THE EFFECTS OF TESTOSTERONE SUPPLEMENTATION ON THE HEART IN CD-1 MALE MICE

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PROJECT SUMMARY
Testosterone supplementation has become increasingly popular among older men. Despite the increasing popularity the risks and effects on the heart are poorly understood. This proposal intends to study the effects of testosterone supplementation on the electrical activity of the heart and measureable heart damage. To examine this, control mice and castrated (orchitectomized) mice will be supplemented with testosterone propionate for 16 weeks and then compared to similar mice who don't receive this treatment. Electrocardiograph (ECG) recordings will be done on mice to calculate QT intervals. Blood samples will be collected throughout the experiment to measure Troponin I concentrations. Results will determine whether testosterone supplementation has a significant influence on QT interval length. The possible role of testosterone supplementation on heart damage will also be observed. If testosterone supplementation aids in the shortening of QT interval and no significant heart damage is observed, then it may be a safe treatment to individual who are testosterone deficient.

INTRODUCTION
- Over the past decade testosterone supplementation and testosterone replacement therapy have become increasingly popular among older men in the US (Finkle et al. 2014). This increase in testosterone use is partly due to increases in marketing. Television advertisements have been very effective at convincing men that they might be suffering from low testosterone (Finkle et al. 2014).
- Testosterone levels gradually decline as men get older. Testosterone in men reaches maximum levels at around age 30, and then levels steadily decline at a rate of 1% to 2% annually (Reckelhoff et al. 2005). Controversy exists regarding whether the decline in testosterone with increasing age is a normal physiologic process or whether it is a result of poor lifestyle choices.
- Low testosterone is associated with many problems, some of which include erectile dysfunction and decrease in libido, energy, strength, and muscle mass (Grunenwald and Matsumoto 2003).
- Despite the increased promotion and use of testosterone supplementation in older men, its risks and effects are not well understood. Studies examining the effects of testosterone supplementation haven't been able to provide definitive evidence of its positive or adverse effects, particularly its effects on cardiovascular outcomes. Furthermore, research on the effects of testosterone supplementation on the heart and cardiovascular outcomes has yielded inconsistent results.
- My research will evaluate the effects of testosterone supplementation on the heart in mice with normal testosterone levels vs. those that are testosterone deficient. This study will assess the effects testosterone supplementation has on QT interval and heart health.

REVIEW OF LITERATURE
- Finkle et al. (2014) examined the risk of nonfatal myocardial infarction following an initial testosterone prescription from individuals in a large healthcare database (n = 55,593). Results from this study found increased risk of nonfatal myocardial infarction in men who used testosterone. Also the risk of nonfatal myocardial infarction did not only apply to older individuals. Men younger than 65 with pre-existing heart disease had an increased risk of nonfatal myocardial infarction shortly after starting testosterone therapy.
- Baillargeon et al. (2014) examined 6,355 men aged 66 and older, from a national sample of Medicare recipients who received at least one injection of testosterone between January 1, 1997 and December 31, 2005. Results showed that testosterone supplementation was not linked with any increased risk for myocardial infarction. In fact, men at greater risk for heart problems who used testosterone actually had a lower rate of myocardial infarction than similar men who did not receive this treatment.
- The electrical activity of the heart is produced by the flow of ions in and out of the cells of the heart, and cardiac tissues, there are two isoforms (troponin I and troponin T) that are only present in cardiac muscle tissues (Kolmanova, et al. 2015). When there is damage to heart, troponin I and troponin T proteins are released into the blood. And the amount of troponin I and troponin T in the blood is proportional to the amount of heart damage (Kolmanová, et al. 2015).

OBJECTIVES
- Determine the effects testosterone supplementation has on heart electrical activity by measuring QT interval. Observe differences in QT interval length between mice who receive testosterone supplementation and those who do not.
- Evaluate differences in the severity of heart damage associated with testosterone supplementation by measuring troponin I concentrations in mice who receive testosterone supplementation and those who do not.

EXPECTED RESULTS

LITERATURE CITED

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