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Genetics of Hypertension

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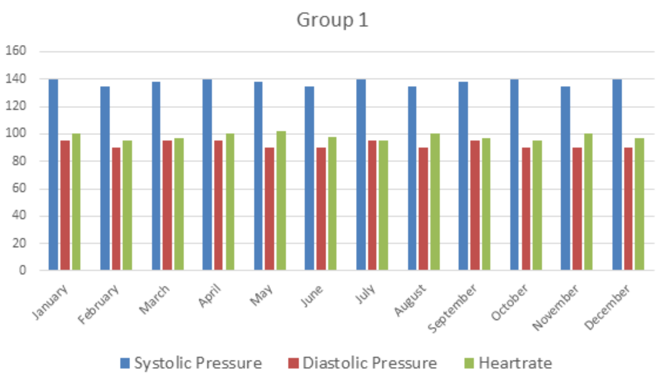
Graphical Abstract



Abstract

Review of the literature helped to establish hypertension as a multifactorial disease, meaning that malfunctions in certain genes predispose individuals to developing the condition but the genes are not particularly dominant and the expression of the final phenotype is heavily influenced by the patient's lifestyle and environment. There is also a disparity concerning the prevalence of chronic illness between individuals of a lower and higher socioeconomic status. It has been shown that people coming from low socioeconomic backgrounds are disadvantaged in terms of disease management. In this study, 30 Zucker rats were used in the first trials of a medication for patients genetically predisposed to hypertension who struggle to manage their condition. The test subjects were separated into 3 groups: a control group who merely got fed twice a day, group 2 who got fed twice a day and received the medication with their first meal, and group 3 who were fed twice a day and received the medication with both meals. The results showed that the test subjects that received the lower dosage did have a decrease in blood pressure although it was slower and less stable compared to the rats that received the higher dosage. Studies must still be conducted although the medication has been deemed safe enough to continue on to the next phase: non-human primates. The hope is that within 5 years, through government assistance such as grants, the medication will be distributed throughout community health centers for the at-risk patient base.

Note: This paper was an assignment for a nursing school General Education Capstone course. The student writer did not conduct a real

	study; she rather simulated a study to demonstrate writing/research skills, creativity, scientific knowledge, and an understanding of how to generate and analyze data. The corresponding author is the student's instructor, who guided the student on each section of the scientific paper, providing feedback on how to "conduct" the study and on how to revise the writing.

Introduction

Literature Review: Scientific

It is essential to understand the basis of inheriting genetic disorders in order to understand the genetic foundation of an illness such as hypertension. According to Coy (2005), there are four types of genetic disorders: single-gene, chromosomal, mitochondrial, and multifactorial. Single-gene disorders occur due to mutations in the DNA sequence on one particular gene versus chromosomal diseases which originate from a mutation in the structure of a chromosome such as deletion or copy of a particular gene (Coy, 2005). A defect or mutation in mitochondrial DNA, inherited solely from the patient's maternal DNA, can result in a mitochondrial disease (Coy, 2005). Hypertension is a multifactorial disease because although individuals may present with malfunctions in several genes, neither gene malfunction is particularly dominant and the patient's lifestyle and environment play an important role in producing the final phenotype (Coy, 2005). This being said, there have been rare presentations of Mendelian forms of hypertension; where a single gene mutation results in deviations of blood pressure (Singh et al., 2016).

Blood pressure is defined as the force of blood as it pushes against the walls of the arteries when the ventricles of the heart contract (National Heart, Lung, and Blood Institute, 2015). There are two readings seen when noting a patient's blood pressure, the systolic and diastolic pressure. Systolic pressure is the pressure of blood against arterial walls when the heart is contracting while diastolic is the pressure when the heart is at rest in between beats (National Heart, Lung, and Blood Institute, 2015). The National Heart, Lung, and Blood Institute (2015) denotes that high blood pressure, also known as hypertension, is a blood pressure reading of 140/90mmHg and above. This same article mentions that there are two main types or stages of high blood pressure: primary, or essential, which is the type that generally develops over time as a person ages. A study done by Marrie et al. (2012) reinforced that the risk associated with developing hypertension increased with age. There is also secondary high blood pressure which is caused by a separate medical condition or a particular medication; this type can be easier to treat as it will generally be resolved once its causative agent has been treated or removed (National Heart, Lung, and Blood Institute, 2015).

There are several genes that are considered in the synergistic association between genetics of hypertension and external environmental factors (Sousa et al., 2017). The angiotensinogen gene is responsible for coding for the substrate renin, indirectly responsible in lowering blood pressure (Singh et al., 2016). There are two genes that are considered as relatively similar and mutations in them could have the same effect: the angiotensin-converting enzyme gene and the renin gene (Singh et al., 2016). A silent mutation can exist on the angiotensin II receptor type I gene which promotes vasoconstriction and growth that provides for an especially aggressive form of essential hypertension (Singh et al., 2016). A polymorphism of the gene responsible for producing G-proteins was linked to lower levels of renin and prorenin, dually responsible for lowering blood pressure in normal healthy individuals (Singh et al., 2016) A population study revealed that polymorphisms of cystathionine β-synthase resulted in a higher risk factor for developing essential hypertension (Ying et al., 2014). Mutations in the adducin gene can provide another risk factor for persons who contain the mutation in their DNA as alterations in the gene have been shown to affect tubular sodium reabsorption (Singh et al., 2016). In total there have been alterations in 27 genes identified as providing a predisposition for developing primary/essential hypertension in adults, further investigation and genetic testing could reveal even more (Coy, 2005). Varga et al. (2016) discussed the case of a white male aged 62 who presented with persisting dyspnea and signs of right heart failure (2016). In the case of this patient, genetic testing was able to identify his genetic predisposition for hypertension and gave his son the initiative to undergo the same genetic testing and take precautionary measure so as to hopefully not develop the condition later on in life.

Due to the status of hypertension as a multifactorial disease, environmental factors are crucial in the final phenotype of the condition (Coy, 2005). According to Chalmers, MacMahon, & Mancia, several of these risk factors include age, sex, family history of hypertension, demographic factors, overweight, diabetes mellitus, physical inactivity, smoking, excess consumption of sodium, coffee, and alcohol (as cited in Singh et al., 2016). Although age is thought of as a risk factor, this only becomes the case after adulthood, age is not a risk factor in childhood and adolescence (Beeman, 2013). A case report presented a 62 year old white male, his case involved a history of smoking combined with a genetic predisposition resulting in a particularly severe form of pulmonary hypertension (Varga et al., 2016). Common features seen in a hypertensive patient are obesity, sedentary, history of smoking, and/or diagnosis of diabetes mellitus (Coy, 2005). The sad reality is that most of these factors are modifiable, meaning that although they are predictive of the development of hypertension, they can be fixed with lifestyle changes (Beeman, 2013).

According to the American Heart Association, it is imperative to understand that hypertension is one of the leading contributors for developing coronary heart disease or having a stroke, worldwide (as cited in Ho & Rumsfeld, 2006). There are individuals who can be unaware of their hypertensive status or who have difficulty in receiving a proper diagnosis because they have a type called masked hypertension. A recent study defines masked hypertension as “a blood pressure in the hypertensive range outside the office setting” (Unsal et al., 2016, p. 1). This same study found that this type of hypertension is associated with a greater prevalence of target-organ damage. This being said, it is high blood pressure/hypertension in general that can damage a patient’s body for years before symptoms develop or if left untreated (Mayo Clinic, 2016). Damage that can be done to the patient’s body as a result of untreated hypertension includes damaged and narrowed arteries or an aneurysm as a result of the constant high pressure within arterial walls, heart failure or an enlarged left heart due to the thickening of the heart wall from the extra work put forth by the left ventricle of the heart, damage to the brain like a stroke or dementia, and even kidney failure through damage of the renal arteries leading to the tiny blood vessels that filter waste from the body (Mayo Clinic, 2016).

There are multiple methods considered to assist in regulating blood pressure, one identified by Behuliak et al. (2017) is the activation of myosin light chain phosphatase in vascular smooth muscle, this results in the dephosphorylation of myosin light chain and promotes vasorelaxation. Drug therapy has been the standard method of treatment for hypertension for over half a century (Rodman, 1969). For the most effective treatment, the right drug or even combination of drugs and supplements must be identified for the individual case of each patient (Rodman, 1969). An example of a particular case study involves a patient with a particularly severe case of hypertension who received oral anticoagulation, loop diuretics, aldosterone antagonists, and oxygen supplementation (Varga, 2016). This patient’s anticoagulation regimen had to be constantly adjusted to maintain ideal therapeutic levels. Other common pharmaceutical treatments for hypertension include thiazide diuretics, loop diuretics, angiotensin II receptor blockers, calcium channel blockers, beta blockers, and even more (Beeman, 2013).

Literature Review: Cultural

It is known that the homeless population in the United States is rising although their mean age of survival is not; this could be because of their lack of proper healthcare for chronic illnesses (Bernstein et al. 2015). A study done that examined a low-income neighborhood found three major themes arose: social connectedness, stress factors, and availability of food options (Al-Bayan et al., 2016). This same study noted that these factors along with the disorder of the neighborhood and lack of proper healthy food choices led to an increase in hypertension within its population. The study found that out of the participant sample, 24% were pre-hypertensive and 35% were hypertensive. This is a stark contrast from the U.S. national average of 29.1% (Nwanko et al. 2013). It has also been found that patients of community health centers were 4% more likely to be on two or more blood pressure medications than those patients from a private physician's office (Fontil et al. 2017). The community health center patients Fontil et al. (2017) analyzed were also approximately 9% more likely to have stage 2 or severe hypertension than those who attended a private care physician's office.

A study conducted by Fontil et al. (2017) found that patients from community health centers were approximately 5% more likely than those who attended a private physician's office to have uncontrolled hypertension. This same study also found that patients at community health centers were less likely than those of private offices to be on fixed-dose combination drugs, this likely contributes to the higher rate of uncontrolled hypertension in these lower income communities. Rosemberg & Hsin-Chun Tsai, (2014) found that hypertension management was increasingly difficult in patients of a lower socioeconomic status. The participants underlined a lack of ability to both pay for the medication that could manage their hypertension and their bills. What many payers and insurance companies fail to realize is that between the comorbidities and complications that can arise from uncontrolled hypertension, effective treatment from the start can be drastically more effective in the long run (Cohen et al., 2001).

An essential portion of effective hypertension management is proper nutrition, Swinburne, Garfield, & Wasserman (2017) say that hospitals need to take it upon themselves to teach effective nutrition to patients. These authors say that it is not only the moral responsibility of the care provider but also their legal responsibility as a stipulation of the hospital readmission reduction program of the Affordable Care Act which enforces penalties on hospitals with excessive patient readmissions. Many communities where the residents are of a lower socioeconomic status are statistically inclined to developing hypertension as residents of neighborhoods with better safety, social connectedness, accessibility and availability of healthy were less likely to be hypertensive (Mujahid et al., 2008). It has been shown that a more cohesive social environment creates an environment less conducive to food insecurity (King, 2017). It has also been shown that there are other factors leading to an individual being disadvantaged from a perspective of disease management: being a woman, black, lower class, and an immigrant all seem to impact the patient's ability to effectively manage their hypertension (Rosemberg, & Hsin-Chun Tsai, 2014). Many of these risk factors are non-modifiable such as being a woman or black (Beeman, 2013).

The rate of patients with uncontrolled hypertension is excessively high, especially considering its increased damage on the body (Cohen et al., 2001). Oftentimes, patients are simply not aware of their hypertensive status or they receive a high blood pressure reading that is simply not reciprocated in the presence of a healthcare professional (Unsal et al., 2016). This phenomenon is known as masked hypertension and is important clinically because of the increased risks of cardiovascular disease (Unsal et al., 2016). In the study analyzed, it appears that the participants found to have masked hypertension had a mean BMI of 30.6 versus the other groups assessed, true normotension and true pre-hypertension, with a mean BMI of 25.9 and 28.5, respectively. The mean waist circumference was also 6 points higher than in the other groups, possibly alluding to a correlation between higher weight and masked hypertension (Unsal et al., 2016). A study conducted by Wang et al. (2017) tells us that the prevalence of masked hypertension is quite astounding, approximately 1 in 8 adults. This statistic is surely a contributing factor in terms of receiving effective treatment for patients with this condition as they are oftentimes misdiagnosed as non-hypertensive (Wang et al., 2017).

Stress has a profound impact on increasing an individual's blood pressure. It is recommended that if you are not able to simply eliminate your stressors, you can still make an effort to reduce your stress levels by changing your expectations, making time to relax, and do other activities you enjoy (Mayo Clinic, 2015). Things have changed quite drastically in terms of the patient's ability to be able to monitor his or her blood pressure at home and knowing when it is imperative to seek support, whether it is in their family or friends to help them manage their illness or their healthcare provider for immediate care (Mayo Clinic, 2015).

Patients must consider at the end of the day that while many factors leading to increased risk for the development of hypertension are considered as non-modifiable, most of them are not (Beeman, 2013). There are approximately 27 genes that lead to a genetic predisposition for hypertension, however there is often a synergistic involvement between genetic factors and external environmental influences such as weight, diet, salt intake, alcohol consumption, smoking, and various other lifestyle choices (Coy, 2005).

Fortunately, according to the Mayo Clinic (2015), hypertension can be controlled by non-pharmaceutical means for many individuals. Weight does have an impact on an individual developing high blood pressure and hypertension as they are more likely to have a buildup of plaque within their arteries (Unsal et al., 2016). The staff at the Mayo Clinic (2015) tells of how losing just 10 pounds can reduce your blood pressure. The Mayo Clinic also recommends exercising regularly and eating a healthy diet with plentiful whole grains, fruits, and vegetables. Reducing your salt intake can also have a profound impact in terms of lowering your blood pressure (Behuliak et al., 2017).

Materials and Methods

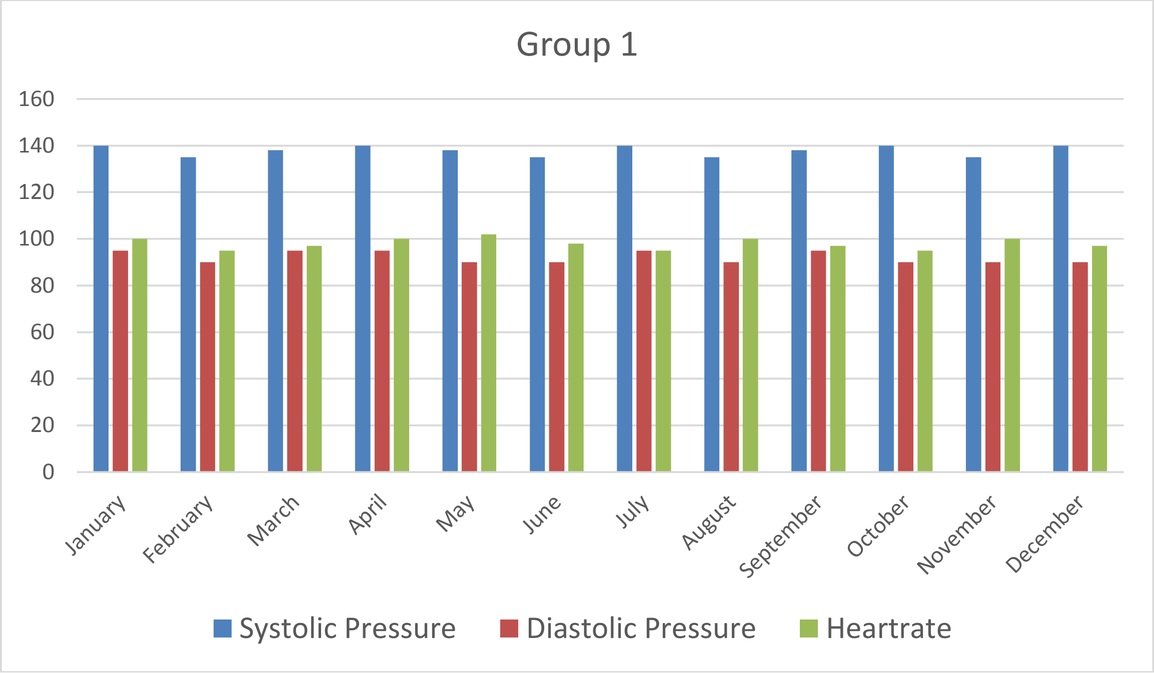
The development of this drug was conducted over a period of 1 year at a research lab in Miami, Florida. The researchers involved with this project consistently complied with all the guidelines set for ethical conduct in the care and use of nonhuman animals in research by the committee on animal research and ethics (CARE) affiliated with the American Psychological Association (2012). This experiment began by obtaining 30 young female Zucker rats and running various tests in the laboratory setting to insure that they did not have any medical conditions that would interfere with the procedures of this study such as Diabetes. The rats in this experiment were fed their normal caloric intake through two meals each day. They were kept in air controlled units so as to keep them comfortable and not raise their stress levels and cause erroneous blood pressure or heart rate results. The rats were kept in cages of an appropriate size, 40 square feet, and each cage kept a consistent supply of water to the rats along with appropriate ventilation (American Psychological Association, n.d.).

The 30 rats were divided into three groups; a first group which received their two meals a day with nothing added, a second that received one crushed pill of the experimental drug in the morning meal only, and a third group which received one pill crushed in each meal daily. Each pill contains 50 mg of the medication, group 2 would only receive this singular dosage while group 3 would receive a total of 100 mg of the medication. The control group in this experiment was group 1 while the experimental groups were groups 2 and 3. The effects of two doses were measured in this case in the effort to figure out what the appropriate amount of medication would be to stabilize, at a consistent rate, the blood pressure and heart rate of the 'patients'. The independent variables in this experiment would be the amount of medication provided to the rats. The dependent variables in this experiment would be the resulting heart rate and blood pressure measurements.

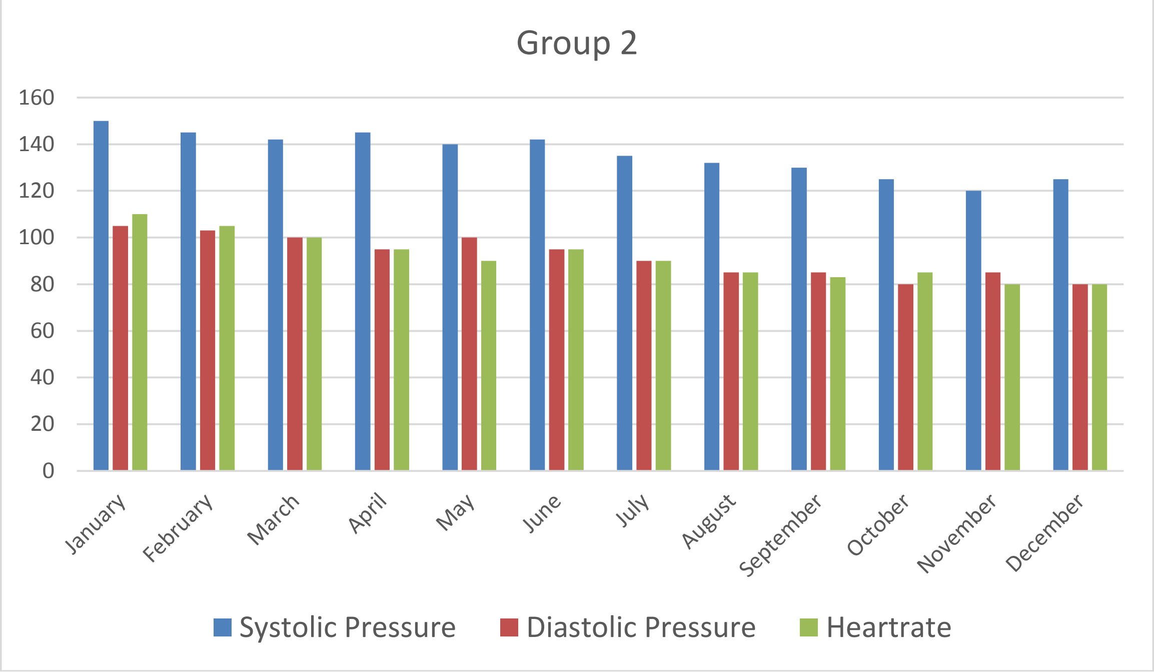
Every day, after their morning feeding and after their evening feeding, the blood pressure, heart rate, and temperature of each rat was taken with the use of a Passive Infrared Transponder (PIT) and a CODA surgical monitor. The PIT was chosen as it includes a sensor for temperature and could be injected subcutaneously while still obtaining an accurate reading, it is able to withstand internal body temperature. The CODA surgical monitor is a tail cuff system that allows for an accurate reading of systolic, diastolic, mean BP, heart rate, tail blood volume, and blood flow in rodents as small as 8 grams to rats as large as 950 grams. This CODA surgical monitor is also applied through a noninvasive procedure, helping maintain the stress levels of the rats used in the experiment low.

Once a month, the rats underwent a complete blood count (CBC) to check their levels of blood glucose, potassium, sodium, and cholesterol. These levels were obtained to ensure that the rodents would be able to withstand the pharmaceutical treatment throughout the duration of the experiment. To ensure that the hearts of the lab rats would be able to withstand the experiment, an EKG was also conducted each month with the Animal Bio Amp including PowerLab with LabChart software. The measurements obtained each day were kept diligently in a log; this included systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate, tail blood volume, and tail blood flow. Along with these measurements were the cholesterol levels for each rat. Meal times and measurement times were strict so as to prevent faults throughout the experiment and eliminate much of the chance of obtaining erroneous results.

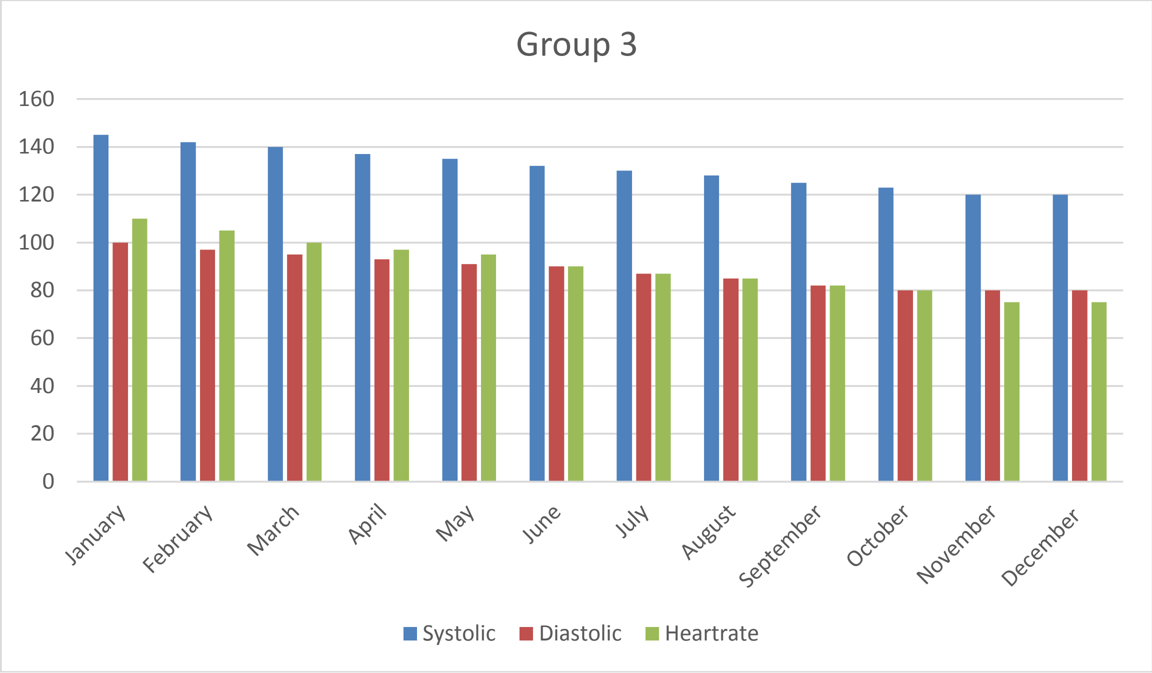
Results



This graph represents the average blood pressure, systolic and diastolic, along with heart rates for the group 1 control Zucker rat group, each month for the year tested. In the month of January, the average systolic pressure was 140mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 100 bpm. In the month of February, the average systolic pressure was 135mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 95 bpm. In the month of March, the average systolic pressure was 138mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 97 bpm. In the month of April, the average systolic pressure was 140mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 100 bpm. In the month of May, the average systolic pressure as 138mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 100 bpm. In the month of June, the average systolic pressure was 135mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 98 bpm. In the month of July, the average systolic pressure was 140mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 95 bpm. In the month of August, the average systolic pressure was 135mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 100 bpm. In the month of September, the average systolic pressure was 138mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 97 bpm. In the month of October, the average systolic pressure was 140mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 95 bpm. In the month of November, the average systolic pressure was 135mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 100 bpm. In the month of December, the average systolic pressure was 140mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 97 bpm.



This graph represents the average blood pressure, systolic and diastolic, along with heart rates for the group 2 Zucker rat group receiving one pill, each month for the year tested. In the month of January, the average systolic pressure was 150mmHg, the average diastolic pressure was 105mmHg, and the average heart rate was 110 bpm. In the month of February, the average systolic pressure was 145mmHg, the average diastolic pressure was 103mmHg, and the average heart rate was 105 bpm. In the month of March, the average systolic pressure was 142mmHg, the average diastolic pressure was 100mmHg, and the average heart rate was 100 bpm. In the month of April, the average systolic pressure was 145mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 95 bpm. In the month of May, the average systolic pressure was 140mmHg, the average diastolic pressure was 100mmHg, and the average heart rate was 90 bpm. In the month of June, the average systolic pressure was 142mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 95 bpm. In the month of July, the average systolic pressure 135mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 90 bpm. In the month of August, the average systolic pressure was 132mmHg, the average diastolic pressure was 85mmHg, and the average heart rate was 85 bpm. In the month of September, the average systolic pressure was 130mmHg, the average diastolic pressure was 85mmHg, and the average heart rate was 83 bpm. In the month of October, the average systolic pressure was 125mmHg, the average diastolic pressure was 80mmHg, and the average heart rate was 85 bpm. In the month of November, the average systolic pressure was 120mmHg, the average diastolic pressure was 85mmHg, and the average heart rate was 80 bpm. In the month of December, the average systolic pressure was 125mmHg, the average diastolic pressure was 80mmHg, and the average heart rate was 80 bpm.



This graph represents the average blood pressure, systolic and diastolic, along with heart rates for the group 3 Zucker rat group receiving two pills, each month for the year tested. In the month of January, the average systolic pressure was 145mmHg, the average diastolic pressure was 100mmHg, and the average heart rate was 110 bpm. In the month of February, the average systolic pressure was 142mmHg, the average diastolic pressure was 97mmHg, and the average heart rate was 105 bpm. In the month of March, the average systolic pressure was 140mmHg, the average diastolic pressure was 95mmHg, and the average heart rate was 100 bpm. In the month of April, the average systolic pressure was 137mmHg, the average diastolic pressure was 93, and the average heart rate was 97 bpm. In the month of May, the average systolic pressure was 135mmHg, the average diastolic pressure was 91mmHg, and the average heart rate was 95 bpm. In the month of June, the average systolic pressure was 132mmHg, the average diastolic pressure was 90mmHg, and the average heart rate was 90 bpm. In the month of July, the average systolic pressure was 130mmHg, the average diastolic pressure was 87mmHg, and the average heart rate was 87 bpm. In the month of August, the average systolic pressure was 128mmHg, the average diastolic pressure was 85mmHg, and the average heart rate was 85 bpm. In the month of September, the average systolic pressure was 125mmHg, the average diastolic pressure was 82mmHg, and the average heart rate was 82 bpm. In the month of October, the average systolic pressure was 123mmHg, the average diastolic pressure was 80mmHg, and the average heart rate was 80 bpm. In the month of November, the average systolic pressure was 120mmHg, the average diastolic pressure was 80mmHg, and the average heart rate was 75 bpm. In the month of December, the average systolic pressure was 120mmHg, the average diastolic pressure was 80mmHg, and the average heart rate was 75 bpm.

Conclusions

The lower dosage of the results shows the effectiveness of the drug. However, in contrast to the higher dosage which resulted in a more stable decline in blood pressure, the lower dosage was less stable in lowering and regulating the test subjects' blood pressure. The higher dosage of the experimental medication led to a steady decline from hypertensive status to one of normotension and effectively maintained it at that level. The lower dosage of medication could work well for patients who have just reached hypertensive status as they have not already sustained extensive damage to their cardiovascular system and body. Having the higher dosage of medication which lead to a steadier decline in blood pressure would be better for a patient whose condition necessitates a much faster solution.

The hope of these results is that the scientific community will only continue to make these advances in terms of treating hypertension. The more widespread these types of medications become the more people will be able to access them in order to regulate their high blood pressure. With a chronic illness such as hypertension affecting 29.1% of the adult population in the United States (Nwankwo et al., 2013) and a lower likelihood that patients with Medicaid will be on fixed dose-combination drugs and have their hypertension controlled (Fontil et al., 2017), it is imperative that the scientific community, insurance companies, physicians or other medical professionals, and even legislators all come together to ensure that people of any socioeconomic status are able to access effective medication.

The scientific community has an ethical responsibility to make an effort to inform the public about the dangers of hypertension, especially if the condition goes uncontrolled. Public health officials can initiate a community outreach program that involves going out to schools to educate students at an early age and also making visits to community health centers or areas that are underprivileged and thus will tend to have a higher rate of uncontrolled hypertension (Conen et al., 2009). Government medical assistance for managing chronic illness for individuals of a lower socioeconomic status would be one good solution for effectively managing hypertension in this group. Another could be allotting more money for the supplemental nutrition assistance program (SNAP) while simultaneously placing stricter guidelines on what can be purchased with the benefits. This would save money in the long run as a preventative measure, it would cost more to then pay for these individual’s medical treatments for end-stage hypertension and the possible complications.

Making healthy food choices and maintaining a steady balanced diet is one of the most important factors in managing hypertension in the vast majority of patients. However, availability of food options in lower socioeconomic neighborhoods contributes to a higher rate of hypertension occurring in these households. One of the pieces of legislation affecting the cost of healthier food options is the farm bill. The farm bill is currently comprised of regulations surrounding farm commodity price and income supports, agricultural conservation, farm credit, trade, research, rural development, bioenergy, foreign food aid, and domestic nutrition assistance (Johnson & Monke, 2017). One of the problems with this bill is that it is written by Congress members and not by experts or those who it would affect. The purpose of the farm bill is to create an alliance with farms and promote healthy living but trends indicate otherwise (Roberts et al., 2012). The legislation has allowed for unhealthy food choices to become less expensive and healthier food options have grown into the more expensive option. This only increases the health disparity in the United States.

The research conducted is certainly limited in terms of its patient base which happens to be Zucker rats. Studies and trials still need to be conducted to determine not only the effectiveness of the drug in human patients but also any possible complications. The study was also limited by time, it was conducted over the course of only one year while an ideal trial of a medication would be conducted over a course of time closer to at least three years. It would be recommended to conduct more trials of the proposed medication on patients whose hypertension is otherwise uncontrolled by other combined-dose drug treatments and who provide informed consent for the experimental medication. Before this point however, another trial can be conducted with non-human primates to ensure the medication is safe for the next phase with humans. Not only would they indicate further safety but also effectiveness of the medication as the genome of the primates is even closer to humans than the Zucker rats.

Particular organizations such as People for the Ethical Treatment of Animals (PETA) and the Humane Society would have serious objections over the utilization of animals as test subjects. They argue that animals used in a laboratory setting are treated inhumanely, that they needlessly suffer and then die in vain. There is legislation such as the Animal Welfare Act (AWA) and organizations such as the Committee on Animal Research and Ethics (CARE), affiliated with the American Psychological Association, who exist for the purpose of ensuring the fair and humane treatment of animals in experimentation. Another issue surrounding the proposed pharmaceutical is cost. Being a generic versus a name brand medication the hope is that the medication tested in this study will be more accessible to the general public. We would also like to propose a government grant for further accessibility to the general public. A grant covering at the bare minimum the manufacture of the medication would allow the drug to be offered at low-cost or even free at community health centers for at-risk populations.

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