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Carvedilol Reverses Standing Parasympathetic Excess in Non-Diabetics

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Introduction: There is a segment of the patient population that present with beta-blocker on board and with difficult to control BP, or blood sugars in diabetics, or hormone levels in hypothyroid or menopausal patients. They also present with fatigue or exercise intolerance, depression-like symptoms, sleep difficulties, GI upset, or frequent headache or migraine. The established need for a beta-blocker indicates a previous or continued sympathetic excess. The additional symptoms are associated with parasympathetic excesses that occur during sympathetic challenges in a standard autonomic study (Valsalva and Stand). Anti-cholinergic therapy to address the additional symptoms is contra-indicated given the need for the beta-blocker.

Carvedilol was administered in place of the beta-blocker to address these additional symptoms.

Methods: Serial ANS assessments were administered to 238 Patients (145 Female, 60.8%; averages: 60.1 ± 12.0 years; 63.3 ± 3.8 inches; 150.4 ± 36.7 pounds) in 12 ambulatory clinics. ANS assessment was performed with the ANX-3.0 (ANSAR Medical Technologies, Inc., Philadelphia, PA) and included five minutes of rest and a quick stand followed by five minutes of quiet standing. HR variability analysis concurrent with respiratory activity analysis was performed to independently and simultaneously compute sympathetic (LFa) and parasympathetic (RFa) activity throughout the phases of the ANS study. **Results:** Patients, on average, were well maintained at rest. They presented with (see Table) low normal HR, normal BP), normal sympathetic activity (LFa), low-normal parasympathetic activity (RFa), and normal sympathovagal balance (LFa/Rfa). Upon standing they presented with normal sympathetic responses (an increase from rest), but abnormal parasympathetic responses (an *increase* from rest). These patients were switched from their beta-blocker to dose equivalent or lower Carvedilol (6.25mg bid on average) and retested 4.1 ± 1.1 months later. Their resting responses remained normal, but sympathovagal balance became low-normal which indicating extra parasympathetic activity as recommended to minimize morbidity and mortality. Their stand

responses were normalized. The stand sympathetic response was reduced, yet remained normal and the stand parasympathetic response was corrected from the abnormal increase to the normal decrease. Clinically, patients reported less fatigue or exercise intolerance, improvements in sleep habits (falling asleep in under 20 minutes and fewer waking episodes during the night), a reduced dependency on any prescribed anti-depressants, reduced GI upset, and fewer headache or migraine. **Conclusion:** The two agents included in Carvedilol seems to provide additional benefits for non-diabetics requiring a beta-blocker.

Measure	Pre-Carvedilol	Post-Carvedilol
Resting HR (bpm)	61.5±8.5	60.8±8.0
Resting Systolic BP (mmHg)	137.4±26.7	128.5±23.4
Resting Diastolic BP (mmHg)	65.8±10.1	62.4±8.4
Resting Sympathetics (bpm ²)	1.10±0.7	0.63±0.2
Resting Parasympathetics (bpm ²)	0.77±0.3	0.80±0.4
Resting Sympathovagal Balance	1.72±0.2	0.90±0.4
Stand Sympathetic Response	4.67±2.1	1.19±1.0
Stand Parasympathetic Response	2.02±0.4	-1.17±0.3