



Hypertensive Patient Compliance with Pharmacist Intervention: A Systematic Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Systematic Review

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ABSTRACT

Background: Pharmacists and physicians can work together to improve patient compliance especially for the management of hypertension. Medication adherence leads to advance health and reduces hospitalizations (morbidity), death (mortality) and healthcare costs.

Objectives: Involvement of pharmacist in treatment intervention can result in improved understanding about hypertension and it can increase medication adherence to antihypertensive therapy which ultimately advance overall quality of life.

Study design and methods: A comprehensive research study was conducted using two eminent databases i.e. PUBMED and EMBASE. The research articles from 1996 to 2015 were analyzed. All the selected articles were about pharmacist intervention, hypertensive patient compliance and hypertension medication adherence.

Results: Some studies show no control in BP; however, there was significant difference in the systolic and diastolic BP pre and post pharmacist intervention (Systolic from 158.1±14.4 to 143.8 ± 10.7, Diastolic from 100.6 ±11.5 to 89.8 ± 9.7). Conversely, in some studies BP was controlled in about 29.9% of control group and in 63% of the intervention group.

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Conclusion: Results showed many methods can improve medication adherence and blood pressure including counseling patients in person, collaboration between pharmacists and physicians, and using technology like telecommunication to intensify patients counseling. Pharmacist intervention can significantly increase disease-related knowledge, blood pressure control and medication adherence in patients with hypertension.

Keywords: Pharmacist; Hypertension; Counseling.

1. INTRODUCTION

Hypertension is a non-communicable chronic disease frequently asymptomatic or sometimes with minor symptoms [1]. When there is no obvious underlying cause of hypertension it can be classified as essential hypertension, secondary hypertension, Cushing syndrome and malignant hypertension [2].

Hypertension disease is the major risk factor for cardiovascular disease and affects approximately 20% of adults in North America [3]. Hypertension is defined as blood pressure at 140/90 mmHg or greater. In the United States, 29% of the population, 85.4 million individuals have been diagnosed with hypertension [4].

Hypertension is a well-known risk factor for many chronic diseases including cardio-cerebrovascular, metabolic and kidney diseases and a leading risk factor for mortality due to these complications [5].

Due to poor medication adherence and compliance to current therapeutic guidelines, hypertension is poorly managed [6].

Pharmacists can play an important role in helping patients with hypertension to manage their condition. Helping as a partner and instructor, pharmacists can provide medication therapy management services and can educate patients about Hypertension [7].

Pathophysiologically, hypertension can be stated in terms of systolic blood pressure, which replicates the blood pressure when the heart is contracted (systole), and diastolic blood pressure, which replicates the blood pressure during relaxation (diastole). Hypertension can be diagnosed when whichever systolic pressure, diastolic pressure, or both are elevated

New guidelines issued by the National Committee on Prevention, Detection, Evaluation, and Treatment of Blood Pressure (JNC 7) encourage health providers to help those who

have uncontrolled blood pressure. Moreover, guidelines have been issued by American Diabetes Association (ADA) and World Health Organization-International Society of Hypertension (WHO-ISH) that emphasize the need to control blood pressure [9]. Complications, such as renal failure [10], myocardial infarction, heart failure and stroke, can occur as a result of uncontrolled hypertension. [11]

A study was conducted where the pharmacist and the physician worked together to improve patient compliance especially for patients diagnosed with hypertension and showed that there was a significant improvement from baselines of the mean BP [12-14].

Furthermore, medication adherence leads to improved health and reduced hospitalizations (morbidity), death (mortality), and the healthcare costs. Addressing factors that positively affect medications adherence for hypertension patients is very important to reduce the burden of hypertension disease and other diseases that may be caused by hypertensions such as chronic kidney diseases [15].

2. METHOD

2.1 Information Sources

A comprehensive research study has been conducted by using two databases; PUBMED and EMBASE (1996-2015). Search terms that had been used in PUBMED were “pharmacist intervention” and “hypertensive patient compliance” and using MeSH terms to do the advanced research for each term and then combined them by using AND coin to include the two terms in the research. After that, searching on EMBASE was performed by using “hypertension medication adherence” and to narrow the research, it was joined to pharmacist intervention and the language that has been used was the English for both databases.

2.2 Inclusion Criteria

The inclusion criteria are hypertensive patients with other *comorbidities*, including *cardiovascular*

diseases, *kidney diseases* or *diabetes mellitus*. Pharmacist intervention was defined as *counseling the patients in person* or using *technology (telecommunications, emails, etc.)*. Blood pressure is the primary outcome.

2.3 Data Collection & Study Selection

The abstracts with titles were reviewed to determine if the article met predetermined inclusion criteria (see Fig. 1). Some of them were eliminated if they did not include an intervention where the pharmacist interacted with patients to improve high blood pressure and medication adherence/compliance as outcomes.

Chart 1: Searching strategy:

- MeSH Hypertension patient
- MeSH Pharmacist intervention
- MeSH hypertension patient compliance
- Text word: hypertension medication adherence
- Text word: pharmacist intervention

● Process for Eligible Articles

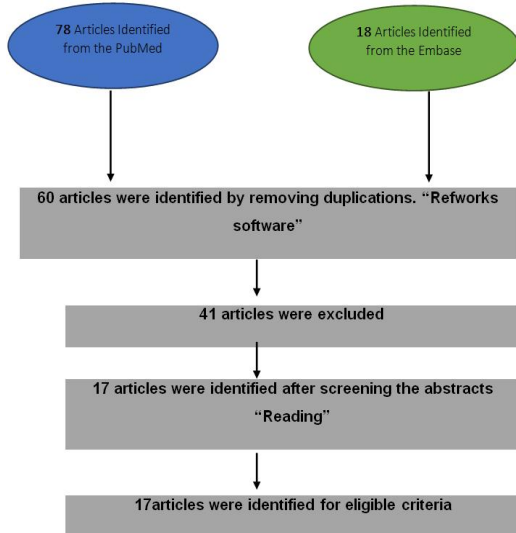


Fig. 1. Process for Eligible Articles

3. RESULTS & DISCUSSION

3.1 Study Selection

Based on the eligibility criteria and removing the duplicate citations a total of 60 articles were

found (see Fig. 1). Then, titles and abstracts were examined and 17 were selected for full text review. There were 10 articles that showed a statistical significant in reducing the blood pressure. Six articles were identified that mentioned a significant improvement in medication adherence. Finally, a one article showed both a statistically significant improvement in blood pressure and medication adherence.

3.2 Study Characteristics & Results of Individual Studies

Table 1 provides a summary of 17 studies that met the eligible criteria that mentioned above. These studies differ from one another according to the sample size, sample population, study design, duration, studies sites, and intervention and control groups description. Sample size in 17 studies ranged from forty to five hundred and eighty-four patients. The length of duration was from one month and eleven days to thirty-six months. Regarding to the sites, places of studies, there were six international studies. Randomized control trials were the most common study design [8,9,3,18,21]. Other study designs included case control study [2], quasi-experimental study with a control group [10], prospective and controlled design [19], non-randomized cross-over design [7,20], nonrandomized retrospective comparison [17]. All studies focused on adult patients who are over 55 years.

Table 2 shows the medications adherence and blood pressure levels in all studies at the baselines and at the end of each study. There are fluctuations and wide range of mean baselines of blood pressure and medications adherence according to various study design. For most of them, to detect medication adherence, qualitative methods like interviewers or self reported surveys were used to determine whether the patient was more adherent to pharmacist and physician instructions for medications adherence. Physical measuring blood pressure as a directly to detect blood pressure included in [8,3,17,19]. However, indirect methods like self-report using a questionnaire or Morisky method to detect the medication adherence along with measuring blood pressure was also used [21].

Table 1. Studies meeting inclusion criteria

| Study(Y) | Patients (n) | Sample population | Duration | Setting | interventions | Study design | Type of control | Ref. |
|------------------------------------|---------------------|---|-----------------------------|---|---|---|---|-------------|
| Aguwa et. al. (2007) | 40 | Hypertensive patients | 10 months | Nigeria Community Pharmacy | Implementing a pharmaceutical care program | Non-randomized, single site, and crossover design | Patients served as their own control | [16] |
| Bodgen et. al. (1998) | 95 | Patients failed to meet JNC-V criteria | 6-months | Queen Emma Clinics, Hawaii. | Physician and pharmacist as team working together | Single blind Randomized control trail | Standard medical Care | [17] |
| Carter BL et. al. (2009) | 402 | Patients of community-based medical offices | 6-months | Davenport, Des Moines, Mason city, Sioux city, and Waterloo, Iowa | Recommendations came from pharmacists to physicians, and nurses measured the BP within 24-H with monitoring | Prospective, cluster randomized, controlled clinical trial. | Uncontrolled hypertension patients receiving usual care | [18] |
| Chabot, I. et. al. (2003) | 100 | Patients visit community pharmacy | 9-months | Quebec city | By using PRECEDE-PROCEED model, computerized-aid tool used by the pharmacists | Case control study | Performed usual care | [19] |
| Criswell T. J., et. al. (2010) | 584 | Uncontrolled primary hypertension | 6 and 9 months respectively | 12 university affiliated-primary care clinics | Intensified hypertension management and drug counseling by pharmacist | Randomized controlled trials | Usual care | [20] |
| Fikri-benbrahim N., et. al. (2012) | 176 | Patients visit community pharmacy | 20 weeks | Jean and Granada in Spain | Patient education about hypertension, home BP monitoring, and referral to physician if it necessary | A quasi-experimental study with a control group | Standard Care | [10] |

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|----------------------------|-----|---|-----------|---|--|---|--|------|
| Gum TH., et. al. (2015) | 539 | Patients have uncontrolled BP, patients with diabetes or chronic kidney disease | 24 months | 15 states in USA | pharmacist-patient encouraging: medication history, assessment of patient knowledge of medication, contraindication, and adherence | Prospective, cluster, randomized study | Usual care | [21] |
| Graco JA., et. al. 2002 | 100 | Hypertensive patients with a previous using anti-hypertensive medications at least for 6 months(rural Portuguese population | 6 months | Private pharmacy, rural Portuguese population | Monthly appointment with the pharmacist for management. | Randomized control study | Receiving the usual care | [12] |
| Hunt JS., et. al. (2008) | 463 | Patients with hypertension and having uncontrolled blood pressure | 12 months | <i>"Providence Primary Care Research Network in Oregon"</i> | Pharmacist-Physician collaborative model and Network-approved collaborative hypertension management guidelines | Prospective, single blind, randomized, controlled trial | Usual care | [22] |
| Kuhmmer R., et. al. (2015) | 380 | Public emergency department | 2 months | Restinga district, Porto, Alegre, Southern Brazil | Structured individual counseling session by the pharmacist | Randomized control trial | Just receive a written information about the disease | [23] |

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|-----------------------------|-----|---|---------------------|---|--|--|---|------|
| Morgado M., et. al. (2011) | 197 | Hypertensive patients attending to the clinic for routine follow up | 12 months | University teaching hospital of Cova da Beira Hospital center, Portugal | Quarterly follow-up by the pharmacist during a 9 months long | Randomized control trial | No pharmaceutical care | [24] |
| Neto PR., et. al. (2011) | 194 | Hypertensive or diabetic patients | 36 months | Public health care in Sao Paolo, Brazil | Receiving the pharmaceutical care from the clinical pharmacist | Prospective, randomized control trial | Receiving usual care from medical and nurse staff | [16] |
| O'Neill JL., et. al. (2014) | 126 | Patient poorly controlled hypertension | 1 month and 11 days | Large Midwestern Veterans Affairs (VA) medical center, USA | Patients get benefits from clinical pharmacy specialist instead of physician | Non-randomized, retrospective comparison | Patients get management from the physician | [25] |
| Ramanath K., et. al. (2012) | 52 | Inpatients and out patients dept. and they were diagnosed over 6 months | 7 months | Adichunchanagiri Hospital and Research Center, B G Nagara, India | Patients get counselling, leaflets information(PILS), and frequent telephone reminding | Randomized, prospective and interventional study | Patients did not get counselling and PILS at the baselines and in the first follow-up | [26] |
| Robison JD., et. al. (2010) | 376 | Patients visit 18 chain community pharmacy | Over 12-months | Tampa, Florida, region, USA | Hypertension pharmaceutical care (PC) guidelines that had been developed by college of pharmacy, University of Florida | Prospective, and controlled design | Usual Care (UC) | [27] |
| Saleem F., et. al. (2015) | 412 | Patients with medical diagnosis of hypertension in previous 6 months | 3 months | 2 cardiac Units of two hospitals, UK | Patients get educational through hospital pharmacists | Non-randomized control trial | Usual care | [28] |

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|------------------------------|-----|--|-------------------------------|---------------------------|--|--------------------------|------------------------------------|------|
| Svarstad BL., et. al. (2013) | 576 | Patients with hypertension in community pharmacies | 27 months (Dec 2006-Feb 2009) | Five Wisconsin cities USA | Implementing 6-month intervention by the schedule visit, brief medication questionnaire, and novel toolkits to patients by pharmacists and give feedback to them and to physicians | Cluster randomized trial | Patients received information only | [29] |
|------------------------------|-----|--|-------------------------------|---------------------------|--|--------------------------|------------------------------------|------|

Table 2. Medication adherence of studies meeting inclusion criteria

| Study (Year) | Mean ± SD baseline medication adherence | Intervention mean ± SD change in medication adherence | Control mean ± SD change medication adherence | Statistical significance | References |
|--------------------------|---|---|--|---|------------|
| Aguwa et. al. (2007) | Sys:158.1 ±14.4 Dia.: 100.6 ± 11.5 | Sys: 143.8 ± 10.7 Dia. : 89.8 ± 9.7 | No control | Significant reduction in both systolic and diastolic BP; pharmaceutical p care program can give a beneficial effect to the patients | [7] |
| Bodgen et. al. (1998) | Intervention: Sys: 155 (42), Dia.:96 (8) Control: Sys: 156(18), Dia.: 95(10) | Sys: Declined 23±22 Dia. : Declined 14±11 | Sys: Declined 11±23 Dia. : Declined 3±11 | Patient failed to get benefits from standard care and they could get the benefits from physician-pharmacist team | [30] |
| Carter BL et. al. (2009) | Intervention: Sys: 153.6(12.8), Dia.: 87.4(11.9), Control: Sys: 150.6(14.1), Dia.: 83.6(12.3) | Sys: Declined 132.9(15.5), Dia.: 77.7(11.2) | Sys: Declined 143.8(20.5), Dia.: Declined 79.1(14.3) | BP was controlled for about 29.9% of control group, and 63% of intervention group | [31] |

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|------------------------------------|---|---|---|---|------|
| Chabot, I. et. al. (1998) | Intervention: Sys: 141, Dia.: 78, Control: Sys: 139, Dia.: 78 | High income; Sys: Declined -7.8; 133.2, Dia.: Declined -6.5; 71.5 | High income; Sys: NOT declined 139.5, Dia.: Declined 74 | A significant results showed a reduction in both systolic and diastolic BP and especially to the high income patinets | [32] |
| Criswell T. J., et. al. (2010) | Intervention: Sys: 153.3±11.9, Dia.: 86.5±11.9, Control: Sys: 150.5 ± 12.9 Dia.: 84.1±12 | Sys: Declined 129.7±14.2, Dia.: Declined 76.6±10.7 | Sys: Declined 150.5±12.9, Dia.: Declined 78.9±13.4 | Social support and self-efficacy improved at the end of the pharmacist intervention | [33] |
| Fikri-benbrahim N., et. al. (2012) | Intervention: Sys: 140.5±16.1, Dia.: 78.4±9.1, Control: Sys: 139.5±15.1, Dia.: 79.6±9.2 | Sys: Declined -6.8; 133.7±13.7, Dia.: Declined -2.1; 76.3±8.9 | Sys: Declined -2.1; 137.4±8.9, Dia.: NOT declined and (not significant), 0.1; 79.7± 6.2 | A protocol-based community pharmacist intervention was significantly reduced the DBP and SPD in combination with HBPM | 10 |
| Gum TH., et. al. (2015) | Intervention: Sys: 148(14.4), Dia.: 85(12), Control: Sys: 149.8(15.2), Dai.: 83.6(12.8) | Not found | Not found | There is a significant improvement to the BP by PPCM and by involving the pharmacist in intervention arm that have affected for decreasing the doses and removing medications | [34] |
| Graco JA., et. al. 2002 | Intervention: Sys: 151.68(23.16), Dia.: 85.66(13.16), Control: Sys: 147.71(15.98), Dia.: 83.9(9.19) | Sys: Declined 128.54(15.06), Dia.: Declined 73.32(8.2) | Sys: Declined 142.9(20.42), Dia.: Declined 78.59(8.55) | Pharmaceutical care program are played an important role for decreasing the BP by a significant results | [12] |

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|-----------------------------|---|---|---|--|------|
| Hunt JS., et. al. (2008) | Intervention: Sys: 173(15), Dia.: 90(14), Control: Sys: 174(15), Dia.: 92(14) | Sys: Declined 137(17), Dia.: Declined 75(9) | Sys: Declined 143(18), Dia.: Declined 78(17) | Collaborative primary care-pharmacist management was significantly better to improve PB without difference in QoL or satisfaction | [35] |
| Kuhmmer R., et. al. (2015) | Inclusion criteria: Sys: over 160mmHg, and Dia.: over 100 | Not found | Not found | Pharmaceutical care intervention has a feasible and effective to increase medication adherence in hospitals and community pharmacy | [36] |
| Morgado M., et. al. (2011) | Intervention: Sys: 141.6(16.3), Dia.: 85.2(10.2), Control: Sys: 141.9(16.8), Dia.: 86.4(11.7) | Sys: Declined 134(16), Dia.: Declined 82.2(8.7) | Sys: Declined 141.1(18), Dia.: Declined 85.3(8.9) | Pharmacist can improve the adherence to the medication for controlling BP | [37] |
| Neto PR., et. al. (2011) | Intervention: Sys: 156.7(21.8), Dia.: 106.6(17.7), Control: Sys: 155.9(20.8), Dia.: 108.7(16.9) | Sys: Declined 133.7, Dia.: Declined 91.6 | Sys: Declined 155.5, Dia.: Declined 106.8 | In a better clinical measurements, the pharmaceutical care program could significantly reduced the risk of cardiovascular scores in elderly patients | [38] |
| O'Neill JL., et. al. (2014) | CPS Sys: 149(12), Dia.: 78(12), Physician: Sys: 145(9), Dia.: 78(11) | Clinical pharmacy specialists: Sys: Declined 135(14), Dia.: Declined 72(11) | Physician: Sys: Declined 135(11), Dia.: Declined 73(11) | Patients who received CPS had a great improvement in the both systolic and diastolic BP compared to those receiving physician-directed RNCM | [17] |

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|------------------------------|---|--|---|---|------|
| Ramanath K., et. al. (2012) | Intervention: Sys: 147.54(20.45), Dia.: 86.62(11.35)., Control: Sys: 138.85(16.03), Dia.: 81.12(7.16) | Sys: Declined 128.27(6.35), Dia.: Declined 77.73(3.63) | Sys: Declined 131.08(5.16), Dia.: 78.46(4.14) | The pharmacist showed in this study has a positive impact on patients counseling which led to medication adherence improvement | [18] |
| Robison JD., et. al. (2010) | Pharmaceutical Care, PC: Sys: 151.5(14), Dia.: 82.4(13.2), Usual Care UC: Sys: 151.5(14.9), Dia.: 87.4(9.9) | PC: Sys: Declined -9.9: 141.6(2), Dia.: Declined -2.9: 79.5(1.3) | Sys: Declined -2.8: 148.7(2.3) Dia.: Declined -1: 86.4(1.5) | Community pharmacists could positively affect patients adherence within 6-months and improve PB | [39] |
| Saleem F., et. al. (2015) | Intervention: Sys: 144.5(17.2), Dia.: 90.5(10.2), Control: Sys: 144.1(16.5), Dia.: 90.9(11.1) | Sys: Declined 137.5(17.2), Dia.: Declined 84.6(9.9) | Sys: Declined 143.9(19.4), Dia.: Declined 90.1(10.5) | Pharmacist can increase medication knowledge, medication adherence in hypertensive medication | [40] |
| Svarstad BL., et. al. (2013) | Intervention; TEAM: Sys: 151.2(15.2), Dia.: 92(10.1), Control; Sys: 153.1(16.6), Dia.: 92.9(10) | Sys: Declined 137.46(16.16), Dia.: Declined 82.69(11.69) | Sys: Declined 143.37(20.41), Dia.: Declined 84.71(13.03) | Team Education and Adherence Monitoring involving community chain pharmacists led to a significant and sustained improvement in SBP | [41] |

4. CONCLUSION

According to the results, pharmacists had a positive impact on medication adherence and hypertension measurements as an outcome. However, results showed many methods can improve medication adherence and blood pressure including, counseling patients in person, collaboration between pharmacists and physicians, and using technology like telecommunication to intensify patients counseling. However, additional research is needed to develop standards for guidelines and interventions that assist patients with hypertension who have trouble with medication adherence.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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