint ECTRIMS-ACTRIMS Meeting in Paris held in October. The results that Fox presented strengthened earlier findings demonstrating that siponimod slows the progression of secondary progressive multiple sclerosis (SPMS).

His presentation focused on magnetic resonance imaging measurements of lesions during the Phase 3 EXPAND trial (NCT01665144). It was titled "Effects of siponimod on MRI outcomes in patients with secondary progressive multiple sclerosis (SPMS): results of the phase 3 EXPAND study."

The trial covered 1,645 patients randomly assigned to treatment with either siponimod or a placebo. For every patient receiving a placebo, two received siponimod, with a total of 1,099 siponimod-treated patients.

Participants had MRI scans at the beginning of the study and every 12 months afterward. Researchers recorded both the number of new lesions and the number of existing ones that were growing. They also recorded the number of lesions with active inflammation, and patients' brain volume loss.

A key finding was that siponimod reduced the number of patients' gadolinium-enhancing inflammatory lesions by 86.6 percent after a year. After two years, the average reduction was even better — 91.1 percent. Gadolinium-enhancing lesions indicate that inflammation is ongoing. Another important finding was that siponimod-treated patients had experienced 39 percent less brain volume loss than placebo-treated patients after a year.

"Siponimod significantly reduced MRI lesion activity and slowed brain volume loss in patients with SPMS as early as month 12, with effects sustained to month 24," Fox said.

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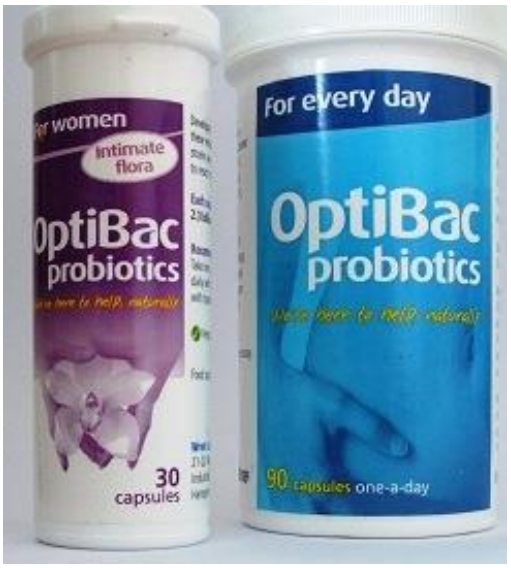

Taking probiotics could reduce disability, say researchers

Probiotics may improve the health of people with MS by reducing disability, an Iranian study claims.

In the study researchers investigated the impact of probiotics on a group of MS patients, looking at a variety of factors including disability scores. Researchers at Tehran's Shahid Beheshti Hospital recruited 60 MS patients, divided them in half, and assigned 30 to take a probiotic capsule and 30 a placebo once a day for 12 weeks.

The probiotic contained the healthy bacteria Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum and Lactobacillus fermentum. Researchers measured patients' health and disability scores at the start and after treatment.

The results showed that probiotic intake after 12 weeks improved MS patients' disability scores (assessed by the expanded disability status scale, EDSS) when compared to placebo controls. Although this improvement was statistically significant, it was not clinically significant — which is defined as a change of 1.0 point or more at EDSS levels less than 5.5, or 0.5 point or more at EDSS levels greater than 5.5).

Moreover, benefits were also detected in several mental health measures – Beck Depression Inventory, general health questionnaire-28 (GHQ-28), depression anxiety and stress scale. Consuming probiotic capsules also significantly decreased insulin levels and high-density lipoprotein (HDL) cholesterol in circulation, researchers also found. It also lowered certain markers of inflammation and oxidative stress, such as serum high-sensitivity C-reactive protein (hs-CRP) and malondialdehyde (MDA).

The researchers say live microorganisms linked to health benefits, known as probiotics, have long been known to help patients with chronic diseases

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Gut bacteria may play role in MS progression

Two newly published studies have established a potential role for specific gut bacteria in the progression of MS, suggesting that targeting the microbiota in people with MS has a potential role for treating the disease.

In one study, published in Proceedings of the National Academy of Sciences, (PNAS) a team led by University of California, San Francisco (UCSF) researchers using a mouse model of the illness discovered certain gut microbes play a role in the neurodegeneration inherent in MS.

In the study, researchers sequenced the gut microbiome of 71 MS patients as well as 71 healthy control subjects. They identified distinct species of bacteria that were in higher concentrations in people with MS than in the general population. The UCSF team found two species more common in people with MS, that triggered human immune cells to become pro-inflammatory. As well as this one bacteria found at lower than usual levels in MS patients, triggered an immune-regulatory response as well.

In another study published in the same issue of PNAS, a team led by researchers from the Max Planck Institute of Neurobiology compared the gut microbiota of 34 twin pairs – one of whom had MS. While they found no major differences in the overall human microbial composition, the researchers saw a significant increase in certain bacteria in the twin with MS, The researchers' data suggests that MS-derived microbiota potentially contain factors that precipitate an MS-like autoimmune disease in mice, and more importantly, in humans.

Study suggests possible role for low dose naltrexone in MS treatment

A team of US researchers have identified Opioid Growth Factor (OGF) as a biomarker for the progression of MS. Their work has focussed interest on Naltrexone which affects levels of OGF levels and is claimed by some to help their MS

The latest research was published in Experimental Biology and Medicine (Volume 242, Issue 15, September 2017) and carried out in the US. It demonstrated that OGF levels were decreased in patients with MS relative to non-MS patients. Low dose naltrexone (LDN) is an off-label therapeutic which intermittently blocks opioid receptors that control pain, reward, and addictive behaviour, resulting in an increase in production of OGF. In the current study researchers examined OGF levels in MS patients as well as an MS animal model. Serum levels of OGF were significantly reduced in MS patients when compared to normal individuals.

Collaborative studies found that in the experimental autoimmune encephalomyelitis (EAE) mouse model of MS reductions in OGF were linked to disease development.

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Asthma drug Significantly Slows Brain Atrophy in Progressive MS

An anti-inflammatory drug called Ibudilast used in the treatment of asthma slowed the rate of brain atrophy by 48% without inducing significant toxicity among patients with primary and secondary MS according to findings from a phase II trial presented at the 2017 ACTRIMS/ECTRIMS MS Meeting held recently in Paris.

This figure of 48% is slightly higher than the 43% annualised reduction rate in brain atrophy recorded among patients with secondary progressive MS who took the statin called Simvastatin for two years in research published in the Lancet in 2014. Simvastatin is currently in phase III trials.

In the Ibudilast trial – results of which were presented at the 2017 ACTRIMS/ECTRIMS MS Meeting - criteria for inclusion were that patients had to be up to 65 years old, and have primary or secondary progressive MS. Patients who were taking beta interferon and glatiramer acetate were allowed on the trial. 86% finished the trial and about 5% more people stopped taking Ibudilast.

The main side effects were gastrointestinal problems including pain, vomiting and diarrhoea. There was an increase in rashes and depression. In addition, fatigue was slightly worse

Ibudilast is affects levels of macrophage migration inhibitor factor (MIF), PDE-4, PDE-10, and Toll-like receptor 4. These two factors are believed to give it a potential neuroprotective effect. Ibudilast is approved in Japan as a treatment for bronchial asthma and post-stroke dizziness.

The other suggested reason for its success in MS is that Ibudilast has been found to be a macrophage inhibitor, and many researchers believe this may be the key to its action because for some time scientists have said that macrophages/microglia are at the centre of the inflammatory response in MS.

A third possible explanation for the success of Ibudilast is that Ibudilast also inhibits TNF (tumor necrosis factor). TNF is a primary neurotoxic molecule in progressive forms of MS so inhibiting TNF may also be a good thing. As Ibudilast is already in use, getting it over the various regulatory hurdles (EMA/ NICE) for MS should be easier and quicker than with new drugs.

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Over-the-counter antihistamine drug repairs myelin damage in MS patients

An antihistamine drug used to treat common allergies has the potential to repair myelin, according to research published in the Lancet. The research, if reproduced in larger trials, could represent a milestone in developing a radical new treatment for progressive MS.

In the research, carried out at the University of California, a 150-day trial treated patients with MS who experienced chronic demyelinating optic neuropathy. The researchers chose to focus on this symptom in particular because it is more commonly one of the first symptoms people with MS experience. The researchers measured so-called visual evoked potentials (VEPs), which is a well-established method of assessing how quickly nerves conduct messages.

Fifty patients were randomly assigned to two groups. Group 1 saw patients receive active treatment over the first 90 days followed by a placebo for 60 days and group 2 received a placebo for 90 days, followed by active treatment for 60 days without a washout between the two periods. Each patient was given unmarked capsules of 5.36 mg clemastine fumarate or a placebo twice daily. Neither the groups nor scientist knew which treatment they were being given and when.

Visually Evoked Potentials were measured by showing participants flickering patterns on a screen. Electrodes placed over the visual areas of the brain detected how long it took signals to travel from the eye to the relevant area of the brain. The results showed that the drug increased the speed of the neural signals from the eye to the back of the brain. Even once the experimental group stopped taking the medication and moved on to the placebo, the increased speed persisted.

The scientists were not able to measure myelin regrowth using MRI scans because of the limited technology available. However there was still strong evidence that re-myelination occurred because there was no other explanation as to how VEPs could be increased. There are currently no drugs available that are able to recreate myelin, so clemastine could be an important milestone for a possible future treatment. **Continued on page 7**

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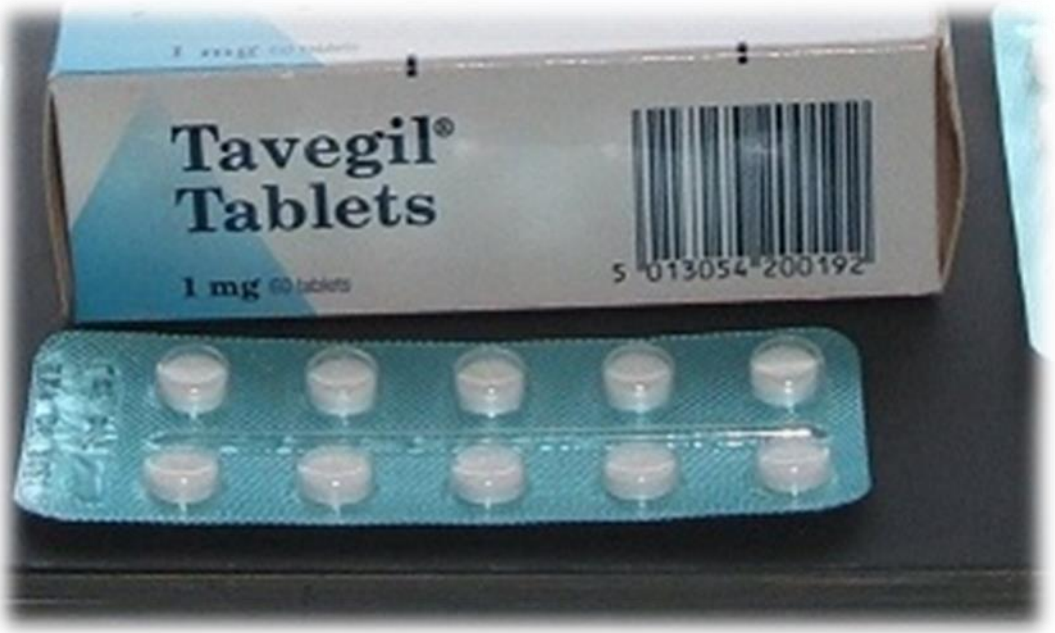
Clemastine fumarate, brand name Tavegil, was first approved by the Food and Drug Administration (FDA) in 1977 and is currently available over the counter in pharmacies for the treatment of other conditions, such as allergies. The dose used in the research (5.36 mg twice daily) is far higher than the dose contained in over the counter Tavegil tablets which are 1 mg).

A further phase III study will need to be conducted before Clemastine fumarate can be considered and approved by NICE as a treatment for MS.

It is significant that the scientists behind the research said the following: **To our knowledge, this is the first randomised controlled trial to document efficacy of a remyelinating drug for the treatment of chronic demyelinating injury in multiple sclerosis. Our findings suggest that myelin repair can be achieved even following prolonged damage**."

In the past clemastine fumarate was found to stimulate differentiation of oligodendrocyte precursor cells (myelin making cells) in lab tests carried out in animal models and in human cells.



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Fats and oils impact on disability in prog-MS

A study has shown a significant link between the intake of saturated fatty acids and disability and fatigue in MS patients with progressive MS .

The study consisted of 126 MS patients including 21 with primary progressive (PPMS)and 21 with secondary progressive (SPMS) who were recruited with MRI assessment of the brain and spinal cord from an MS clinic in Kashani Hospital of Isfahan University of Medical Sciences in Iran.

All participants were assessed using a 168-item food questionnaire to assess dietary intakes of fatty acids, a medical history questionnaire, the expanded disability status scale (EDSS) and a fatigue questionnaire.

There was a significant correlation between intakes of polyunsaturated fatty acids (PUFAs) including linolenic acid and linoleic acid with EDSS in all participants. In addition, there was a significant negative correlation between intakes of mono unsaturated fatty acids (MUFA) with EDSS in all participants. Correlation between saturated fatty acids (SFAs) with EDSS and fatigue scale was significantly positive in all participants. Correlation between total dietary fats with EDSS and fatigue scale in all participants and subgroups were positive, but not significant.

Researchers concluded that the study demonstrated that there is a positive and significant correlation between intakes of saturated fatty acids with EDSS. In addition dietary intakes PUFAs and MUFAs can decrease EDSS in all patients with MS.

Falls surprisingly common among wheelchair and scooter users

The majority of people living with MS who use wheelchairs or scooters for mobility reported falling at least once during a six-month period, according to a new study.

A new study recruited 44 MS patients from May 2014 to July 2015 who required wheelchairs or scooters to move about. These patients were from medical centres across the United States and Asia. They were asked to complete a survey focusing on the prevalence of falls, the frequency of injuries, the circumstances surrounding the falls, and quality-of-life indicators. Thirty-three of the 44 participants (75 percent) reported falling at least once in the previous six months. This number is higher than any of the other studies that assessed the prevalence of falls in MS patients. Many of these people experienced more than one fall within those six months. Of these falls, 87.5 percent occurred inside the home.

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References contact details etc

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Siponimod story

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Page 3 Probiotics story

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Page 4gut microbes

Source: https://www.genomeweb.com/autoimmune-disease/gut-bacteria-may-impact-multiple-sclerosis-progression

Page 4 Naltrexone

Source: Medical Express https://medicalxpress.com/news/2017-09-biomarker-multiple-sclerosis.html

page 5 Ibudilast

Source; Source: http://www.mdmag.com/conference-coverage/ms-paris-2017/ibudilast-significantly-slows-brain-atrophy-for-progressive-ms

P 6-7 clemastine/Tavegil

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P8 Iranian study on fats and oils

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Page 8 wheelchair/ scooter user falls

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To Contact me email iancookjournalist@yahoo.co.uk or via twitter@iancookMSer