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Cardiac differences between "White coat syndrome" and true hypertension

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Title Cardiac differences between “White coat syndrome” and true hypertension.

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Abstract

White coat syndrome or hypertension is a condition where patients in a clinic setting exhibit above-the-normal-range blood pressure level, but a normal blood pressure range when in other settings such as home. White coat syndrome often progresses to sustained hypertension, alters left ventricular diastolic function and the elastic properties of the aorta. The variability of blood pressure that is the fluctuations of blood pressure with time increases stiffness of the major arteries in the body. These changes may eventually lead to target organ damage or stroke. It is believed that these changes are the cause for end target organ damage that occurs. There are different opinions when it comes to treating white coat syndrome, the general consensus by the researchers (which will be discussed in subsequent paragraphs) is to perform further studies with larger population sizes over a longer time frame of study. This is relevant since the percent of adults ages 20 and over with hypertension is 33.5% (CDC, 2017). This number is growing in our society and any and all information is important in the diagnosis and treatment of this condition to prevent the detrimental effects of end target organ damage, high costs of treatment, lost productivity of employees in the workforce and mortality.

Background

My clinical topic focused on researching into white coat syndrome comparing to essential or true hypertension and noting if any possible cardiac differences exist between the two. A 67-year old white female who came into the office for a three-week follow-up after prescribed lisinopril 20mg taken once daily. The patient developed an angiotensive converting enzyme inhibitor (ACEI)-induced cough, severe enough to consider alternative therapies and different medications, not only for the unpleasant side effects from lisinopril but also to better manage her blood pressure (BP). Since the patient continued to have elevated blood pressure additional investigation and treatment was warranted. Further querying of the patient's history revealed that her BP readings at home were also high in the 160/90 mmHg range.

White coat hypertension (WCH), or as it is commonly known as white coat syndrome (WCS), is a phenomenon when patients exhibit above-the-normal-range blood pressure level, in a clinical setting and not in other settings. There is some belief that this phenomenon maybe related to anxiety experienced by patients during a clinic visit**.** There is evidence to show that increases in BP are the leading cause of coronary artery disease (CAD), stroke, arrhythmia, and death (Ermis et al., 2016). White coat syndrome prevalence increases with age, progresses to true hypertension, and causes end target organ damage (Puchales et al., 2010).

Although numerous studies have been conducted on WCS in determining the prognostic significance, it remains unclear. There is some controversy when it comes to diagnosis and treatments of WCS. The instrument BP cuff used to measure the BP, activities before the appointments, and anxiety could all cause a false high BP reading. The purpose of this report is to learn more about WCS, whether there are different cardiovascular outcomes between this and true hypertension.

Case Report

A 67-year-old Caucasian female presented to the primary care office for follow-up on hypertension (HTN). She denied any significant past medical history other than “the occasional seasonal sinus issues” for which she used over the counter antihistamine Claritin, which relieved the sinus symptoms. Also, she was diagnosed with hypertension three-weeks ago, and was prescribed lisinopril 20mg daily at that appointment. Since starting the medication she voiced noticing a dry, irritating cough that was worse at night and even woke her from sleep. She monitors her blood pressure every morning with readings usually in the 160/80mmHg range and a heart rate between 60 to 70 beats per minute. She voiced health maintenance lab work was completed about six months prior to this visit. The results of the lab work showed her basic metabolic panel (BMP) to be within normal range, but the results of the lipid panel revealed elevated low density lipoprotein (LDL); She was advised by the health care provider to engage in exercise program as well as weight-loss to decrease the risk of cardiovascular diseases.

She denied dizziness, palpitations, or chest pain. She was one pack per day smoker for fifteen years and quit for ten years. She admitted alcohol consumption weekly. Health maintenance practice includes annual eye exams, dental visits, and regular exercise of water aerobic. Her familial history includes coronary artery disease in her father, mother, and oldest brother who had multiple coronary bypass surgeries.

The physical exam reveals a well nourished, non-toxic appearing female who is age appropriate and answered questions appropriately. Her heart rate was regular, no jugular venous distention (JVD) or murmur appreciated, and lungs were clear bilaterally on auscultation. Her hands and feet showed no edema. She had normal bowel sounds auscultated in all four quadrants, abdomen was soft and non-tender, and had no CVA tenderness appreciated, and

genitourinary exam was deferred by patient. Blood pressure reading in office was 160/80mmHg with a pulse of 80.

Diagnosis of uncontrolled Hypertension, Angiotensive Converting Enzyme Inhibitor (ACEI) induced cough, and Borderline low density lipoproteins (LDL) were made. The lipid panel was repeated to monitor LDL as well a comprehensive metabolic panel (CMP) in the office which showed only elevated LDL level.

The treatment plan for the uncontrolled hypertension and ACEI-induced cough include:

- Discontinuing Lisinopril due to ACEI-induced cough and starting on hydrochlorothiazide (HCTZ) 25mg to be taken orally daily starting following morning.
- Monitoring blood pressure randomly together with heart rate and bring results with to next appointment in one month.
- Encouraging to continue with water aerobics three times/week.
- Advised on risk factors of cardiovascular events and to cut down salt intake.
- Informed that we plan to do another BMP on next appointment to monitor kidney function and for any electrolyte imbalance

Pertaining to the borderline LDL treatment she will be started on fish oil 1000mg twice a day.

Literature Review

The fore mentioned case report about hypertension raised the question about white coat hypertension or white coat syndrome does it exist? It was postulated that it may not be real. Also, could there be any cardiovascular outcomes between WCS and "normal"/ true hypertension. Researching current literature revealed some interesting information, which will be discussed in the subsequent paragraphs.

The prevalence of WCS increases with age and about 45% of patients over the age of 65 have been diagnosed with this condition. The authors defined WCS as systolic blood pressure of greater than 140 mmHg and a diastolic blood pressure greater than 90 mmHg without any antihypertensive treatment in the office setting (Puchales et al., 2010). Left ventricular hypertrophy was also found in WCS, the prevalence of left ventricular hypertrophy (LVH) in WCS was found to be about 50%. Also, the more abnormalities that are present in the left ventricle, the higher the chances of increased mortality (Puchales et al., 2010). This suggests that WCS over a prolonged time may be associated with cardiac damage, and may have prognostic implications for morbidity or mortality. Huang et al. (2017) researched whether or not WCS is a risk factor for cardiovascular disease and mortality. WCS without antihypertensive treatment was associated with long-term risk of cardiovascular disease (CVD) and total mortality in patients, and suggested that more monitoring or close follow-up should be performed in these WCS patients (Huang et al., 2017). In elderly people, WCS is linked with cardiac structural abnormalities comparable to what is seen in people with sustained hypertension (Puchales et al., 2010). Ermis et al. (2016) also found that WCS was linked with a higher risk of developing persistent hypertension, and it also had an effect on target organ damage.

Ermis et al. (2016) did a study looking at left atrial volume and function in patients with WCS using real-time 3-D echocardiography. The authors also looked at ambulatory BP monitoring in WCS individuals. The results showed there were no significant differences between the control individuals and the WCS individuals for ambulatory BP monitoring. Krakoff (2015) discussed using ambulatory or out of office BP readings to help diagnose and treat WCS patients. Krakoff felt this was important to have accurate home BP readings as these will help decrease unnecessary treatment of WCS patients. Krakoff found that in some prospective studies WCS has a slightly higher risk for future target organ damage than sustained hypertension (Krakoff, 2015). Research has been done evaluating the most appropriate medical treatment for WCS but it has yet to be determined if these treatment are effective in preventing cardiovascular disease in this population (Krakoff, 2015). Krakoff recommended using ambulatory or out of office BP readings to detect WCS as it can often reduce the many burdens associated with drug treatment for these patients.

White coat syndrome often progresses to sustained hypertension, and it can alter left ventricular (LV) diastolic function and the elastic properties of the aorta. The latter two have been identified as markers of target organ damage in hypertension (Ermis et al., 2016). The authors discuss another study that showed that 42% of 1412 patients who had WCS had developed sustained hypertension during the ten year follow-up. Any changes in the left atrial volumes (LAV) can affect the expansion index and ultimately help predict cardiac arrhythmia in these patients. The authors concluded that due to the small sample size of the participants, there is the need for a large scale prospective study with a longer term follow-up (Ermis et al., 2016). The authors concluded that the impaired left atrium may lead to atrial arrhythmia, but further

studies are required to determine the prognostic power of atrial measurements for cardiovascular events in WCS patients.

Shehab and Abdulle (2011) in their study focused on cognitive and autonomic dysfunction (specifically heart rate variability) in WCS, the authors also found WCS did contribute a risk for cardiovascular disease. The authors explored the hemodynamic differences and presence of any functional changes. The results found that patients with WCS performed less in the memory test, and echocardiogram revealed no significant differences in left ventricle mass indices and diastolic function. The authors concluded that WCS may not be a benign condition as previously thought and may contribute to an overall risk for left ventricle damage and cardiovascular disease. A recommendation is to do a longitudinal study of WCH patients to clarify the progressive nature of this condition (Shehab & Abdulle, 2011). There is existing evidence that indicates that WCS may develop into persistent or true hypertension over time.

Briasoulis, Androulakis, Palla, Papageorgiou, and Tousoulis (2016), performed a systematic review to determine the effects of WCS on cardiovascular events, stroke, and death. They found that patients with WCS had a slight, higher rate of cardiovascular disease, morbidity and mortality compared to normotensive patients. Also, WCS may develop into true hypertension which carries slightly, higher, cardiovascular risk especially if other risk factors are present. Briasoulis et al. (2016) recommend further studies that will focus on participants with WCS who are at higher risk of progressing to sustained or true hypertension since these patients would benefit from treatment to decrease cardiovascular morbidity and mortality. Based on the results of their study WCS is real, and there was no mention of cardiac difference between this and sustained or true hypertension (Briasoulis et al., 2016).

Another study performed by Cacciolati, Hanon, Dufouil, Alpérovitch, and Tzourio (2013) looked at a one-year follow-up in elderly patients with untreated WCS and the risk of developing sustained hypertension. The elderly with high office BP readings had a three-fold increased risk of developing sustained or normal hypertension a year later. The authors went on to say that the elderly are at higher risk for developing hypertension-related diseases such as strokes, heart and renal failure; thus it is important to understand the risk of sustained hypertension in the elderly (Cacciolati et al., 2013). The study mentioned conflicting thoughts as to whether WCS increases a patient's risk of target organ damage.

Franklin, Thijs, Hansen, O'Brien, and Staessen (2013) looked at cardiovascular risk associated with WCH. Patients with untreated WCH failed to show a progressive increase in cardiovascular risk over time and did not progress to sustained hypertension. This could also be due to the fact that patients were selected inappropriately with high-normal blood pressure and not WCS, and this could also be the reason for the failure to progress to sustained hypertension. There is the belief that it may be beneficial to treat high-risk patients with white-coat hypertension, but this is untested by randomized controlled trials. A small study was performed treating WCS in elderly patients but there was no evidence of beneficial effect of active treatment on ECG voltages or stroke incidence. Patients with high cardiovascular risk and showing evidence of hypertensive target organ damage should not only institute lifestyle changes but to make a treatment decision based on documented elevated 24-hour ambulatory or home BP readings (Franklin et al., 2013).

Muntner, Booth III, Shimbo, and Schwartz (2017) performed a meta-analysis study looking at data from previous studies to determine if WCS led to higher risk of cardiovascular outcomes; and diagnosing WCS accurately to prevent unwarranted use of antihypertensive

medication. There is a tremendous need to identify the cardiovascular risk in the WCS population due to the high prevalence of WCS. The authors after reviewing the meta-analysis suggested screening for WCS with ambulatory or home BP monitoring thus avoiding the unwarranted initiation of antihypertensive medication.

Kaplan and Townsend (2015) had suggestions for minimizing WCS such as decreasing anxiety, which is one of the contributors of WCS. This could include having the nurse or technician take the BP reading rather than the clinician, or using an automated oscillometric blood pressure monitor. Also, it takes about three to six visits for a new patient to a doctor's office to reach a stable BP value; therefore if the patient has a mild to moderate elevation in BP, it would be reasonable to delay diagnosis of WCS until about the sixth visit. Exceptions to this include the patient's blood pressure that remains elevated after three to six visits or there is evidence of ongoing end-organ damage. The cardiovascular risk connected to WCS may be slightly higher than in a normotensive patient as well as a significantly higher rate of mortality during a sixteen-year follow-up. WCS patients are at a high risk of developing sustained hypertension. This seems to be the general consensus that is the progression to sustained or normal hypertension (Kaplan & Townsend, 2015).

In conclusion whether WCS is an innocent phenomenon is controversial. Ermis et al., Puchales et al., Huang et al., Briasoulis et al., and Krakoff concluded from their studies WCS increased the risk of cardiovascular disease. Also, there was slightly higher risk of causing target organ damage and if not treated could lead to mortality. Shehab and Abdulle also found WCS may contribute an overall risk for cardiovascular disease. When it comes to treating or not to treat there are divided opinions as well. There is not enough data to support the effectiveness of drug treatment in reducing the potential for cardiovascular disease risk. Krakoff and Briasloulis

et al., recommended using ambulatory or out of office BP readings to detect WCS as it can often reduce the many burdens associated with drug treatment for these patients. There are no cardiovascular differences between WCS patients and patients with sustained or true hypertension as confirmed by the studies in previous paragraphs, but further studies with larger population size and a longer time frame of study is needed.

Learning Points

- White coat hypertension is a known medical phenomenon. Research while somewhat limited has not been able to identify cardiac differences between those diagnosed with WCS and essential hypertension.
- White coat syndrome is a well-documented medical condition affecting an estimated 33.5% of people in America. Some research has evidence to support that it does eventually lead to target organ damage, increases risk of stroke, and cardiovascular disease. Left ventricular hypertrophy may be an early sign of end-organ damage, which is otherwise undetectable, and the best way to do so is to perform an echocardiogram.
- The role of white-coat hypertension (WCH) in development of cardiovascular disease (CVD) risk remains poorly understood. There is evidence to show changes in the left ventricle, left ventricle hypertrophy, and stiffness in the artery over time increases the risk for CVD. The research recommends a larger population sample to be used and also long-term follow-up.
- There may be some benefit to treat high-risk patients with white-coat hypertension; this is however untested by randomized controlled trials.
- In a small study performed elderly patients with WCS were treated but there was no evidence of beneficial effect of active treatment on ECG voltages or stroke incidence.
- Patients with high cardiovascular risk and showing evidence of hypertensive target organ damage should institute lifestyle changes. Treatment decision should

be based on documented elevated 24-hour ambulatory or home BP readings and not in office readings.

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