**Treating Agitation in Alzheimer Disease .... Is Donepezil Effective?**

*Donepezil found to be no more effective than placebo for behavioural problems.*

Previous studies, sponsored by the pharmaceutical industry have reported that cholinesterase inhibitors such as donepezil (Aricept) reduce agitation and have a beneficial effect on cognitive ability in patients with Alzheimer disease. The cognitive ability and agitation levels of 221 Alzheimer patients were assessed over a 12 week period in a British study. The study subjects were selected from a group of patients who were unresponsive to a 4 week trial of psychosocial therapy. The patients were blinded to receive either a placebo or donepezil (titrated to 10 mg daily). Patients taking psychotropic medications were included in the study group.

No improvement in agitation was observed in the patients taking donepezil contrary to the results of previous industry-sponsored studies. There was however a significant but modest improvement in the cognition scores.

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**Fructose Linked to Gout**

*Sugar-sweetened soft drinks contribute to the development of gout.*

Sugar-sweetened soft drinks containing high-fructose corn syrup cause a rapid increase in blood uric acid levels. The consumption of regular, non-diet soft drinks in the U.S. has increased dramatically in the past few decades and parallels the increased incidence of gout.

A prospective study of over 46,000 males during a 12 year period found that the consumption of one sugar-sweetened soft drink a day increased the risk of developing gout by 1.45 compared with the consumption of one soft drink a month. The relative risk increased to 1.85 when two soft drinks a day were consumed. People with a high fructose intake from other sources such as fruit juices, fruits or other dietary products experienced more cases of gout in relation to their total daily fructose consumption. Diet soft drinks are not associated with a higher risk of developing gout.

Concern with the study design has been expressed due to the selection of patients, since only patients unresponsive to psychosocial measures to control agitation were included. These patients may have been more severely ill and refractory to treatment “however, patients’ baseline agitation scores were relatively low”. It was also noted that “the psychosocial intervention did not include sleep-wake cycles and using a night light”.

The authors concluded that it is inappropriate to use cholinesterase inhibitors (e.g. Aricept) to manage agitation in Alzheimer patients since it appears to be ineffective. “Clinicians should assess agitated demented patients carefully for reversible medical and environmental factors as well as use of medications that could be contributing to the problem before adding new medications that appear, at best, to be ineffective”.

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**Statins Implicated in Tendon Problems**

*Clinicians should routinely assess patients for symptoms of tendon problems during the first year of statin therapy.*

An online publication, *Arthritis & Rheumatism*, suggests that tendonitis and tendon rupture, particularly in high risk patients, may occur in patients taking statins. It should be noted that tendon effects with statins is extremely rare (occurring in about 2% to 5% of patients). Statin trials have not reported tendon problems but anecdotal reports over a 15 year period were noted at 31 French Pharmacovigilance Centres.

Most tendon complications were tendinitis but tendon rupture did occur and some patients required hospitalization. Patients reporting tendon effects were an average age of 56 years and experienced symptoms within the first year of treatment. About 30% of patients had concomitant conditions such as diabetes and hyperuricemia and participated in sports. Drugs such as steroids or some antibiotics (e.g. fluoroquinolones) were thought to possibly increase the toxicity of statins. In all cases tendon problems occurred after starting a statin and “cleared up or improved after stopping the drugs and returned in 7 patients who were restarted on statins”. Pain, swelling, warmth and stiffness were the most commonly reported symptoms.
Zeldox 20, 40, 60 & 80 mg capsules
ziprasidone hydrochloride

Pfizer (not currently a benefit of ODB)

Zeldox is a new atypical antipsychotic drug indicated to treat schizophrenia and related psychotic disorders. It is not indicated in elderly patients with dementia due to an increased risk of death. Zeldox is as effective as other atypical antipsychotics (e.g. Zyprexa, Seroquel and Risperdal) in the treatment of schizophrenia and often results in less weight gain. Zeldox has a greater tendency to prolong the QT interval.

Contraindications, Warnings & Precautions:
- Zeldox is contraindicated in patients with a known history of QT prolongation, recent MI or uncompensated heart failure.
- Zeldox should be used in pregnancy only when the benefits outweigh the risks. Breastfeeding is not recommended.
- Geriatric patients may be more sensitive to Zeldox’s effects and experience poorer tolerance or orthostatic hypotension.
- Zeldox is contraindicated in elderly patients with dementia.
- Caution should be exercised in patients with dysphagia due to the risk of aspiration pneumonia.
- Patients with hepatic impairment may require lower doses.
- Serum potassium and magnesium levels should be measured before starting treatment with Zeldox. Low levels should be corrected before starting treatment.
- Zeldox may disrupt the body’s ability to regulate core body temperature. Caution is advised where patients are at risk of overheating (e.g. strenuous exercise, extreme heat, concomitant medication with anticholinergic activity or dehydration).
- Patients with a history of drug abuse should be observed closely for signs of misuse or abuse (e.g. development of tolerance, increase in dose, drug seeking behaviour).
- Zeldox has been associated with the development of neuroleptic malignant syndrome.
- Patients should be monitored for signs of hyperglycemia.

Adverse Effects:
Common adverse effects include somnolence, extrapyramidal symptoms and respiratory tract infections. Less commonly reported adverse effects include nausea, dry mouth, digestive disturbances, anorexia, myalgia, dizziness, akathisia, rhinitis, cough, fungal dermatitis and abnormal vision.

Drug Interactions:
- Zeldox should not be used with any drugs that prolong the QT interval (e.g. chlorpromazine, thioridazine, dolasetron, quinidine, sotalol, moxifloxacin, etc.).
- Use Zeldox with caution when administered concomitantly with other central nervous system drugs (e.g. alcohol, opioids, etc.).
- Use of Zeldox with antihypertensive drugs may induce hypotension.
- Zeldox may antagonize the effects of levodopa and other dopamine agonists (e.g. bromocriptine, pergolide, pramipexole, etc.).
- The administration of ketoconazole (and other potent CYP3A4 inhibitors) has the potential to increase Zeldox serum concentrations.
- Zeldox drug levels may be reduced with concomitant use of carbamazepine.
- Lithium, when given with Zeldox, may increase the risk of developing arrhythmias.

Dose & Administration:
Zeldox should be administered with food to increase absorption. Zeldox therapy should be evaluated periodically to determine the need for maintenance therapy.

Initial adult dose (18 years of age & older): 20 mg to 40 mg twice daily with food.

Maintenance dose: Dose adjustments may be made at intervals of not less than 2 days. The maximum recommended dose is 80 mg twice daily.

Hepatic impairment: Lower doses should be considered in mild to moderate hepatic impairment. There is a lack of experience in patients with severe hepatic impairment.

Refer to the product monograph for complete information

Beginning April 1, 2008, Canadians will have access to timely, easy-to-use and credible public health information through the Public Agency of Canada’s Web site: http://www.phac-aspc.gc.ca. Visit the site and subscribe to a new e-alert feature available soon.