The Effect of Vardenafil, a Selective PDE5 Inhibitor, on Ischemic Threshold, Exercise Tolerance, and Circulatory Responses During Treadmill Exercise in Men With Stable Angina Pectoris

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Background: Erectile dysfunction (ED) is common among men with CAD. Vardenafil (5, 10, and 20mg) is an efficacious oral treatment for ED. The effects of vardenafil 10mg on exercise parameters in patients with stable angina and reproducible exertional cardiac ischemia were previously evaluated; this study examined the effects of vardenafil 20mg in a similar patient population.

Methods: In this double-blind, crossover, single-dose, multicenter study, 39 men randomized to vardenafil 20mg or placebo were evaluated by symptom-limited exercise treadmill test (ETT) one hour post-dose, the time of maximal drug exposure. Nitrates were prohibited during the study.

Results: Majority of men (mean age 63.6 y [range 48-80 y]) received beta-blockers (28/39), aspirin (28/39) and lipid lowering drugs (28/39). Data derived during exercise is shown.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Vardenafil 20mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treadmill Exercise Time, sec</td>
<td>361±484</td>
<td>361±482</td>
</tr>
<tr>
<td>Time to Angina Pectoris*, first awareness, sec</td>
<td>361±484</td>
<td>361±482</td>
</tr>
<tr>
<td>Time to ST-Segment depression&gt; 1 mm a from baseline</td>
<td>361±484</td>
<td>361±482</td>
</tr>
<tr>
<td>Rate-pressure product, peak exercise*, mmHg x BPM x 10²</td>
<td>19±3.2</td>
<td>19±3.2</td>
</tr>
</tbody>
</table>

*: median ± SD, p<0.05, based on LS geometric mean ratio of vardenafil/placebo. *includes 1/3 of patients in vardenafil/placebo groups respectively, excluded from ET-

Vardenafil was well tolerated. The most common adverse events during vardenafil treatment (facial flushing and headache) were mild or moderate and transient. One patient receiving vardenafil exhibited post-exercise transient hypotension and dizziness which resolved following oral fluid replacement.

Conclusion: Vardenafil 20mg did not impair stable CAD patients' ability to exercise or alter ischemic threshold at effort levels considered equal to or greater than sexual intercourse.

An Examination of Atorvastatin Safety When Used in Combination With Verapamil: Evidence From 44 Completed Clinical Trials

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Background: Verapamil is a widely prescribed calcium channel blocker used for the treatment of angina, hypertension and supraventricular arrhythmias. Recently, safety questions have been raised about the concomitant utilization of verapamil with statins.

Methods: A well established database that effectively traces (i) randomized trials and (ii) all patients across the 10-80 mg dose range. We investigated whether there was any indication of an interaction between atorvastatin and verapamil as indicated by an increased rate of common statin-associated adverse events in the atorvastatin clinical trial program.

Results: To date, the program consists of 44 completed clinical trials with 9416 patients that have received atorvastatin. Of these 9416 patients, 202 (2.1%) have received concomitant verapamil (50 mg, 10 mg and 30 mg atorvastatin). There were no incidences of myopathy, rhabdomyolysis or CPK elevations >10xULN among the 292 atorvastatin/verapamil patients. The rate of treatment-emergent myalgia in patients taking atorvastatin/verapamil was 9 (3.7%). Of these patients taking atorvastatin/verapamil, an incidence comparable to the overall rate of 0.5% seen in the entire 9416 atorvastatin cohort across all doses.

Conclusion: In conclusion, data from the atorvastatin clinical trial program does not currently indicate an increase rate of muscle or hepatic adverse events when atorvastatin is used concomitantly with verapamil. Additional data will be collected with over 44000 patients currently ongoing in clinical trials with atorvastatin.

The Resuscitative Value of B-Type Natriuretic Peptide in Patients With Out-of-Hospital Cardiac Arrest Due to Cardiac Causes

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Background: B-type natriuretic peptide (BNP) is released by the ventricular myocardium in response to increased wall tension. Although the circulating level of this neuroendocrine hormone has been shown to have a prognostic value in either congestive heart failure or acute coronary syndromes, no data are available for a resuscitative value in out-of-hospital cardiac arrest.

Methods: We constructed a prospective study of 401 patients whose BNP was measured on arrival at the emergency department. The primary end point was survival to hospital discharge.

Results: A total of 63 of the 401 patients survived to discharge from the hospital and the BNP level was lower among such patients than among those who died (<0.001). A value of 100pg/ml or less for BNP was the significant independent predictor of the survival with an odds ratio of 0.04 to 0.45, 0.10 (95% CI, 0.03 to 0.36), and 0.008 (95% CI, 0.0 to 0.17). A value of 100pg/ml or less for BNP was the significant independent predictor of the survival with an adjusted odds ratio of 1.0.

Conclusion: The measurement of BNP on arrival at the emergency department provides predictive information for survival to hospital discharge in patients with out-of-hospital cardiac arrest due to cardiac causes.