Low Testosterone Levels in Postmenopausal Women Associated with Increased Cardiac Risk

Researchers in California evaluating the role of naturally occurring testosterone in older women followed 678 postmenopausal women 50 to 90 years of age over a 20 year period. None of the women were taking estrogen. They were divided into 5 groups based on their testosterone levels. The normal testosterone level for postmenopausal women is about 170 pg/ml or less. The study group with the lowest testosterone levels had values of 80 pg/ml or less.

The results indicated that “women with testosterone levels in the lowest quintile had twice the risk of prevalent coronary heart disease, incident coronary heart disease (defined as first ever myocardial infarction or revascularization procedure) and coronary heart disease mortality. Increased cardiac risk was independent of the presence of coronary heart disease risk factors, diabetes and the metabolic syndrome”.

The researchers concluded that low testosterone levels were associated with an increased risk of mortality due to coronary heart disease. It is not known whether these results apply to women receiving estrogen supplementation because this group of women were excluded from the study.

Drug Interaction Updates

Venlafaxine & Antipsychotic Interaction

Venlafaxine (Effexor) has been shown to prolong the QTc interval at recommended doses. Antipsychotics known to prolong the QTc interval include risperidone (Risperdal) and quetiapine (Seroquel). Although no formal studies have been done with the combination, “the coadministration of drugs known to prolong the QTc interval is not recommended”. It is thought that coadministration of these drugs would likely have an additive effect on the QTc interval posing a major risk factor for cardiac toxicity.

Cranberry Juice & Warfarin Interaction … No Longer Considered a Problem

Several years ago reports surfaced that cranberry juice could significantly increase the INR in patients taking warfarin. Researchers now say that drinking cranberry juice is “not likely to cause a problem for most people”. With that in mind it is important to note that significant dietary changes can alter warfarin response.

Chondroitin Not Effective for Osteoarthritis Pain

Earlier studies suggested that chondroitin was beneficial for osteoarthritis. Subsequent larger, higher quality studies have shown that chondroitin alone shows no benefit and there is no evidence that the combination of glucosamine and chondroitin is more effective than glucosamine alone. The use of glucosamine sulfate alone is best supported by the current evidence.

Warfarin & Corticosteroids

New data has emerged indicating a significant interaction between warfarin (Coumadin) and oral corticosteroids (prednisone, prednisolone). It is thought that corticosteroids alter the hepatic metabolism of warfarin resulting in either a decrease or an increase in INR values. Changes in INR’s may occur between 2 and 20 days after starting a corticosteroid. The effect on warfarin levels in some patients can be extreme with INR’s increasing from a therapeutic range to greater than 5.

Monitoring of INR’s is recommended if these drugs are coadministered.
**Champix 0.5 mg & 1 mg varenicline tartrate tablets**

**Pfizer**

(not currently a benefit of ODB)

Champix is a new oral smoking cessation therapy which partially stimulates the nicotine receptors in the brain (but less than nicotine itself). The stimulation of nicotine receptors (i.e. the ?482 nicotinic acetylcholine receptors) partially stimulates the release of dopamine which is thought to be responsible for the reward and reinforcement experienced when smoking. Champix also helps to block the pleasurable effect of smoking derived from the binding of nicotine to the nicotine receptors. The craving and symptoms of withdrawal are reduced when Champix is administered.

**Precautions:** Champix is not indicated in patients under 18 years of age or in patients with end stage renal disease. Reduced doses are recommended in patients with severe renal impairment. The use of Champix has not been studied in psychiatric patients. “Smoking cessation with or without pharmacotherapy has been associated with the exacerbation of underlying psychiatric illness”. Champix has demonstrated reproductive toxicity in animals, therefore should not be used in pregnancy. It is not known if the drug is excreted in human breast milk.

**Drug Interactions:**

- The incidence of adverse reactions (nausea, headache, vomiting, dizziness, dyspepsia and fatigue) may be greater in patients taking concomitant nicotine replacement therapy and Champix. The addition of nicotine replacement therapy is not expected to be of greater benefit than the administration of Champix alone.

- In severe renal impairment the concomitant administration of Champix and cinmetidine, trimethoprim, ranitidine or levofoxacin is not recommended due to the resulting significantly increased blood levels of Champix.

Champix does not appear to inhibit or induce the cytochrome P450 system.

**Adverse Effects:** The most common adverse effect is nausea which occurs in 30% of patients taking the 1 mg twice daily dose and in 16% of patients taking the 0.5 mg twice daily dose. Nausea is generally mild to moderate in intensity, dose-dependent and usually resolves with time. Other adverse effects include abnormal dreams (13%), constipation (8%), flatulence (6%) and vomiting (5%).

**Dose & Administration:** Champix is available in two formats: a 2 week starter pack and a two week continuation pack. The recommended dose is as follows: days 1 to 3 … 0.5 mg once daily
days 4 to 7 … 0.5 mg twice daily
days 8 to 14 … 1.0 mg twice daily
weeks 3 to 12 … 1.0 mg twice daily

**Dosing in severe renal impairment:**
days 1 to 3 … 0.5 mg once daily
days 4 to end of treatment … 0.5 mg twice daily

Patients begin treatment 1 to 2 weeks before their target quit date. For best results Champix administration is most effective when combined with patient counselling and/or support services for smoking cessation. At the end of 12 weeks of treatment, patients who do not stop smoking or who experience a relapse after treatment may continue Champix for another 12 week course. Dose adjustments are not necessary for patients with mild renal disease (estimated creatinine clearance greater than or equal to 50 ml/min and less than or equal to 80 ml/min) to moderate renal disease (estimated creatinine clearance greater than or equal to 30 ml/min and less than or equal to 50 ml/min).

**Availability & Storage:** Champix is available as a 0.5 mg capsular biconvex, white to off-white, film-coated tablet debossed with “Pfizer” on one side and “CHX0.5” on the other side. The 0.5 mg tablets are supplied in bottles of 56 tablets and blister strips of 11 tablets.

The 1.0 mg capsular biconvex, light-blue, film-coated tablet is debossed with “Pfizer” on one side and “CHX1.0” on the other side. The 1.0 mg strength is supplied in blister strips of 14 tablets.

The initial dosing pack includes 0.5 mg tablets in blister strips of 11 tablets and 1.0 mg tablets in blister strips of 14 tablets.

Champix tablets should be stored at room temperature (15° to 30°C).

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**Congratulations to both Syd Shrott, Sr. VP and Carole McKee, VP (retired) of Medical Pharmacies on receiving Centennial Pharmacists Awards at the 100th Anniversary conference of the Canadian Pharmacists Association. The award recognizes leadership in CPhA and the pharmacy profession.**