Effects of Hydrogen Sulfide on Corpus Cavernosum Function following Testosterone Deprivation

Kaylee Parizo, Meghan Peoples Research Mentors: Clifford Pierre & Dr. Justin La Favor
Department of Nutrition and Integrated Physiology
Florida State University, Tallahassee, FL

Introduction

Testosterone plays a major role in penile structure and function. As men age, many experience a decrease in testosterone production, which correlates to an increase in Erectile dysfunction (ED). ED is the inability to achieve or maintain an erection satisfactory for sexual performance.[4] It is often associated with other underlying health problems such as obesity, cardiovascular disease, diabetes, and Hypogonadism. Hypogonadism is the inability of the testes in producing testosterone.[4] Research has found that lowered levels of testosterone can lead to an increase in oxidative stress which then decreases nitric oxide (NO) and hydrogen sulfide (H2S) levels.[1,2] These two are important gasotransmitters that mediate relaxation. Current research has shown H2S has vasorelaxant properties and its production is stimulated by testosterone.[2] However, there is no evidence of its effects on ED in a model deprived of testosterone.

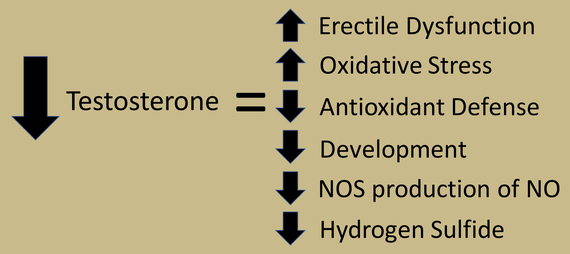

Figure 1. The effects of testosterone deprivation. [4,1]

Our research project aims to assess penile function following treatment with two H2S-enriched diets in mice deprived of testosterone via castration. Function will be measured through myograph experiments with various dilators and constrictors. We hypothesize that H2S treatment in mice deprived of testosterone will experience more relaxation and less constriction than the non-treated castrated group.

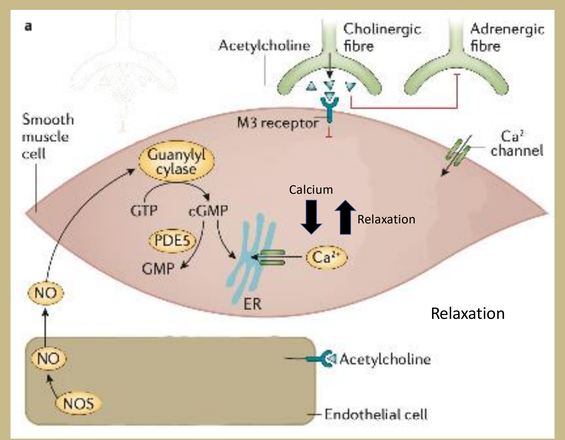

Figure 2. Penial smooth muscle relaxation– erect state. [4]

Results

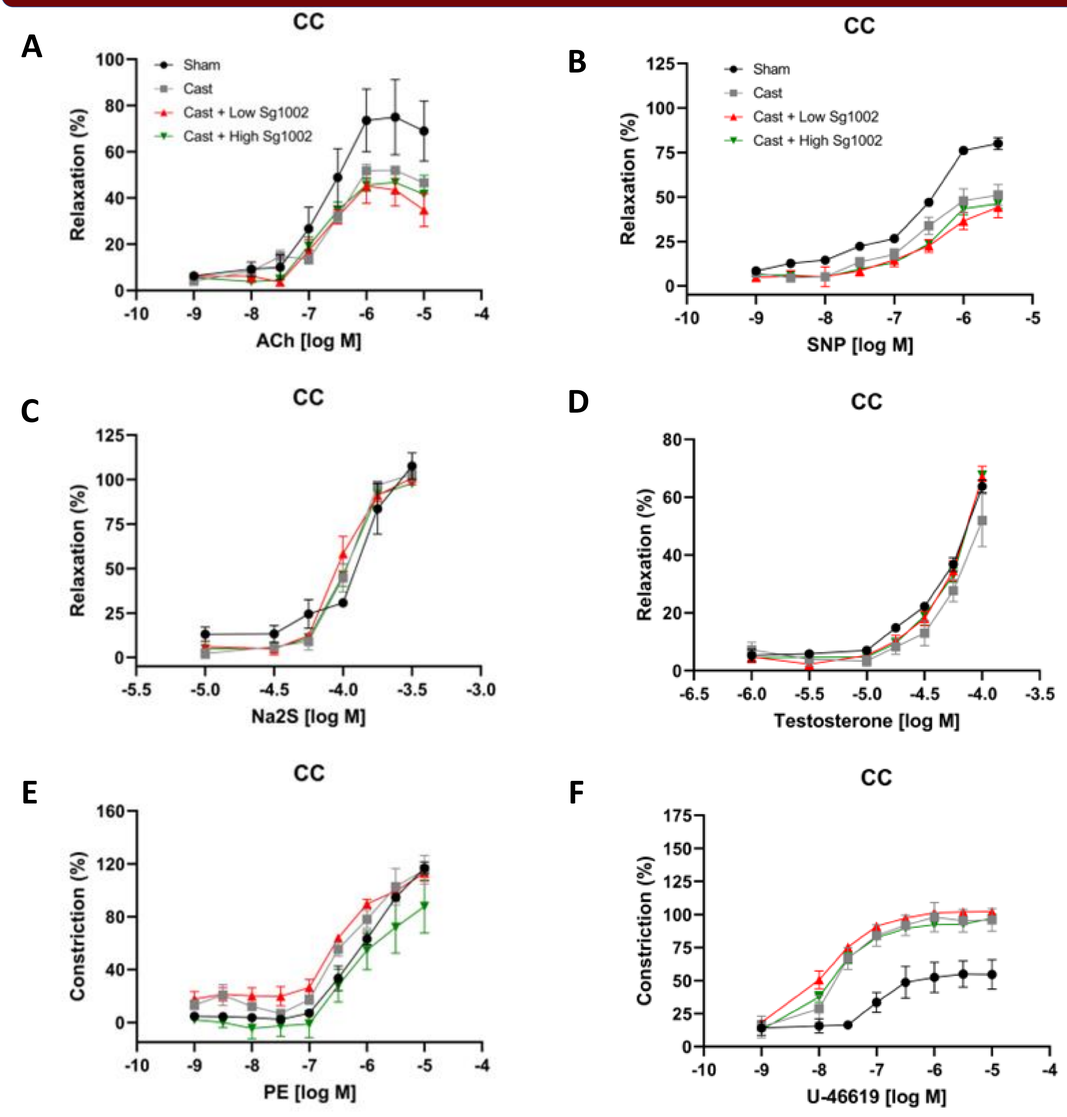

Figure 3. Assessment of vasoreactivity of the corpus cavernosum (CC). (A) Relaxation was tested with 0.001 µM-10 µM of acetylcholine (ACh). (B) Relaxation was tested with 0.001 µM-3 µM of sodium nitroprusside (SNP). (C) Relaxation was tested with 10 µM-300 µM of sodium sulfide (Na2S). (D) Relaxation was tested with 1 µM-100 µM of testosterone. (E) Constriction was tested with 0.001 µM-10 µM of phenylephrine (PE). (F) Constriction was tested with 0.001 µM-3 µM of U-46619. Values represent means ± SEM for n = 3-4 animals per group.

References

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Methods

Animals: 12-week-old C57BL/NH6SD mice
- SHAM- Sham surgery & Normal Diet (n=3)
- CAST- Castration surgery & Normal Diet (n=3)
- CLS- Castration & Low Dosage SG1002 (n=4)
- CHS- Castration & High Dosage SG1002 (n=4)

Experimental Design
Day 0: Start dietary intervention
Day 3: Mice underwent castration surgery
Week 5: Mice were sacrificed

Erectile Function Assessment
Erectile function was assessed using DMT myograph system. Vasoreactivity was tested in corpus cavernosum using several dilator and constrictor agonists.

All relaxation protocols were pre-constricted with 10 µM PE

Dilators
- Acetylcholine - promotes NO production from endothelial cells. Endothelial dependent relaxation
- Sodium Nitroprusside - NO donor. Test smooth muscle reactivity to NO. Endothelial-independent relaxation
- Testosterone – male sex hormone
- Sodium Sulfide (Na2S) – an H2S donor

Constrictors
- Phenylephrine- Mimics norepinephrine and constricts smooth muscle
- U-46619- a prostaglandin/ thromboxane A2 agonist and initiates constriction via different mechanisms

Statistical Analysis
Two-Way Repeated Measures ANOVA were used to compare differences between groups. Significance was set at $p \leq 0.05$ for all analysis.

Conclusion

- H2S diets seems to improve the loss in testosterone-mediated relaxation and lowers PE-induced constriction following testosterone deprivation. However, H2S diets does not appear to reverse the dysfunction in endothelial-dependent and independent relaxation and U-46619-induced constriction caused from testosterone deprivation.
- As this is an on-going project, we are unable to make a conclusive statement.
- More data and statistical analysis is required before making a conclusion
- Future projects include western blots and qRT-PCR.