

Commonly Prescribed Hormonal Therapies and their Relationship to Cardiovascular Disease

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Identify commonly prescribed hormonal therapies

Describe the effect of hormonal therapies on the cardiovascular system

Discuss the role of hormonal therapies in the prevention and treatment of cardiovascular disease (CVD)

Objectives

◦ Hormon, horman, horme ...




What are hormones?

- Endogenous Molecules
 - Internally secreted compounds, formed in endocrine glands and transported by body fluids, that specifically effect function of target organs or tissues

What are hormones?

- Exogenous Molecules
 - Synthetic substance used in medicine to act like such a compound when introduced into the body
 - Calcitriol, Melatonin, Thyroid, Insulin, Glucagon, Dopamine, Vasopressin, Norepinephrine, Calcitonin, Erythropoietin, Prednisone, Growth Hormone, Testosterone, Estrogens

Prescribed Hormonal Therapies



Do hormones effect the Heart?

- Endogenous Cardiovascular hormones
 - Regulate homeostatic processes and are also targeted in clinical syndromes
 - Affects hemodynamics, oxidative stress, and inflammation
 - Include the following:
 - Renin-angiotensin II-Aldosterone System (RAAS)
 - Norepinephrine, Epinephrine, Dopamine
 - Brain-Natriuretic Peptide (BNP)
 - Endothelin
 - C-reactive protein and Cytokines

Do hormones effect the cardiovascular system?

Rainier U. Piquett, Raff Paschke, Christen A. Koch. Hormones of the Cardiovascular System. Nov 29, 2008. 25. www.endotest.org

	Target	SVR	HR	SNS	Ox Stress	CRP
Epinephrine	Endothelial Cell/Vascular Smooth Muscle Cell	↓↑	↑	↑	↑↓	↑
Norepinephrine	VSMC	↑	↑	↑	↑	↓
BNP	EC, VSMC	↓	↔	↓	ND	ND
Angiotensin II	EC, VSMC	↑	↑↓	↑	↑	↔
Aldosterone	EC, VSMC	↑	↔	↑	↑	ND
Endothelin	VSMC	↑	↑↓	↑	↑	↑

Hormonal effects on the cardiovascular system

Rainier U. Piquett, Raff Paschke, Christen A. Koch. Hormones of the Cardiovascular System. Nov 29, 2008. 25. www.endotest.org

- Hormonal therapies
 - Testosterone
 - Androgen replacement therapy
 - Hypogonadism
 - Pharmacological androgen therapy
 - Anemia, steroid dependent autoimmune disease, AIDS
 - Drug abuse
 - Estrogen
 - Post-menopausal therapy, birth control
 - Growth hormone
 - Growth hormone deficiency (GHD)
 - Growth failure associated medical conditions
 - AIDS wasting syndrome
 - Drug Abuse

Effect of hormonal therapies on the cardiovascular system

Pharmacotherapy: a pathophysiologic approach. 6th Ed.

- Surrogate Effects
 - Acute and chronic vasodilation
 - Eugonadal, not hypogonadal men
 - Blood pressure
 - Sodium retention, endothelin production, vasodilation
 - Lipid panel
 - Lowers HDL, LDL, TC, lipoprotein a (Lp (a)) and apo-protein B
 - Obesity
 - Reduce visceral fat mass, enhances insulin sensitivity
 - Prothrombotic factors and inflammatory mediators
 - Reduce fibrinogen, c-reactive proteins and cytokines
 - Erythropoiesis
 - Potential for polycythemia

Testosterone

Mandakovic et al. Reproductive Biology and Endocrinology. 2009; 7:44.
Klein, T et al. Kidney Blood Press Res. 2008; 31:71-79.
Pharmacotherapy: a pathophysiologic approach. 6th Ed.

- Clinical Cardiology
 - Men 2x greater risk of Cardiovascular Heart Disease (CHD) death than women
 - Low-testosterone associations:
 - EPIC-Norfolk data – increased all-cause CVD, CHD, cancer mortality
 - Atherosclerotic progression in men and women
 - Hypertension
 - Testosterone supplementation
 - Positive effect on cardiac ischemia, anginal symptoms, quality of life
 - Symptomatic improvement in elderly men with heart failure
 - No increase in CV death among female to male transsexuals
 - Severe aorta atherosclerosis increased when co-administered w/estrogen in post-menopausal women
 - Increase prostate size and PSA levels, no evidence of increased malignancy
 - Treatment or prevention of CVD??

Testosterone

Mandakovic et al. Reproductive Biology and Endocrinology. 2009; 7:44.
Carroll, C et al. J Am Coll Cardiol. 2009; 54:19-22.
Makris, C.J. et al. Q J Med. 2003; 96:521-529.

- Treatment or prevention of CVD?
 - Intriguing, however more studies necessary

Testosterone

- Case Studies
 - Mr. Fit is a 68 year old male who presents to the community pharmacy complaining of dizziness and lightheadedness... "My pressures are lower than usual, I almost fell getting out of bed!". A review of his medications indicates he was recently initiated on testosterone replacement therapy. He is currently taking four medications for high blood pressure.
 - Does Mr. Fit have a drug therapy problem?

Testosterone

- Surrogate Effects
 - Lipid profile
 - increase HDL and TG, reduce LDL
 - Blood pressure
 - reduce systemic vascular resistance (SVR) and sympathetic activity
 - Improve glucose tolerance
 - Reduce weight and waist circumference
 - Thromboembolism
 - increase coagulation factors
 - Inflammation and oxidation
 - increase c-reactive protein, but reduce oxidative stress

Estrogen

Raher U, Piquart, Rafi P, Zachar, Christen A, Koch. Hormones of the Cardiovascular System. Nov 29, 2008. 25. Pharmacotherapy: a pathophysiologic approach. 6th Ed. Heart Disease: a textbook of cardiovascular medicine. 7th Ed.

- Clinical Cardiology
 - Men 2x greater risk of CHD death than women
 - WHI
 - CHD increased w/estrogen/progestin at 1 yr, overall no difference vs. placebo
 - Increased risk of ischemic stroke and venous thrombosis
 - HERS
 - No effect on recurrent coronary events at 4.1 & 6.8 yrs
 - Additional findings
 - No cardiac protection (Papworth and ESPRIT)
 - Estrogen increased risk of stroke in first 6 months of treatment (WEST)
 - No reduction in atherosclerotic progression in women w/CHD (ERA)

Treatment or prevention of CVD?

Estrogen

Raher U, Piquart, Rafi P, Zachar, Christen A, Koch. Hormones of the Cardiovascular System. Nov 29, 2008. 25. Pharmacotherapy: a pathophysiologic approach. 6th Ed. Heart Disease: a textbook of cardiovascular medicine. 7th Ed. Menopause: Part of Reproductive Biology and Endocrinology 2008, 744.

- Treatment or Prevention of CVD?
 - No, not recommended for primary or secondary cardiovascular protection

Estrogen

- Case Studies
 - Ms. Edith is a 53 year old former equestrian champion who enters the community pharmacy to fill her new Prem-Pro prescription. Her competitive nature appears to have once again gotten the best of her as she carries on-and-on about how now she will dominate her goal HDL and maybe prevent those heart attacks/strokes that run in her family. She also requests to refill her warfarin for "the clots".
 - Does Ms. Edith have a drug therapy problem?

Estrogen

- Surrogate Effects
 - Impair glucose handling
 - Lipid panel
 - reduce TC, LDL, increase HDL and Lp (a)
 - Blood pressure
 - decrease SVR, increase cardiac output (CO)
 - initially, enhance endothelial function
 - improve diastolic blood pressure & diastolic filling
 - increase sodium and water retention
 - Body composition
 - increase lean mass, decrease visceral fat

Growth Hormone

Ng T et al. Pharmacotherapy. 2009. 29(9). Clinics in Clinical Endocrinology 2008; 169:347-356. Pharmacotherapy: a pathophysiologic approach. 6th Ed.

- **Clinical Cardiology**
 - GHD and cardiovascular impairment
Reduced cardiac mass, diastolic filling, left ventricular peak response w/exercise, increased intima-media thickness (IMT), endothelial dysfunction
 - Cardiac performance in GHD
non-sustained enlargement, increase in ejection fraction (EF), reverse dilated cardiomyopathy
 - Improved performance
exercise endurance and capacity
 - Heart failure - mixed results
Prevent progression, improve CO and decrease SVR, left ventricular hypertrophy (LVH)?, edema? Arrhythmias? Quality of life?
 - Edema and Benign intracranial hypertension
Pediatrics, 1.2:1000 cases (OZGROW database)
 - Reduction in common carotid artery IMT
- Treatment or prevention of CVD?

Growth Hormone

Ng T et al. Pharmacotherapy. 2000. 20(9).
Cohen A. Clinical Endocrinology 2008. 69:347-358.
Pharmacotherapy: a pathophysiologic approach. 6th Ed.

- Treatment and prevention of CVD?
 - Yes, when clinically indicated
 - Growth hormone deficiency


Growth Hormone

- **Case Studies**
 - Mr. Sweets is a 6'2", 235 lb, 72 yom presenting to the community pharmacy with new Glucophage, Lantus, and Norditropin Rx's from his off-shore physician, F. Rod Uland. Mr. Sweets has an extensive history of diabetic medication refills dating back to 1992. He claims to have joined the gym and plans to once and for all get his diabetes under control.

Does Mr. Sweets have a drug therapy problem?

Growth Hormone

- **Summary**
 - Multiple prescriptive hormonal therapies are available for a variety of medical indications
 - Similar to exogenous hormones, prescriptive hormonal therapies effect cardiovascular hemodynamics, oxidative and inflammatory processes, and other surrogates including lipids, blood glucose, and metabolic processes
 - Despite an assortment of provocative data, no prescriptive hormonal therapies are specifically indicated for the treatment or prevention of cardiovascular disease at this time



Questions?

- **Questions**
 - True or False?

Testosterone and estrogen have similar effects on the lipid profile?