

UNIVERSITY OF WISCONSIN-LA CROSSE

Graduate Studies

EFFECTS OF PDE5 INHIBITORS (VIAGRA) ON EXERCISE BLOOD PRESSURE

A Manuscript Style Thesis Submitted in Partial Fulfillment of the Requirements for the
Degree of Master of Science in Clinical Exercise Physiology

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By David Steenstra

We recommend acceptance of this thesis in partial fulfillment of the candidate's requirements for the degree of Master of Science in Clinical Exercise Physiology.

The candidate has completed the oral defense of the thesis.



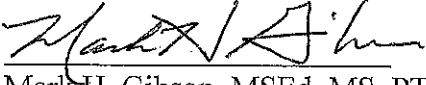
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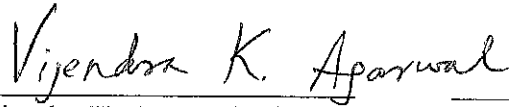
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ABSTRACT

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Introduction: Phosphodiesterase inhibitors (PDE₅-i) (e.g. Viagra) inhibit the destruction of nitric oxide, and contribute to vasodilation, both in target tissues and generally. In the setting of heavy exercise, this may lead to a reduction in systemic vascular resistance and a decrease in blood pressure. **Purpose:** To evaluate the effect of PDE₅-i on blood pressure responses during heavy exercise. **Design:** Controlled laboratory investigation. **Methods:** Well-trained, middle aged men completed 40 min exercise bouts beginning one hour after ingestion of a (double blind randomly ordered) PDE₅-i (Viagra 50mg) or placebo. Blood pressure was measured at rest prior to exercise, throughout the exercise bout, and during the cool-down. **Results:** There was a significant reduction in Systolic blood pressure throughout the course of exercise. SBP at 0, 3 (warm-up), 15, 25, 35, 45 and 47 (cool-down) min on PDE₅-i vs control was 116 vs 109, 129 vs 122, 162 vs 152, 166 vs 152, 167 vs 148, 166 vs 154 and 142 vs 134. Diastolic blood pressure was also significantly lower at each time period. **Conclusions:** Exercise after taking a PDE₅-i reduces systolic blood pressure significantly throughout the exercise bout, but not to levels associated with hemodynamic compromise.

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INTRODUCTION

The benefits from exercise and physical activity are profound and have been studied thoroughly. Some of the benefits that come from regular exercise are: increase in lean body mass, decrease in percent fat, improved self-efficacy, increase in cardiovascular health and many others. One important cardiovascular benefit that is elicited by exercise is a control of high blood pressure. Post Exercise Hypotension (PEH) is a term used to define a decrease in blood pressure following a single exercise bout.^{1,2} One area of exercise research includes questions such as how much exercise, how hard to exercise, and what kind of exercises should be performed to elicit a hypotensive response.

Researchers have completed studies that have looked at the specific effects of exercise and blood pressure. A study completed by Mark Hamer evaluated the effects of chronic and acute bouts of exercise on blood pressure. He found that both acute and chronic bouts of exercise elicit a decrease in blood pressure following exercise; post exercise hypotension.¹ Post exercise hypotension (PEH) was further researched in a study completed by Smelker et al. The results of the study suggest that working subjects at 70, 80, 90, and 100 percent VT all elicit a PEH effect that peaks at one hour of recovery. However, working the subjects at 100% VT elicited the greatest hypotensive effect and occurred earlier into recovery.² Another study looking at exercise effects on blood pressure was completed by Christopher Mach et al. The study researched the effect of exercise duration on PEH. Results showed that there was a decrease in blood pressure in

all bouts, but the decrease was greater in both magnitude and duration with longer exercise bouts.³ Guidry et al found that both short and long duration bouts of exercise caused a decrease in systolic blood pressure by 4-6 mmHg. However, the longer the exercise bout was, the more effect it had on PEH. The study suggests that even short duration; low to moderate intensity exercise can decrease blood pressure significantly for the day. However, the main findings from the study imply that as the intensity of a workout increases the decrease in blood pressure is greater.⁴

One of the presumptive reasons that blood pressure is lowered by exercise is because the role of nitric oxide (NO) plays in the body. NO works as a vasodilator in the body by relaxing the smooth muscles of the vascular tissues. The vasodilatory effect of NO is also the cause of an erection when a man becomes sexually aroused.

Between 15 and 30 million males in America with erectile dysfunction (ED) are prescribed medications that are made to treat this problem. Tadalafil (Cialis), sildenafil (Viagra), and vardenafil (Levitra) are the most commonly prescribed medications for ED. These medications are known as Phosphodiesterase Type 5 inhibitors, or PDE-5i and are most commonly used for the treatment of ED and pulmonary hypertension.^{5,6} It is very important to understand the risk factors involved with taking PDE-5i because many people with ED have some type of heart failure. The use of PDE-5i for treatment of ED is safe in individuals with mild to moderate heart failure, but requires caution with higher risk patients.⁷ Information about how PDE-5i influence exercise in active individuals is generally lacking.

PDE-5i's prevent the destruction of NO which leads to relaxation of the smooth muscle of the arterial walls. NO works as a vasodilator to allow for proper blood flow.

Nitric oxide naturally occurs within our bodies. During physical activity or sexual arousal the body releases significantly more NO to increase blood flow to the muscles being used or the genital tissue. However, older individuals with atherosclerotic disease may have impaired endothelial function and thus may have a reduced capacity to produce NO. Thus, the administration of a PDE-5i reduces the rate of NO destruction and allows adequate accumulation of NO to allow effective erections and to increase systemic blood flow, causing a widespread vascular effect. With increased NO associated with exercise and the effect of PDE-5i on inhibition of NO destruction, there could be a significant and dangerous decrease in blood pressure.

Research has also been completed on the specific effects of PDE-5i combined with exercise. Sildenafil was the PDE-5i used in a study completed by Andrew Hsu et al. The basis for his study was to determine if sildenafil had an ergogenic effect when exercising during acute hypoxia. Results from this study suggest that while exercising in hypoxic conditions, sildenafil increased stroke volume, cardiac output, and SaO_2 , but had no significant effects while exercising at normoxia.⁸ Ergogenic effects of PDE-5i were researched in another study completed by Guidetti et al. The study used the long acting PDE-5i tadalafil. Results from this study show there was only a increase in time to peak power during a 30 s Wingate anaerobic power test.⁹ Studies completed on persons with known cardiovascular problems have also been completed. A study conducted by Arruda-Olson et al examined the cardiovascular effects of sildenafil during exercise in men with known coronary artery disease. Results showed that at rest, SBP decreased significantly after sildenafil administration but DBP was not significantly decreased. Sildenafil and placebo trials elicited similar SBP and DBP results.⁵

The purpose of this study is to identify hemodynamic effects PDE-5i's have during an aerobic exercise bout at approximately VT in apparently healthy middle aged men. This study hypothesis is that blood pressure will be significantly lower during exercise when a PDE-5i has been ingested.

METHODS

Procedures

The subjects in this study were ten apparently healthy middle-aged men. All the subjects regularly performed moderate-intensity aerobic exercise. This age range was chosen because these are the men who are most commonly affected by erectile dysfunction, who may be using PDE-5i and may also be physically active. None of the subjects had documented coronary artery disease, prior myocardial infarction, symptoms suggestive of angina pectoris, or a history of revascularization procedures. Three of the ten men in the study were taking anti-hypertensive medications. The subjects who were receiving anti-hypertensive medications took medication as usual. The characteristics of the participants are presented in Table 1. Before participation in the study each subject completed a thorough health history questionnaire and provided written informed consent. The research protocol was approved by the University of Wisconsin-La Crosse Institutional Review Board for the Protection of Human Subjects.

Table 1 MEAN ($\pm$ SD) CHARACTERISTICS OF SUBJECTS

Age, Y	54 $\pm$ 13
Height, cm	177 $\pm$ 14
Weight, kg	93 $\pm$ 21
VO _{2max} , mL/kg/min	34 $\pm$ 12
Percent Predicted VO _{2max} , %	108 $\pm$ 24

Initially, each subject completed an incremental exercise test to rule out occult cardiovascular disease and to estimate their ventilatory threshold (VT). VT was estimated by performing the Talk Test.¹⁰ During this initial exercise test, the electrocardiogram, hemodynamic responses, symptoms, and RPE were monitored. After this, each subject participated in two randomly ordered exercise bouts with the exercise intensity near VT, performed at least 48 hours apart. All exercise sessions were 50 minutes in duration; including a 5 minute warm-up and a 5 minute cool-down. The subjects were encouraged to have similar diets on days of exercise sessions.

Blood pressure was measured by auscultation. Prior to the first measurement, the subject was allowed to sit quietly for five minutes. At least three BP measurements were performed at rest to acquire a consistent value. During the remainder of the protocol one blood pressure measurement performed at each necessary point, every ten minutes. The two exercise bouts consisted of working at an intensity approximately VT. Prior to each exercise session the subject was given a placebo or 50mg Sildenafil which was ingested one hour prior to exercising. Drug administration was double-blind and randomized.

On initial entry into the laboratory, subjects were given five minutes of seated rest, after which blood pressure and heart rate (via radiotelemetry) measurements were obtained. After initial blood pressure and heart rate values were obtained the subject began exercising. A five minute warm-up was completed prior to the 40 minute exercise bout. Heart rate and blood pressure was taken at minute 3 of the warm-up, 15, 25, 35, 45, and 47 minutes of exercise. The category ratio RPE scale (0-10) was measured at the same points.

Statistical Analysis

Statistical analysis was performed using repeated measures analysis of variance (ANOVA) to examine the differences in systolic and diastolic blood pressures, heart rate, % maximum heart rate, RPE, and mean arterial pressure, and to test for differences between placebo and 50 mg Sildenafil. The alpha level indicating statistical significance was set at 0.05 or less.

RESULTS

Each subject completed the two randomized trials according to the protocol with no complications. There was no postural hypotension observed. The response of heart rate and % heart rate max are presented in Figure 1. There was no significant difference in HR or % HR max between placebo and 50mg Sildenafil trials. The average %HR max during both control and PDE-5i exercise bouts fell within ACSM's guidelines for moderate intensity exercise.

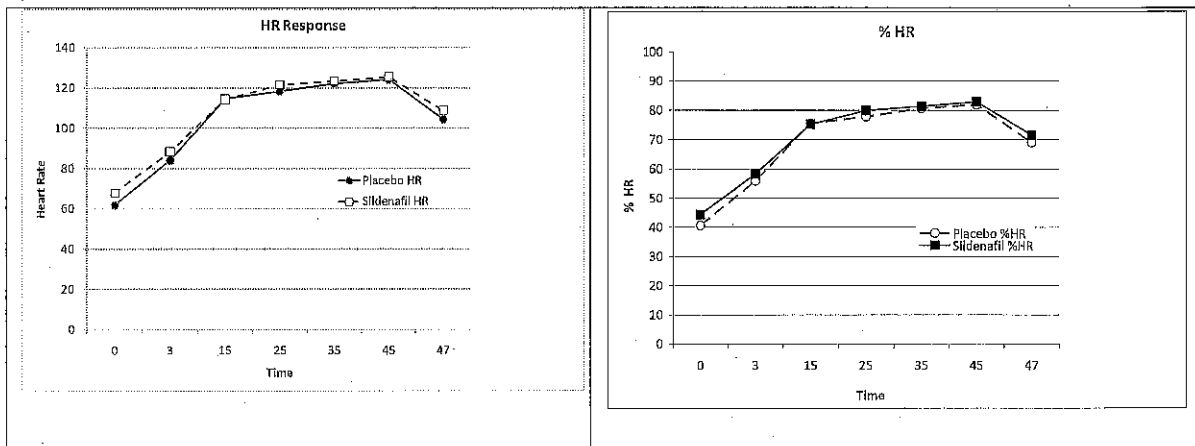


Figure 1. The pattern of heart rates and % heart rate max at specific times during the two exercise bouts.

The response of Rating of Perceived Exertion (RPE), (1-10) is displayed in Figure

2. There was no significant difference between the two trials attributable to drug. The RPE response increased with the duration of exercise.

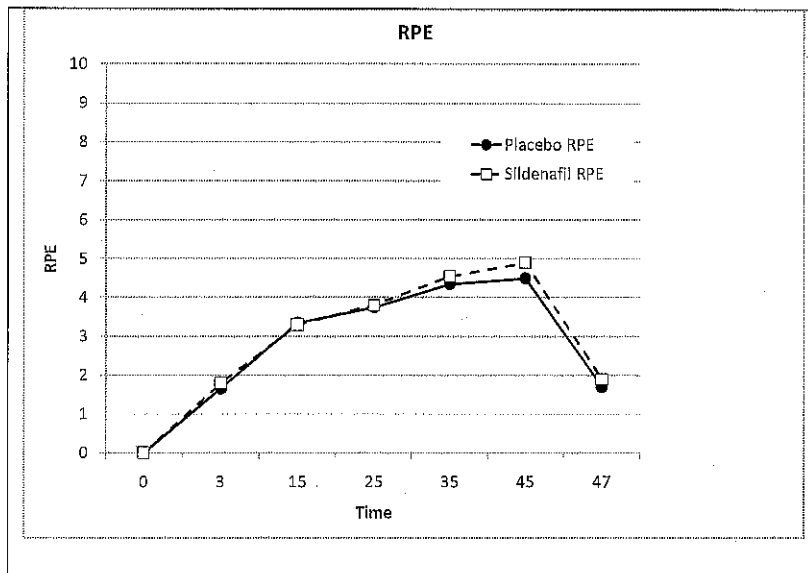


Figure 2. RPE in both placebo and 50mg Sildenafil exercise bouts.

The response of systolic and diastolic blood pressure is displayed in Figure 3.

There was no significant difference with drug and time over the 40 min work bout combined, but there was a significant drug effect and a significant time effects for systolic blood pressure. Systolic blood pressure, both prior to exercise and throughout the exercise bout following PDE-5i were lower (Figure 3). Diastolic blood pressure showed no significant difference between the two trials in regards to the 40 min work bout (time) or drug and time combined, but did show a significant difference due to drug effects. Changes in diastolic blood pressure are also shown in Figure 3.

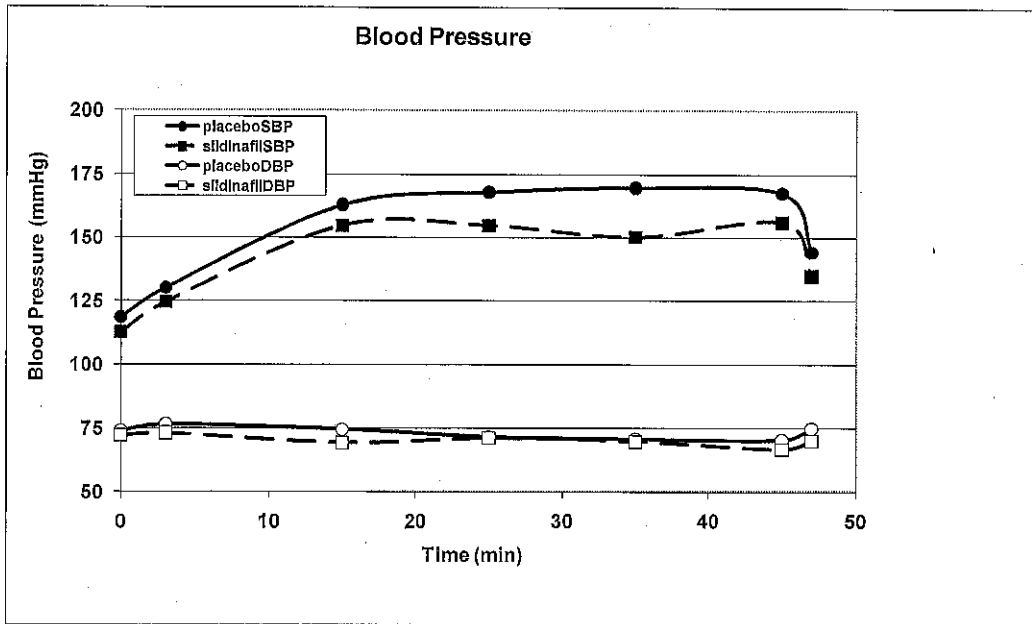


Figure 3. Systolic and diastolic blood pressures in placebo and 50mg Sildenafil exercise bouts.

The response of mean arterial pressure is displayed in Figure 4. There was no significant difference between the two trials attributable to time or drug and time, but there was a significant decrease due to drug effects.

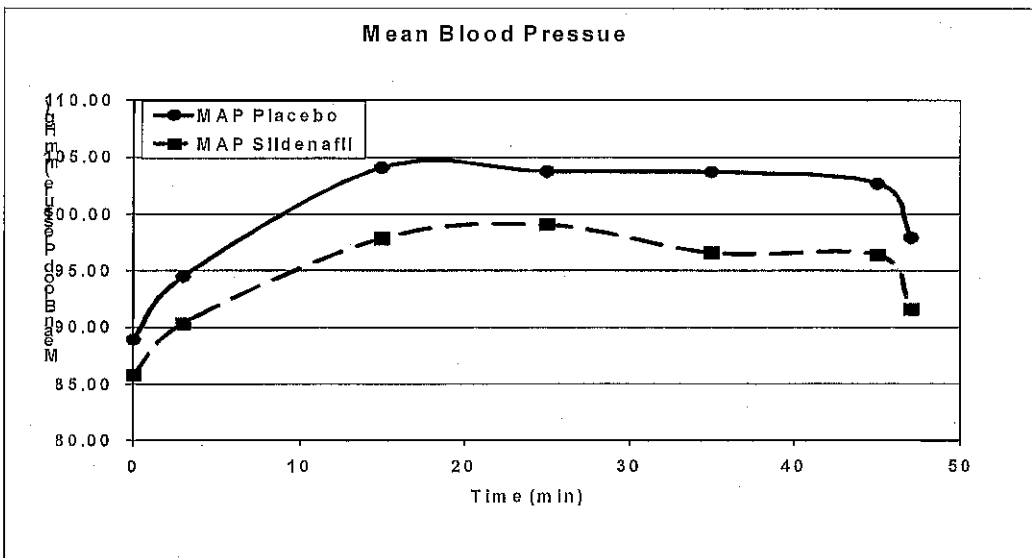


Figure 4. The differences in mean blood pressure between the two trials.

The results of this study suggest that there is a significant difference in exercise blood pressure when the subjects had ingested 50mg of Sildenafil. There were no significant responses in HR, %HR max, or RPE between the trials.

DISCUSSION

The findings of this study suggest that there is a hemodynamic change in near VT intensity exercise bouts when the subjects ingested 50mg of PDE-5i prior to exercise. Both systolic and diastolic blood pressures were significantly lower at rest and throughout the entire exercise bout when taking PDE-5i. Mean blood pressure was significantly lower with PDE-5i. Heart rate, RPE and % heart rate max all increased significantly across the exercise bout, but there was no significant drug effect.

The data here agrees with the findings of Arruda-Olson et al regarding heart rates and systolic blood pressure.⁵ Arruda-Olson found that there was no significant difference in the heart rate but there was a significant decrease in systolic blood pressure at rest after administration of Sildenafil.⁵ However, the findings of the present study are in opposition of Arruda-Olson in regards to diastolic blood pressure. Exercise intensity and exercise blood pressure was monitored in a study conducted by Smelker et al.² The harder someone is exercising elicits a higher systolic blood pressure. Most studies prior to this study looked at the cardiovascular effects within cardiovascular disease subjects. This study looked at the hemodynamic response in apparently healthy middle aged males working near VT (eg. heavy exercise). Heart rate and blood pressure were taken prior to exercise as well as throughout the exercise bout. In this study the RPE is suggestive of the subjects working at moderate intensity. The % heart rate max also is in the moderate intensity, training zone according to ACSM (60-90%).

Blood pressure depends on the interaction between cardiac output (CO), arterial compliance, and total peripheral resistance (TPR). Vasodilation decreases TPR and decreases the work of the heart. NO derived vasodilation is likely to decrease TPR. Since the work intensity was the same in both exercise trials, the same CO is required. The observed difference in systolic blood pressure during exercise is reasonably attributable to PDE-5i, secondary to a general decrease in TPR.

Future studies working with PDE5-I could deal with increased intensity, increased amount of drug administered, subject demographics. Intensity is one variable that can be manipulated. The subjects in this study were exercising near their VT. Exercising the subjects at a higher intensity may elicit a different or more profound effect hemodynamically. Also, the dosage of drug administered could cause a different effect. This study used 50mg of Sildenafil which is a common dosage used in the treatment of ED. Increasing the amount of drug used could cause more substantial reduction in vascular resistance, making effects more profound. Sildenafil is one of many PDE5-I and was used in this study due to the short half life. Studies were performed 48 hours apart to allow for the proper removal of the drug. Other PDE5-i could be used in a similar study to see if their effects differ from this study's. Some of the subjects that participated in this study were on cardiac related medications that could blunt the heart rate and blood pressure response. Future studies may look to find subjects that are not on any, or are on more cardiac related medications.

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APPENDIX A
INFORMED CONSENT FORM

Protocol Title: Effects of PDE5 Inhibitors (Viagra) on Postexercise Hypotension

Principle Investigator: Jenna Shatzer
3520 Crown Blvd.
La Crosse, WI 54601
(608)-788-6584

Emergency Contact: Carl Foster
(608)785-8687

Purpose and Procedures

- The purpose of this study is to examine the effects of Sildenafil (e.g. Viagra) on the blood pressure response following a high-intensity bout of exercise.
- My participation will involve a maximal exercise test and two high-intensity workouts on a cycle or treadmill. Before each high-intensity work bout I will take a tablet, which in one case will be Sildenafil and in the other will be a placebo (non-active agent). The sequence of which tablet I take first will be decided by chance.
- The total time commitment will be seven hours over a two month period.
- Testing will take place in room 3026 of the Health Science Center, UW-L.
- During all tests I will be wearing a heart rate monitor and have my blood pressure monitored every ten minutes.
- I will be asked my rate of perceived exertion every ten minutes.

Potential Risks

- I may experience local muscle fatigue from the workouts.
- I may experience exertional fatigue from the maximal exercise test.
- I may experience a significant drop in blood pressure following a high-intensity exercise bout in conjunction with taking Sildenafil. When I take Sildenafil, I may experience flushing in my face, a stuffed up nose and a mild headache. If, after the study, I am in a sexually stimulating situation I may find that I have a strange reaction. Should an erection lasting longer than 4 hours occur, I should seek medical attention.
- Individuals trained in CPR, Advanced Life Support and First Aid will be in the laboratory, and the test will be terminated if complications occur.
- The risk of serious or life-threatening complications, for healthy individuals, like myself, is near zero.

Rights and Confidentiality

- My participation is voluntary.
- I can withdraw from the study at any time for any reason without penalty.
- The results of this study may be published in scientific literature or presented at professional meetings using grouped data only.
- All information will be kept confidential through the use of number codes. My data will not be linked with personally identifiable information.

Possible Benefits

- I will gain a better understanding of the possible effects that Sildenafil can have on post-exercise blood pressure in active individuals.

Questions regarding any procedures in this study can be directed to the primary investigator, Jenna Shatzer (608-788-6584) or overseeing faculty member, Carl Foster, Department of Exercise and Sport Science, UW-L (608-785-8687). Questions regarding the protection of human subjects may be addressed to the UW-La Crosse Institutional Review Board for the Protection of Human Subjects, (608-785-8124 or irb@uwlax.edu).

Participant _____ Date _____

Researcher _____ Date _____

APPENDIX B
REVIEW OF LITERATURE

REVIEW OF LITERATURE

The purpose of this paper is to review the literature pertaining to the phenomena of Postexercise Hypotension (PEH), the changes in blood pressure due to certain types of exercise, and the role of PDE5 inhibitors on hemodynamics.

There have been several studies that take a look at different aspects of exercising. To go along with these studies, it has been shown that exercise elicits numerous health benefits. The topics of postexercise hypotension and the role of different types of exercise are very highly correlated. Significant data was found surrounding the influence of short and long duration acute bouts of exercise on blood pressure. In one such study, 45 male subjects between the ages of 18 and 55 years with known stage 1 hypertension participated in a study. The study was broken into 2 study groups: 1. light and 2. Moderate. Every participant went through an incremental maximal test to rule out cardiovascular disease and to establish appropriate workloads. During the exercise tests blood pressure (BP) was taken every other minute. BP was also monitored by an ambulatory monitor until the following morning upon waking. This test was effective in showing significant data, showing that short and long duration exercises of light to moderate intensity decreased systolic blood pressure for the waking hours of the day.¹

Another study was conducted by Hamer that explored the anti-hypertensive effects of exercise, more specifically, the acute and chronic exercise bouts. Conclusions of this study suggest that the anti-hypertensive effects appear to be multi-factorial. With every individual being different, the proper prescription of exercise to combat hypertension is highly individualistic. Acute and chronic bouts of exercise seem to show similar results in PEH, according to this study.²

In two similar studies published by the Journal of Cardiopulmonary Rehabilitation, the effect of exercise intensity and the effect of exercise duration were closely examined. Both of these research studies were performed at the University of Wisconsin-La Crosse. The study conducted by Smelker et al focused on the effect of exercise intensity on PEH. Ten subjects with a history of hypotension partook in the study. Each participant performed an incremental exercise test to identify peak oxygen uptake and ventilatory threshold (VT) to set appropriate workloads for the training sessions. The subjects completed four exercise bouts in which they worked at 70%, 80%, 90%, or 100% of VT. Each subject's BP was monitored during exercise and every ten minutes post exercise for 120 minutes. Results showed that PEH occurs after a wide range of exercise intensities, but BP is decreased the most in exercising near 100% VT. Also, at 120 minutes postexercise BP remained below baseline, but was the same as all other intensities of exercise.³ Nine subjects volunteered to participate in the study conducted by Mach et al dealing with the effect of exercise duration on PEH. A maximal incremental cycle ergometer test was used to establish the proper intensity for each participant. In addition to the maximal test, four other exercise bouts of varying duration were completed. BP was monitored every ten minutes during exercise and also every ten minutes post exercise for 90 minutes with the BP taken immediately following exercise serving as the zero minute measurement. This study shows that PEH occurs in any bout of exercise, no matter the duration or intensity; however, the greater the intensity and longer the duration produces a larger decrease in PEH.⁴

A study completed by Williams et al attempted to find the exact effects of exercise on postexercise hypotension and the different aspects of exercise that play

certain roles in those effects. They posed a question asking if postexercise hypotension is related to excess post exercise oxygen consumption (EPOC) through leg blood flow. In this study, 16 apparently healthy subjects between 20-31 years of age participated. Results showed that leg blood flow was elevated by over 70 ml/min for an hour post exercise, however; leg blood flow decreased back to normal levels by 105 minutes post exercise. The conclusions from this study show that there is no correlation between PEH and EPOC.⁵

A decrease in blood pressure following exercise has garnered the term post exercise hypotension, but there are different aspects that attribute to this phenomenon of PEH. One of the key aspects of PEH is the role of nitric oxide (NO) in the body. NO plays role of a vasodilator in the body and produced in mass quantities during different activities performed by the body. Two main times where more NO is produced is during exercise and sexual arousal. The NO vasodilates the smooth muscle of the vascular tissue as well as genital tissue to allow for proper blood flow to the muscles being used or genital tissue. For men who are incompetent, a form of medication known as PDE5 inhibitors has shown to assist in the increase of blood flow to the genital tissues. When the drug is in the body it does not allow for NO destruction which in turn allows for vasodilation. Tadalafil (Cialis), sildenafil (Viagra), and vardenafil (Levitra) are the most commonly prescribe medications prescribed to help with ED. The nature of these drugs is what sparks the controversy and the need for further research to be done. This class of medication has become very popular and several studies have been done to view its possible positive and negative effects it has on exercise.

The studies pertaining to different PDE5 inhibitors and their effects on the body are very vast and sporadic; therefore, this literature encompasses many positive and negative effects of this type of medication.

Even though the use of PDE5 inhibitors is primarily used in the older population, one study examined the possible ergogenic effects of the drug tadalafil on anaerobic performances in healthy athletes. 12 well trained athletes were to perform a 30 second Wingate anaerobic power test one week apart. The day before the test, the subjects were double-blinded to receive an oral dose of 20mg of tadalafil or placebo. Blood lactate, mean power, peak power, time to peak power and fatigue index were assessed. Findings from this study showed that the long term PDE5 inhibitor, tadalafil, did not result in a substantial difference in anaerobic performance. The results did show an increase in blood lactate at minute 3 of the recovery as well as a decrease in time to peak power.⁶

Another study in which a PDE5 inhibitor was looked at in the sense of an ergogenic aid was a study performed by Hsu et al. His study posed the question of whether the PDE5 inhibitor sildenafil improves cardiac output and exercise performance during hypoxia and normoxia. After proper screening was taken place to eliminate possible contraindications to the study, the study was performed by 10 trained athletes with one practice trial and three experimental trials. The experimental trials were performed using a placebo, 50mg, or 100mg of sildenafil in a random double-blind design. For the hypoxic air tests, the percent oxygen was 12.8%. The main findings of this study show that there was an increase in stroke volume and cardiac output during the hypoxic exercise. The results also show that during a cycling exercise in acute hypoxia,

sildenafil can significantly improve cardiovascular function, oxygen saturation levels, and performance for certain individuals.⁷

The next few studies are looking at the effects of PDE5 inhibitors on participants with known heart disease. In a study conducted by Guazzi et al looks at several areas involved with the use of sildenafil in participants with chronic heart failure (CHF). The main objective of the study was to evaluate the effects on lung function and exercise performance. The study combined 16 patients with known CHF and 8 participants with normal coronary angiography. The study is very complex and looks at many different physiological changes within the body, but the main conclusions are that PDE5 inhibitors change pulmonary pressure and vascular tone, improves exercise peak VO₂, and ventilatory efficiencies.⁸

Cardiovascular effects of sildenafil were researched by Arruda-Olson et al. Her study was focused on men with probable coronary artery disease (CAD) and the effect sildenafil had on their cardiovascular system. Males over the age of 40, with erectile dysfunction, and CAD participated in this study. The study was a double-blind crossover study in which the subjects receive either a placebo or 50mg of sildenafil one hour prior to exercise. BP was taken immediately following ingestion of pill as well as monitored during exercise. Heart rate was not affected significantly after the dose of sildenafil was administered; however, systolic blood pressure decreased significantly after sildenafil was taken and not when the placebo was taken. Another significant finding was that most of the subjects in this study produce exercise induced myocardial ischemia. However, they were no more likely to experience ischemia with exercise when they used sildenafil than when they took the placebo.⁹ The last study in this review regarding

diseased populations and their use of PDE5 inhibitors is a study conducted by Lewis et al. The purpose of his study was to see if sildenafil improved exercise hemodynamics and oxygen uptake in patients with systolic heart failure. Results show that in the 13 patients used in this study, sildenafil improved peak VO₂ and was a selective pulmonary vasodilator during rest and exercise.¹⁰

Anytime you are taking a medication the potential for adverse effects or contraindications to that drug are always present. Exercise coupled with the use of PDE5 inhibitors has been studied throughout the years since the drug was released. As mentioned earlier, PDE5 inhibitors prevent NO from being destroyed which could lead to unsafe global vasodilation.

A very important study was conducted by Al-Ameri and Kloner on the role of PDE5 inhibitors in patients with ED and heart failure. As stated in their research, the risk factors of these two problems are commonly present together and are similar in nature. This study suggests that the treatment of ED with PDE5 inhibitors is effective, but should be used with caution in patients with heart failure. PDE5 inhibitors are safe and effective way to treat ED in patients with mild to moderate heart failure, but should be used with extreme caution or should be avoided in patients that are intermediate to high risk.¹¹

One of the most profound contraindication to taking PDE5 inhibitors is if the patient is on nitrates. The patient who is on nitrates already has an increase of NO in their system, and the PDE5 inhibitor does not allow for that destruction. This could cause a dangerous decrease in blood pressure. A study conducted by Kloner et al focused on the time course of the interaction between tadalafil, a long lasting PDE5 inhibitor, and nitrates. The study was random, double-blind, and placebo-controlled. There were a

total of 166 men that participated in the study ranging from 40-83 years. Results showed that systolic and diastolic BP decreased significantly at the 4, 8, and 24 hour marks in more subjects on tadalafil compared to the placebo. After 48 hours of observation the subjects' blood pressures virtually were the same no matter if they received tadalafil or placebo.¹²

An interesting article called: Roundtable Discussion: Tadalafil Study Group was published in *The American Journal of Cardiology*. This was a study group that consisted of several medical doctors talking about different areas surrounding PDE5 inhibitors, their use in certain populations, their use along with nitrate use, and different guidelines. A point Dr. Melvin D. Cheitlin wanted to emphasize and make known was that men with cardiovascular disease are also at an increased risk for erectile dysfunction. Another main focal point that Dr. Kuritzky honed in on was that the only absolute contraindication for the use of PDE5 inhibitors along with cardiovascular disease is the use of nitrates.¹³

SUMMARY

In conclusion to this review, there have been several studies conducted on the effects of exercise on blood pressure. The term postexercise hypotension has been created to define and explain the drop in blood pressure after exercise. Also, the use of PDE 5 inhibitors has become a popular way to combat erectile dysfunction. With the use of PDE5 inhibitors coupled with exercise, you can see significant changes in blood pressure. More research needs to be completed in this area to determine the potentially dangerous decreases in blood pressure when intense exercise is joined with the use of PDE5 inhibitors.

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