Cardiovascular Implications of Viagra

Dear Colleagues,

Viagra (sildenafil) has just been released to the Canadian market. This will have a significant impact on our practises. We all can expect to see many patients who will ask for the medication or who wish to be informed of the safety and suitability of this agent in their case. Many patients with erectile dysfunction have manifest or occult coronary artery disease. In this context it is important that we are all well versed in the cardiovascular implications of Viagra.

Erectile dysfunction (ED) - Clinical context:

- ED is common-52% of men age 40-70 (10% complete;25% moderate;17% minimal)
- > ED is a marker of underlying organic disease:
 - Atherosclerosis (CAD,PVD), hypertension, diabetes, renal failure, hepatic failure
 - Hyper or hypothyroidism, hypogonadism, hyperprolactinemia
 - Alzheimer's disease, multiple sclerosis
 - Depression
 - Spinal injury, autonomic dysfunction
 - Post urologic surgery
- ➤ Medications may be implicated in ED:
 - Anti-hypertensives, anti-depressants, hormones, tranquillisers
 - Alcohol, smoking, diet

Sexual activity and the cardiac patient:

- Energy expenditure of intercourse (3-4 METS)
- Energy expenditure of ejaculation and intercourse (4-5 METS)
- Equivalent activities¹
 - Walking 3 mph, level = 3-3.5 METS
 - Bruce protocol stage I = 5 METS
 - Golf, pulling cart = 3-4 METS/carrying clubs = 4-5 METS
 - Bruce protocol stage II = 7 METS
 - Walking upstairs = 4-7 METS
 - Cycling 12 mph, level = 7-8 METS
 - Swimming- front crawl = 9-10 METS
- Risk of repeat MI triggered by sexual activity in MI survivors²
 - Low risk male (non-smoker, non-diabetic, 50 years old) 1.01/million/hour
 - Clinically high risk male 1.2 /million/hour
 - Risk decreases with regular physical activity ≥ 6 METS
 - 0-1/wk RR 3.0
 - 2x/wk RR 1.9
 - $\geq 3x/wk$ RR 1.2

Patients in Whom Sexual Activity May Carry Significant Cardiovascular Risk:

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¹ Pashkow and Dafoe, Eds. Clinical Cardiac Rehabilitation, Appendix A. 1999.

² Muller JE et al. JAMA. 1996;275:1405-1409.

Reference: ACC/AHA Expert Consensus Document; Use of Sildenafil (Viagra) in Patients With Cardiovascular Disease. Circulation. 1999;99:168-177. (www.circulationaha.org)

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Sexual activity carries a small but defined CV risk, even in asymptomatic patients, however patients with the following conditions should not receive any therapy for ED until the CV condition has been clarified and stabilized.

- Patients with recent acute cardiac ischaemic syndromes (six weeks)
- Patients with angina or ischaemia at low levels of exercise(unable to complete stage I of Bruce protocol or climb 2 flights of stairs; approximately 4-5 METS)
- Patients with poorly controlled, severe HPT (SBP > 180 or DBP > 115 mm Hg)
- Patients with recent Cerebrovascular event (less than 6 weeks)
- Patients with any medical or surgical condition that may be aggravated by sudden increases in BP
- Inactive patients with CV disease or significant risk factors who are presently sexually inactive and in whom functional activity has not been determined.

Which Patients Require Cardiac Evaluation Prior to Starting Viagra?

- All patients with Class III dyspnea or angina
- Post MI or post unstable angina
- Patients receiving complicated multi-drug anti-hypertensive therapy
- Patients with significant aortic stenosis

Patients to Whom Viagra (sildenafil) should be Prescribed with Caution:

- Patients with active coronary ischaemia and are not on nitrates
- Patients with CHF and borderline low BP or borderline low volume status
- Patients with severe renal or hepatic dysfunction (\$\sqrt{\sildenafil}\$ metabolism)
- Patients on drugs that can prolong the half life of Viagra (erythromycin, cimetidine)
- Patients with retinitis pigmentosa

Nitrate / Viagra Interaction:

- Viagra is a potent inhibitor of cGMP-specific phosphodiesterase type 5
- Viagra enhances the relaxant effect of endogenous NO on the corpus cavernosum
- Systemic effects: a balanced modest vasodilator/ anti-spasmodic which will enhance the vascular actions of endogenous NO (nitric oxide). Similar to a weak nitrate. No direct cardiac effects.
- Potentiates the hypotensive effects of exogenous nitrates resulting in severe hypotensive response.
- Administration to patients who are currently using organic nitrates in any form is contra-indicated.
- This includes; Sublingual NTG tablets or spray, oral long acting nitroglycerin preparations, isosorbide mononitrate, isosorbide dinitrate, sodium nitroprusside and amyl nitrate (poppers)

Nitrates in any form are contra-indicated for 24 hours after Viagra administration. Patients should alert ambulance attendants and ER staff that they have <u>Viagra on board</u> should chest pain or ischaemia develop during its use. Anti-ischaemic measures should avoid nitrate administration.

Reference: ACC/AHA Expert Consensus Document; Use of Sildenafil (Viagra) in Patients With Cardiovascular Disease. Circulation. 1999;99:168-177. (www.circulationaha.org)