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A Systematic Review: Relationship Between Medication Adherence

and Hypertension

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A master project completed in partial fulfillment of the requirements for the degree of Masters Science—Nursing, Family Nurse Practitioner at the Valley Foundation School of Nursing, San José State University

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A Systematic Review: Relationship Between Medication Adherence and Hypertension

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Family Nurse Practitioner Program

The Valley Foundation School of Nursing

San José State University

May 1st, 2023

Abstract

Chronic diseases are defined as conditions that are present for over one year and limit activities of daily living or require ongoing medical attention. Heart disease is the number one leading chronic disease in the United States, making up one third of all deaths. In turn it costs the health system \$216 billion per year (Center for Disease Control and Prevention, 2023). Uncontrolled blood pressure is a key risk factor for heart disease and stroke. 1 in 2 adults will need to take prescription medication to control blood pressure and lower the risk of having a cardiovascular event. This systematic review is aimed to explore the relationship between medication adherence and blood pressure. Studies between 2012-2020 will be utilized. This systematic review did find an association between medication adherence and decreased blood pressure. Many factors played a role in medication adherence such as: health literacy, socioeconomic status, frequency of disease monitoring, co-payments and medication taking reminders. Definition of terms in Appendix A.

Keywords: medication adherence, compliance, uncontrolled hypertension, hypertension, blood pressure

Background

Approximately half of the adult population in the United States have high blood pressure or hypertension. One in four adults will have controlled hypertension, leaving 75% of the individuals with uncontrolled hypertension (Center for Disease Control and Prevention, 2020b). The disease burden of hypertension accounts for one third of the total mortality, globally (Kang et al., 2014). Hypertension is a modifiable medical condition that can lead to a cardiac event or stroke if not controlled (Center for Disease Control and Prevention, 2020b). In addition to lifestyle modification, many individuals need to take antihypertension medication to maintain their blood pressure at a healthy level (Center for Disease Control and Prevention, 2020a). Ampofo et al. (2020), states there are excellent clinical outcomes that are associated with medication adherence. Despite the evidence, medication adherence rates remain low, possibly due to the lack of patient education (Ampofo et al., 2020). Lack of proper education leads to a decrease in adherence and may cause debilitating effects (Ampofo et al., 2020). Nonadherence to medication can lead to hospitalization and is estimated to cost the healthcare system \$100 billion dollars (Kini & Ho, 2018). Research have been implemented to improve adherence, yet the rate has not been significantly approved (Hedegaard et al., 2015; Kini & Ho, 2018). The Morisky Medication Adherence Scale (MMAS) is a self-reported scale regarding common medication taking behavior questions (Moon et al., 2018). MMAS is used due to its simplicity, although it is at risk of bias since it is self-reported (Moon et al., 2018). The higher the number in the results, the higher the adherence, and vice versa. The lower the results, the lower the adherence (Moon et al., 2018). Many clinical trials have proven that medication adherence lowers a patient's risk of stroke and myocardial infarction by 30-43% (Delavar et al., 2020; Kang et al., 2014; Matsumura

et al., 2013). Poor medication adherence can lead to poor health management and need to be addressed. Yue et al. (2015) and Kang et al. (2014) conducted research to determine factors that hinder medication adherence. Kini and Ho (2018) discovered six categories of interventions which are used in the following research studies. The six categories are: patient education, regimen management, clinical pharmacist consultation, motivational interviewing, medication reminders and reducing co-payments (Kini & Ho, 2018).

Methods

Study Purpose

Despite educational interventions, medication adherence in patients with hypertension remains uncertain (Ampofo et al., 2020). The purpose of this review is to determine whether medication adherence is directly related to decreased blood pressure and which interventions showed the highest adherence post intervention.

Search Strategy

Systemic search on medication adherence and hypertension was conducted using CINHAL, PubMed, and science direct. Initially, the search yielded thousands of results when using SJSU one search or Google Scholar. To reduce the high yield, each database was utilized individually. By using this method, results yielded were much smaller in quantities, some less than 200. Using this single database method provided more accuracy in resulting articles. Keywords included "medication adherence", "hypertension", "blood pressure". Research published between 2012 and 2022 will be included to ensure relevant data. The outcomes focused on medication adherence and how it affected blood pressure readings. A systemic approach provides the opportunity to fill gaps in knowledge (Thomas et al., 2022). Selected filters will aid in excluding articles that are meta reviews. The Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) checklist was utilized to provide an evidencebased search for systematic review. (Appendix B)

Inclusion & Exclusion Criteria

Adults ages 18 and over with primary hypertension who have high blood pressure will be the population included in the search. Articles that were not full text, available as free, systemic reviews, published within the last ten years, or had subjects other than humans were excluded. Articles that included modifying multiple risk factors in addition to medication adherence will not be included, in other words, articles that focused only on medication adherence were included in this study. The control arm should have not received additional intervention and should only receive usual care from their primary care provider. Usual care is defined as the typical appointments the patient receives from their primary care provider without additional medication education intervention. This meant handouts, text messages, phone call reminders to take medications (Hedegaard et al., 2015).

Participants with secondary hypertension or have controlled blood pressure were excluded from this study. The secondary outcome of this study was to evaluate the effect of medication adherence on blood pressure, and the results will not be accurate of more than one intervention occurred. Articles that used surveys other than the Morisky Medication Adherence Scale (MMAS) or medication possession ratio (MPR) to evaluate medication adherence were excluded. MMAS is preferred due to its specificity to medication adherence. MMAS has been validated with good reliability and validity (α = 0.83) when measuring adherence in an outpatient setting. (Kang et al., 2014).

Data Extraction and Analysis

A literature review matrix was utilized from Walden university (Walden University, 2023) which consisted of eight categories (Appendix C). Those categories were author/date, framework, hypothesis, methodology, analysis/results, conclusions, implications for future research and implications for practice. Each of these eight categories were used to evaluate the final eight articles used in this research. In addition to the review matrix, Melnyk's level of evidence was also utilized to categorize the level of evidence (Fineout-Overholt, et al., 2010).

Quality Appraisal

Melnyk found seven levels of hierarchy when it came to intervention studies. Each level was based on the type of evidence. Level I of evidence consists of systematic reviews or metaanalysis. Level II is for randomized controlled trials (five articles were randomized control trials), level III: controlled trial without randomization, level IV: case control or cohort study (one article was a cohort study), level V: systematic review of qualitative or descriptive studies (two articles were qualitative), level VI: qualitative or descriptive study and level VII: expert opinion or consensus (Fineout-Overholt, et al., 2010). The following chart of levels can be found in Appendix C. Overall, of the eight articles, five were level II, one was level IV and two articles were level V.

Results

As stated above, three search engines were utilized: CINHAL resulted in 99 articles, Pub Med resulted in 156 articles and Science Direct resulted in 127 articles, which in total resulted 382 articles. Articles were excluded if the participants were younger than 18, included subjects other than humans, not in English, no full free text available and was published before 2012. This eliminated 300 articles and 20 remained for eligibility. 12 articles were disqualified for

including multiple modifiable risk factors in addition to medication adherence to lower blood pressure. A total of 8 articles were included at the end of the search.

Literature

Research Study 1

Matsumura et al. (2013) performed a randomized controlled trial of 203 hypertensive subjects to investigate the association between medication adherence and blood pressure control. The study took place at 29 hospitals and clinics in Japan. Subjects were placed into three groups based on their initial adherence (relatively low, moderate, and high) and randomly assigned to a daily regimen. The daily regimen consisted of losartan 50 mg and hydrochlorothiazide 12.5 mg or two pills of an angiotensin II receptor blocker and a thiazide diuretic (Matsumura et al., 2013). Follow up with the participants was performed at one, three and six months. During follow up, residual pills were assessed to determine how many pills the patient did not take. Adherence was determined using the following formula: number of prescribed pills - number of residual pills/numbers of prescribed pills x 100. In addition to calculating adherence, blood pressure was assessed by taking two measurements, five minutes apart and determining the mean. The results of the study showed the mean blood pressure of the low adherence group were significantly higher compared to the moderate and high adherence group. In turn, medication adherence was found to be directly related to blood pressure control (Matsumura et al., 2013)

Research Study 2

Similarly, Kang et al. (2014) performed a cross sectional study to explore the determinants of medication adherence and blood pressure control. Data was collected by self-administered questionnaires and blood pressure management by trained professionals. An eight item Morisky Medication Adherence Scale (MMAS-8) was used to measure medication

adherence while a second questionnaire was used to determine variants in the participants lives. The variants consisted of age, sex, marital status, household income, occupation status, family members with hypertension, self-perceived health status and illness perception and knowledge (Kang et al., 2014). The results showed that marital status and morbidity count was directly associated with blood pressure control while age, employment and self-perceived health status were associated with medication adherence. Kang et al. (2014) stated there should be further investigation on the determinants and relations between medication adherence and blood pressure control.

Research Study 3

Along with Kang et al. (2014), Delavar et al. (2020) utilized the Morisky Medication Adherence Scale in a randomized control trial to determine the effects of education on medication adherence and blood pressure control. Unsuccessful hypertension management is directly related to poor medication adherence (Delavar et al., 2020). Delavar et al. (2020) reports the major factors contributing are altered physical, mental, and psychological function and lack of knowledge. The intervention group received 30–45-minute face to face sessions for two weeks followed by 15-minute phone calls for four weeks. Participants in the control group received routine interventions by their providers. As a result, the intervention group proved that educational intervention could improve medication adherence and decrease blood pressure. Although the intervention group was successful, there were no significant changes in the control group (Delavar et al., 2020).

Research Study 4

Yue et al. (2015) reported that interventions to medication adherence should be focused on risk factors. A cross sectional study was performed to determine the risk factors and how they

effected blood pressure control. Participants who were on a longer duration of drug use, had more access to professional guidance and who were less concerned of medical cost had a higher likelihood of adhering to their medication regimen (Yue et al., 2015). Of the 232 participants, those who had a high adherence according to the MMAS-8, showed a lower systolic blood pressure when compared to those with a low drug adherence (Yue et al., 2015).

Research Study 5

Morawski et al. (2018) aimed to determine whether the association of a smartphone application can increase medication adherence and decrease blood pressure. Morawski et al. (2018) performed a randomized clinical trial with a total of 411 participants. The intervention group was instructed to download an application called Medisafe and the control group was not instructed to download the application. The Medisafe application reminded the participants to take their medication, offer peer support and created adherence reports (Morawski et al., 2018). The Morisky Medication Adherence Scale was used to determine if the intervention was successful. In the intervention group, the adherence increased while the adherence remained the same in the control group. Blood pressure readings decreased by 10.6 mm Hg in the intervention group and decreased by 10.1 mm Hg in the control group. Although both groups had a decrease in blood pressure, there were no significant differences between the two (Morawski et al., 2018).

Research Study 6

Hedegaard et al. (2015) attempted to improve medication adherence in a randomized control trial, with secondary outcomes of lowering blood pressure. The intervention group received usual care from their physician in addition to the following three interventions: medication reviewing which focused on drug related problems, adherence counseling and motivational interviewing via telephone follow-ups (Hedegaard et al., 2015). The control group

received usual care which consisted of two to four outpatient consultations with a physician or nurse. The consultation included blood pressure education regarding risk factors, medication adherence and control of blood glucose (Hedegaard et al., 2015). Results of the study showed medication adherence did not have any effects on clinical outcomes (Hedegaard et al., 2015).

Research Study 7

Shaw and Bosworth (2012) explored the characteristics of 159 patients with hypertension to determine if being medication adherent can predict if a patient will need increased aid in hypertension management. The Morisky Medication Adherence Scale determined which patients we're adherent versus nonadherent. Baseline blood pressure measurements were obtained for both groups at baseline and every 6 months for 24 months (Shaw & Bosworth, 2012). The results of the study showed that blood pressure did not change overtime, for both groups. In turn, this shows a need in clinician care to manage blood pressure. A correlation analysis confirmed that financial status and race played a significant role in blood pressure and medication adherence (Shaw & Bosworth, 2012).

Research Study 8

The Morisky Medication Adherence Scale also determined the participants medication adherence in a randomized control trial conducted by Schoenthaler et al. (2019). A randomized control study was conducted to determine the relation between medication adherence education and blood pressure management in a six-month period (Schoenthaler et al., 2019). The intervention group received education geared towards adhering to antihypertensive medication regimens. Education targeted many factors leading to nonadherence such as: missed dose, extra dose, or refills. The intervention group also received coaching from a trained medical assistant and their primary care physician (Schoenthaler et al., 2019). Similar to Hedegaard et al. (2015), the comparison group received standard health education, blood pressure checks and coaching at the clinic from their primary care physician. As a result, the intervention group had a significant improvement on medication adherence and both groups had a reduction in their blood pressure (Schoenthaler et al., 2019).

Discussion

Yue et al. (2015) and Kang et al. (2014), agreed that an individual's age, lifestyle, education, socio-economic status, and marital status affects a patient's ability to adhere to their medication regimen. Yue et al. (2015) found that patients who are adherent to their antihypertensive medication regimen showed a decrease in blood pressure, as Delavar et al. (2020). presented similar results through an educational intervention. Delavar et al. (2020) and Hedegaard et al. (2015) approached medication compliance through an educational perspective and discovered educational sessions provided to participants led to an increase in adherence. Schoenthaler et al. (2019) agrees with Matsumura et al. (2013) and demonstrated an increase in adherence led to a decrease in blood pressure. Morawski et al. (2018) and Schoenthaler et al. (2019) approached medication adherence through an electronic system and their results differed. Morawski et al. (2018) instructed their participants to download a mobile application that aids in blood pressure monitoring and reminders to take their medication. With the aid of the application, the participants showed an increase in adherence and a decrease in blood pressure (Morawski et al., 2018). In contrast, Schoenthaler et al. (2019) instructed their patients to report to an electronic medical device through a system approach and this intervention did not improve adherence nor blood pressure. Similarly, Shaw & Bosworth (2012) attempted to show correlation to medication adherence and blood pressure control but did not find evidence connecting the two. Hedegaard et al. (2015) agrees with Shaw & Bosworth (2012) that medication adherence

did not have a significant impact on blood pressure. Schoenthaler et al. (2019) and Matsumura et al. (2013) found a relation between increased medication adherence and decreased blood pressure while Hedegaard et al. (2015) and Shaw and Bosworth (2012) have found the opposite. Overall, it has been shown that medication adherence is highly dependent on determinants of the patient and addressing those determinants can aid in a higher adherence (Kang et al. 2014; Yue et al. 2015).

Limitations

When performing a comprehensive search on the databases, there was a lack of current literature. Most research articles ranged between 2010-2015, with select few from 2018-2022. A second concern of this study is that the researcher is a novice, which can lead to a low-quality study.

In addition to limitations, the eight research studies had conflicting results. Five of the eight articles agreed that medication adherence lowered blood pressure, while the remaining three agreed that there were no changes in blood pressure. Further research is needed to determine how medication adherence is directly related to blood pressure.

Gap in Literature

Nearly half of the uncontrolled blood pressure cases are directly related to nonadherence to medication (Morawski et al., 2018). Delavar et al. (2020) found that educational intervention tailored to the patient's health literacy leads to adherence. Many factors lead to nonadherence and these factors need to be explored more to provide evidence-based research on the relation between medication adherence and lowering blood pressure. As mentioned prior, Kini & Ho (2018) discovered six categories of interventions that can be used to aid in adherence. The gap in this research is to determine the interventions which aid in adherence and proceed with this

intervention. In addition to determining the interventions, recognizing early risk factors in patients who are likely to be nonadherent may decrease a patient's risk of a cardiovascular event. Hypertensive patients will benefit from the healthcare system if there are more resources targeted at medication adherence. For the healthcare system to implement targeted medication adherence interventions, more research and evidence needs to be available. The healthcare system can save billions of dollars by focusing on modifiable risk factors that lead to nonadherence.

Conclusions and Practice Implications

Yue et al. (2015) and Kang et al. (2014), agreed that an individual's age, lifestyle, education, socio-economic status, and marital status affects a patient's ability to adhere to their medication regimen. By addressing these barriers, there can be a bridge between the gap of medication adherence and lowering blood pressure. For example, providing education intervention based on the individual's educational level plays a significant role. Approaching medication adherence in an educational perspective has led to an increase in adherence. Yue et al. (2015) found that patients who are adherent to their antihypertensive medication regimen showed a decrease in blood pressure, as Delavar et al. (2020) presented similar results through an educational intervention. Delavar et al. (2020) and Hedegaard et al. (2015) approached medication compliance through an educational perspective and discovered educational sessions provided to participants led to an increase in adherence.

Although it's been shown that medication adherence decreases blood pressure, it's dependent on each individual and their ability to modify risk factors or stay in medication adherent. Yue et al. (2015) and Kang et al. (2014), stated that an individual's age, lifestyle, education, socio-economic status, and marital status affects a patient's ability to adhere to their medication regimen. While attempting to change modifiable risk factors, decreasing blood

pressure is also dependent on the type of antihypertensive medication the patient is taking and if it's effective for that patient. Overall, it has been shown that medication adherence is highly dependent on determinants of the patient and addressing those determinants can aid in a higher adherence (Kang et al. 2014; Yue et al. 2015).

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Appendix A

Definition of Terms Used

Medication adherence: the extent to which a patient's behavior corresponds with the prescribed medication dosing regime, including time, dosing, and interval of medication intake (Gast, et al., 2019).

Blood pressure: the force of blood moving through the blood vessels (American Heart Association, 2022).

Hypertension: when the force of blood through your blood vessels is consistently too high. Systolic >130 mmHg or diastolic 80-89 mmHg (American Heart Association, 2022).

Morisky Medication Adherence Scale (MMAS):8 item self-reported scale that measures patient's antihypertensive medication adherence, specifically. Scores of an 8 was considered high adherence, less than 8 was medium adherence and less than 6 was low adherence (Yue et al., 2015).

Medication possession ratio (MPR): the amount of drug available from the time of refill to the follow up period, relative to the amount prescribed (Hedegaard et al., 2015).

Appendix B





Appendix C

Table of evidence

Author/year	Problem	Design	Sample size	Analysis	Results	Conclusions	Implications for Future research	Implications For practice	Quality Assessment (Fineout-Overholt, et al., 2010).
Matsumura et al., 2013	Does medication compliance relate to a decrease in blood pressure for patients who range from low, moderate and high adherence?	Randomized control trial	203 subjects who have hypertension. Blood pressure was evaluated at 1-, 3- and 6- months post randomizatio n.	The Morisky Medication Adherence Scale (MMAS)	Mean systolic blood pressure were higher in the low adherence group compared to the high adherence group.	Blood pressure is dependent on medication adherence	Number of pills a patient must take may play a role in adherence.	Clinicians play a significant role in medication adherence as they can reduce the number of pills, provide patient education or prescribe a cost-effective medication to aid in adherence.	Level II
Kang et al., 2014	What are the determinants of medication compliance and how does it affect blood pressure control	Cross sectional study	2445 participants	Medication adherence questionnair e MMAS	Marital status, duration of antihypertensive drug use and morbidity count were strongly associated with BP control.	The main factors that affect medication adherence were marital status, morbidity county and duration of antihypertensive medication use.	Underlying mechanisms of medication adherence need to be examined.	Patients may benefit from targeted interventions regarding adherence and blood pressure control.	Level V
Delavar et al., 2020	Does a tailored SME focused on medication	Randomized control trial	118 participants over 3 months	MMAS	Participants who received SME showed a decreased in blood pressure, which is	Patient education tailored to the patient's health literacy can promote adherence	Further research should be done on patient education, health literacy and	Healthcare providers can aid in adherence to medication by	Level II

	adherence lead to a decreased blood pressure				directly related to adherence.	to antihypertensive medication.	the effects on health outcomes.	educating patients.	
Morawski et al., 2018	Can a smartphone application help increase medication adherence and blood pressure control?	Randomized clinical trial	411 participants.	MMAS Self- reported adherence via application.	Adherence increased in the intervention arm while no changed were reported in the control arm.	Patients can benefit from downloading a smartphone application to maintain their adherence and blood pressure, thus decreasing their risk of a cardiovascular event.	Increase in smartphone applications targeted at healthcare is beginning to rise, yet more research needs to be done to evaluate the effectiveness.	Healthcare providers can aid in adherence to medication by educating patients.	Level II
Hedegaard et al., 2015	Will educating patients increase adherence and lower blood pressure?	Randomized trial	532 participants	Medication possession ratio (MPR)	no changes were found except for diastolic blood pressure in the intervention group.	Educational intervention did not have any clinical significance	Studies should be longer than 6 months with participants who have not reached their target blood pressure.	Motivational interviewing did not affect this cohort over a 6-month period.	Level II
Shaw & Bosworth 2012	Self- reported measure of adherence and characteristi cs of individuals to predict adherence.	Longitudinal study in two primary care clinics	with 159 participants	MMAS Blood pressure measuremen t	there were no changes in blood pressure nor adherence	Nonadherence is related to elevated blood pressure. Financial status, minority status, and African Americans are at higher risk for increased blood pressure.	Addressing risk factors can identify patients who are more likely to be nonadherent and behavioral interventions can be done.	Identifying nonadherent patients at baseline will direct nursing to intervene and promote adherence which can improve blood pressure.	Level IV
Schoethaler et al.,	Will systems lead approach with	Randomized control trial	119 participants	Electronic monitoring	(primary) a systems level approach had a greater	This study had null findings as the EMD was not reliable due to self-	Factors other than medication adherence shall be evaluated to control	Medication adherence is directly related to deceased	Level II

2019	educational			device	improvement in	reported measures	blood pressure, such	blood pressure	
	intervention			(EMD)	adherence than the	for the primary	as diet, and lifestyle	and some self-	
	lead to				comparison group,	results. As for	changes.	reported	
	increased			MMAS	when using the	secondary results		measures are	
	medication			WINIAS.	MMAS. As for the	the MMAS		not reliable.	
	adherence				EMD, there were	produced a positive			
					no significant	impact on			
					changes. The	adherence.			
					intervention group				
					also showed a				
					decrease in blood				
					pressure.				
Yue et al.,	What risk	Cross	256	MMAS	adherence, socio-	Patients who have	Adherence has	More studies	Level V
	factors	sectional	participants		demographic and	social support and	strong association	should be done	
2014	contribute to	study		Questionnair	clinical factors are	who are taking	with decreased	to evaluate risk	
	medication			e	directly related to	other drugs	blood pressure and	factors and how	
	adherence				blood pressure	combined with	risk factors should	to address	
	and what is				control.	their	be addressed.	them.	
	the					antihypertensive			
	association					are more likely to			
	between					adhere to their drug			
	adherence					regimen. As for			
	and blood					patients who are			
	pressure					concerned of			
	control?					medical cost have			
						lower chances of			
						adherence.			