

Roles of Family Physicians in Management and Control of Hypertension Review

¹Zahra Ali Almunian, ²Amal Abbas Almarzooq, ³Ahlam Ali Alammam,
⁴Bothaina Jawad Alyousif, ⁵Zainab Mohammed Alhashmi,
⁶Habbab mansour Alkhonaizi

Abstract: This review was conducted to address and discuss the roles of family physicians in diagnosis and management of hypertensive patients, through variant procedures and gridlines worldwide. A literature search was conducted in the following databases: PubMed, The Cochrane Library, and Google scholar for relevant articles published up to, June, 2017. Hypertension is the First threat factor for mortality in the world¹ and also an important danger variable for heart disease as well as stroke. Hypertension is usually diagnosed as well as managed in the outpatient setting and also is just one of one of the most common reasons to visit a family doctor. With virtually a quarter of the adult population and also nearly fifty percent of individuals aged 50 years as well as older having hypertension, the problem of this illness is without a doubt high. As treatment of high blood pressure is associated with a 20% to 25% reduction in cardiovascular occasions, getting control of this usually asymptomatic disease might be one of the most vital safety nets that family physicians can take.

Keywords: family physicians, Hypertension, treatment, family doctor.

1. INTRODUCTION

According to a World Health Organization (WHO) report, hypertension is the solitary essential threat variable, representing 13% of mortality globally⁽¹⁾, and an essential risk factor for cardiovascular disease and stroke^(2,3,4). There is a straight relationship between blood pressure and threat of heart disease. As baseline blood pressure boosts from below 120/80 mm Hg, there is a stepwise increase in cardio event rates^(3,4).

Hypertension is generally diagnosed and also managed in the outpatient setup and also is one of one of the most usual needs to go to a family physician (FP)⁽⁵⁾. high blood pressure instances represent 8.6% of all visits to a medical care medical professional⁽⁶⁾. High blood pressure influences 32% of adults in western society, two-thirds of which are improperly regulated, its occurrence is likely to continue climbing^(7,8).

Regardless of indisputable scientific evidence that lowering blood pressure (BP) is substantially effective in decreasing cardiovascular disease occasions, as pointed out in all significant guidelines on high blood pressure monitoring, arterial hypertension is known to be badly diagnosed and treated generally practice^(9,10). In established countries, the proportion of hypertensive clients with well-controlled BP is typically less than 30%^(11,12). Appropriate antihypertensive treatment is rarely carried out even in risky people, in whom BP reductions can cause fairly huge life-saving results⁽¹³⁾. The asymptomatic nature of this condition offers a considerable difficulty to determining individuals with high blood pressure as well as giving optimal care⁽¹⁴⁾. In addition, the absence of signs renders medicine adherence much more challenging⁽¹⁵⁾.

In spite of the obstacles, high blood pressure monitoring has actually boosted dramatically over the past years, largely in the locations of raised recognition as well as therapy^(16,17). The majority of patients, however, do not reach healing goals and also remain to be at high risk of cardio events⁽¹⁷⁾.

This unsuitable BP control amongst cured hypertensive subjects has multiple reasons, among which physician's habits as well as patient's compliance have actually obtained particular interest.

Therefore, this review was aimed to address and discuss the roles of family physicians in diagnosis and management of hypertensive patients, through variant procedures and gridlines worldwide.

2. METHODOLOGY

A literature search was conducted in the following databases: PubMed, The Cochrane Library, and Google scholar for relevant articles published up to, June, 2017. Keywords used were; (hypertension, high blood pressure, family practice, primary care, and family physicians). Furthermore, references list from founded studies were searched for more relevant studies to be included in our study.

3. DISCUSSION

Hypertension is an important modifiable risk factor for cardiovascular disease and among the leading risk factors for mortality around the world^(18,19). Hypertension is a challenging clinical problem with a significant proportion of patients failing to achieve blood pressure control despite extensive medical therapy, therefore, the family physicians have a great role in management of hypertension of those patients. Studies have identified various barriers for hypertension control in regular care that are structured in physician-, patient-, health care delivery and health care system-related factors⁽¹⁴⁾.

o Management of hypertension by family physicians:

family physician must be aware with the important management of high blood pressure. Treatment needs to make up both way of living adjustment and pharmacologic therapy. The high blood pressure goal in uncomplicated clients is 140/90 mmHg which could be loosened up to 150/90 in individuals above 60 years of age⁽²⁰⁾. A better therapy target in people with end-organ damages is 130/80 mmHg^(21,22).

Non-pharmacologic steps ought to be present in individuals with high blood pressure of any kind of seriousness. Recommendations consist of cigarette smoking cessation, a decrease in alcohol consumption, nutritional salt constraint, healthy eating strategies, boosted exercise and weight management. Lifestyle interventions complement the efficiency of drug therapy as well as, alone, are often sufficient in uncomplicated vital hypertension.

There is little randomised test data to guide choice of drug regimen for clients with immune high blood pressure and also suggestions are mainly empirical. In general, the very best technique is to create a combination treatment that targets different physical devices and also accounts for patient comorbidities.

The recommended first drug options coincide when it comes to crucial high blood pressure⁽²³⁾. The standards of the National Institute for Health and Clinical Excellence (NICE) advise first treatment with an angiotensin-converting enzyme inhibitor (ACE prevention) in people younger than 55 years of age, or a dihydropyridine calcium channel blocker (CCB) in clients older than 55 or black people of any age⁽²⁴⁾. These choices could then be trialled in combination as well as titrated as necessary before including a thiazide as the 3rd medication.

Standards supported commencement of antihypertensive treatment with only one medicine because appropriate monotherapy controls high blood pressure in 30% of instances⁽²⁵⁾. If monotherapy wants the program could be changed depending upon healing result by modifying dose or including an additional class of medication. Due to the fact that ideal application and also drug selection could see blood stress normalise in many people, three-way treatment must be optimised before choosing additional add-on treatment.

Whatever regimen is chosen it is essential that it be customized to the specific client. When picking an antihypertensive agent, comorbidities have to be thought about. As an example, in individuals over 55 years old with evidence of heart failure a thiazide diuretic might be a more suitable first-line option compared to a CCB. If patients are intolerant to an ACEI because of coughing it is appropriate to replace the ACEI with an angiotensin receptor blocker (ARB). This must attain a similar high blood pressure lowering result^(23,25).

A lot of clients with high blood pressure are recommended hydrochlorothiazide as the diuretic of selection. However, numerous recent clinical tests have demonstrated superior blood pressure decrease with chlorthalidone, especially in individuals with resistant high blood pressure^(25,26,27,28,29). Chlorthalidone is a thiazide-like diuretic with a longer half-life as well as greater effectiveness compared to hydrochlorothiazide. An excellent initial action in regulating refractory hypertension is consequently to switch over individuals from hydrochlorothiazide to chlorthalidone. The beginning dosage of chlorthalidone is 12.5 mg daily, taken in the morning, titrated if needed to a maximum of 50 mg everyday⁽³⁰⁾.

Indapamide is a different thiazide-like representative which may be more suitable compared to chlorthalidone in some individuals. Chlorthalidone has a much longer half-life as well as duration of action compared to indapamide as well as is related to a greater danger of kidney problems and also hypokalaemia. Thus in inclined patients such as the elderly or those with renal lack indapamide could be an exceptional replacement⁽³¹⁾. An ideal beginning dose is a 1.5 mg controlled-release tablet each early morning⁽²⁴⁾. Individuals with serious renal disability (GFR below 30 mls/min) should have their thiazide changed by a loop diuretic under expert support⁽³²⁾.

In many cases the medication program might be altered by having clients take one antihypertensive agent at night-time instead of conventional morning-only dosing. Blood pressure typically decreases physiologically throughout rest and nighttime high blood pressure, or supposed 'non-dipping', has actually been connected with poorer cardiovascular diagnosis^(33,34). If one antihypertensive is ingested nocturnally⁽³⁵⁾, there is current trial information on resistant high blood pressure which recommends boosted blood stress decrease with fewer cardiovascular occasions. Notably, there is no significant difference in unfavorable outcomes with this technique⁽³⁶⁾. Moving one agent to bedtime dosing is not an unreasonable choice in patents with immune hypertension. If choosing to trial nighttime therapy it is generally sensible to stay clear of a diuretic as the night-time medication.

Spirolactone is recommended as the fourth antihypertensive medicine^(32,37). The Scandinavian Cardiac Outcomes Trial (ASCOT) showed mean high blood pressure decrease of 22/10 mmHg at one-year follow-up in individuals with resistant hypertension randomised to get spironolactone as the fourth drug⁽³¹⁾. A general policy is to begin individuals on 25 mg per day, which might need concerning 2 weeks for full impact. This dose can be enhanced slowly, preferably over a number of months, to a maximum of 100 mg daily if necessary. Negative results of spironolactone typically show up at greater doses where individuals might complain of gynecomastia and also bust inflammation, menstruation abnormalities and also sex-related dysfunction. Amiloride, a potassium-sparing diuretic, is an affordable choice in those intolerant of spironolactone. Its dosage ranges from 2.5-10 mg daily. A caution for both spironolactone and amiloride is the demand for mindful routine monitoring of serum potassium. If the blood potassium degree surpasses 4.5 mmol/L increase of thiazide therapy ought to be thought about⁽³⁸⁾.

The double renal-angiotensin-aldosterone system clog offered by spironolactone with ACEIs is not matched by integrating ACEIs with ARBs. The site Ongoing Telmisartan Alone and also in mix with Ramipril Global Endpoint Trial (ONTARGET) demonstrated no fringe benefit in between utilizing ACEIs or ARBs alone as well as in combination⁽³⁹⁾. Treatment regimens for that reason ought to not consist of both an ACEI and also ARB at the same time.

Challenging clients will certainly call for recommendation to a high blood pressure professional. Indications for reference include individuals with uncontrolled blood pressure despite obtaining optimum endured dosages of four medications, clients enduring end-organ damages consequently of their hypertension, or people with a presumed secondary reason [Table 1] All individuals less competent to quadruple therapy needs to be reevaluated for an additional reason.

Table 1: Indications for specialist referral in hypertensive patient

(1) severe or unacceptable adverse effects from drug therapy
(2) multiple hypertensive emergencies
(3) problematic comorbid conditions that be contributing to the hypertension and making management difficult
(4) uncertainty about the diagnosis
(5) severe, unexpected hypertension in pediatric patient or young adult
(6) need to perform specialized testing

A lot of patients with immune high blood pressure do achieve blood pressure control via pharmacotherapy supplied they are appropriately assessed as well as treated⁽⁴⁰⁾. Patients that continue to be hypertensive despite four representatives could have additional medicines trialled sequentially with direction from a specialist [Figure 1]⁽⁴¹⁾. Drug selection should be step-by-step with cautious evaluation of scientific conditions at each phase. Individual comorbidities typically dictate drug options as well as it is sensible to start each medication at the most affordable dosage practicable. Periodically these less-frequently utilized agents will certainly need earlier intro relying on clinical circumstances⁽⁴¹⁾.

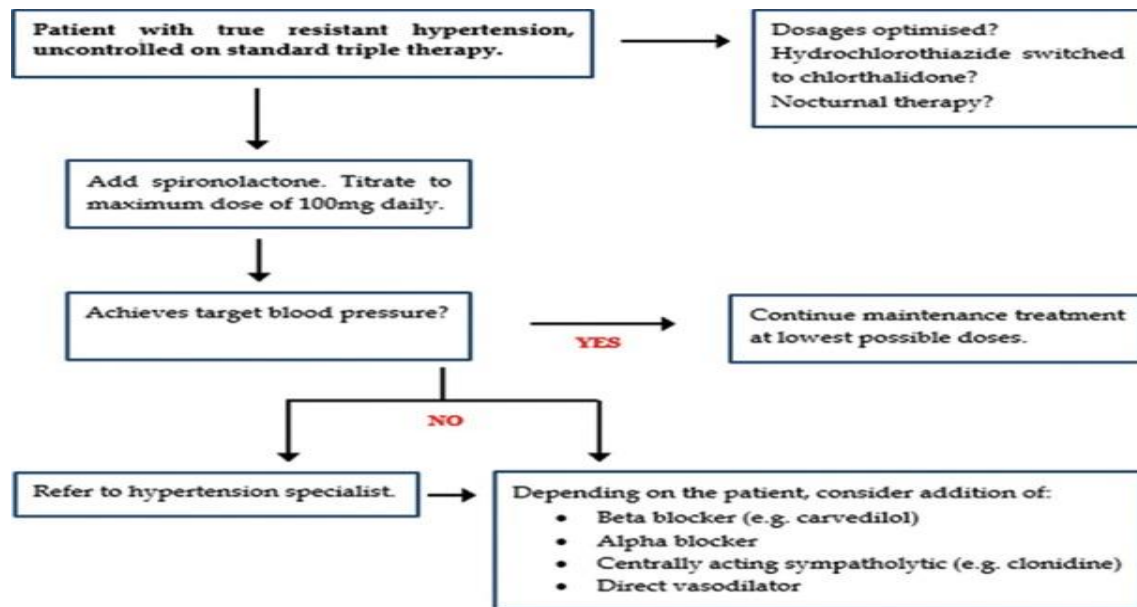


Figure 1: Stepwise pharmacologic management of resistant hypertension

Vasodilating beta blockers, such as carvedilol as well as labetalol, are a more effective following alternative as fifth-line drug therapy⁽³²⁾. They are not recommended as first-line treatment for individuals with uncomplicated hypertension because they offer much less cardiovascular protection compared to various other agents. As an example, individuals treated with beta blockers in the Controlled ONset Verapamil INvestigation of Cardiovascular Endpoints (CONVINCE) trial had higher prices of stroke than with any one of CCBs, ACEIs or thiazides⁽⁴²⁾. Carvedilol must be started at 12.5 mg daily for at least two days, before boosting by 12.5 mg every 2 weeks to a maximum dosage of 50 mg daily. Labetalol is commenced originally at 100 mg two times daily as well as titrated to an optimum of 2.4 g daily. Labetalol needs to not be boosted quicker than by 200 mg increments each day. In some clients such as those with ischemic heart disease or poor glycaemic control, conventional beta blockers like atenolol or metoprolol may rather be suggested. Their antihypertensive advantage is most likely smaller sized although head-to-head comparison data is lacking⁽³²⁾.

Various other choices consist of alpha blockers, clonidine, methyl dopa and straight vasodilators such as hydralazine or minoxidil. These rarely form part of the regular administration of high blood pressure as well as should be recommended with expert recommendations. Such agents are very effective in managing blood pressure their use must be tempered by side result accounts and also the comorbidities of the patient [Figure 2]^(30,37,39,40). These drugs have not been sufficiently examined in resistant hypertension and the selection of representative depends mainly on individual situation and also private prescriber choice. Since experience with their usage is bigger, most medical professionals often tend to choose for centrally-acting agents before the straight vasodilator medications.

Drug class	Examples	Recommended dose	Notes
Alpha blockers	Prazosin	0.5 mg daily, initially nocte, increasing to maintenance dose of 1-10 mg twice daily	Useful option in men with benign prostatic hyperplasia and lower urinary tract symptoms Can cause postural hypotension so use with caution in elderly
Centrally acting sympatholytic	Clonidine Methyldopa	50 mcg twice daily, up to 300 mcg twice daily 125 mg twice daily initially, up to 250 mg twice daily	Adverse effects are relatively common with both agents, such as dry mouth and sedation Abrupt cessation of clonidine can cause severe rebound hypertension so must be weaned carefully Methyldopa is a safe non-teratogenic option in pregnancy and remains widely used in that setting
Direct vasodilators	Minoxidil Hydralazine	5 mg daily, up to 30 mg twice daily 12.5 mg daily, up to 200 mg daily in divided doses	Minoxidil commonly causes reflex tachycardia and fluid retention Minoxidil must be used cautiously in patients with heart failure and coronary artery disease Minoxidil requires co-administration of a beta blocker and loop diuretic to offset tachycardia and fluid retention Minoxidil causes hypertrichosis so should be avoided in women Hydralazine provides less antihypertensive effect but is also associated with fewer adverse effects Most clinicians familiar with their use elect hydralazine in women and minoxidil in men

Figure 2: Specialized medication options for resistant hypertension

○ **Interventional approaches toward hypertension patients in primary care:**

There is a need for alternative therapy methods in refractory people that remain hypertensive regardless of maximum clinical treatment. Two possibly effective interventional treatments are presently being assessed for this purpose. These are kidney denervation and carotid sinus excitement. The quality of treatment that clients with hypertension get from family physicians has a clear influence on their risk of suffering a cardiovascular occasion. Empirical research studies have shown that insufficient control of blood pressure is associated with a considerable danger of stroke ^(43,44). In regards to the procedure of care that hypertensive clients get, characteristics of both the client, health and wellness specialist as well as the health care system in which they are provided their treatment have been linked in poor high blood pressure control. Absence of adherence to medication as well as not having a medical care medical professional were related to inadequate blood pressure control ⁽⁴⁵⁾. More recent research studies have actually revealed that regular contact with health care professionals does not ensure much better blood pressure control unless there is more vigorous use of antihypertensive medicines, and that individual practitioners vary significantly in their professional performance when handling high blood pressure in the neighborhood ^(46,47).

Huge systematic evaluation research study ⁽⁴⁸⁾ involving greater than 90 routes have actually found that there are to a large degree controlled by the findings from the biggest RCT, the HDFP study [Table 2] ^(49,50,51). Mostly meant as a test to analyze the value of systematic identification of hypertensive people, ⁸² the vital ingredients of just how patients with established hypertension were managed totally free care, enrollment, recall and normal evaluation in tandem with a rigorous stepped treatment method to antihypertensive medication treatment need to be stressed as this multi-faceted intervention was reliable in terms of getting to blood stress goals as well as decreasing all-cause mortality ⁽⁵¹⁾. It is interesting to note that a 2-year post trial monitoring study showed that high blood pressure control was undermined when the stepped-care arm of the research study was ceased. This lack of control was associated with a decline in using antihypertensive drug ⁽⁵²⁾. Some caution is called for when analyzing this RCT as it consisted of both untreated and also unchecked hypertensive topics with differential uptake of antihypertensive treatment in the treatment and normal treatment arms of the research study.

Table 2: Summary of results of interventions on systolic and diastolic blood pressure, control of hypertension and follow up at clinic.

Intervention	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Blood pressure control (odds ratio) ^a	
	Pooled estimate (95% CI)	Range of results from individual RCTs	Pooled estimate (95% CI)	Range of results from individual RCTs	Pooled estimate (95% CI)	Range of results from individual RCTs
Self-monitoring		-10-5	-2.0 (-2.7 to -1.4) ^b	-12-0	0.9 (0.8 to 1.1)	0.8-.2
Education (patient)		-16-1		-9-7	0.7 (0.4 to 1.0)	0.3-1.1
Education (physician)	2.0 (-3.5 to -0.6) ^b	-7-1	-0.4 (-1.1 to 0.3)	-2-1		0.8-1.0
Health professional care		-13-0		-8-0		0.1-0.9
Organisational interventions		-12-3		-8-5		0.5-1.8
Intervention	Follow up at clinic (relative risk)					
Appointment reminders		0.1-1.4				

4. CONCLUSION

Hypertension is the First threat factor for mortality in the world¹ and also an important danger variable for heart disease as well as stroke. Hypertension is usually diagnosed as well as managed in the outpatient setting and also is just one of one of the most common reasons to visit a family doctor. With virtually a quarter of the adult population and also nearly fifty percent of individuals aged 50 years as well as older having hypertension, the problem of this illness is without a doubt high. As treatment of high blood pressure is associated with a 20% to 25% reduction in cardiovascular occasions, getting control of this usually asymptomatic disease might be one of the most vital safety nets that family physicians can take.

REFERENCES

- [1] World Health Organization (WHO) Global health risks: Mortality and burden of disease attributable to selected major risks. Geneva: WHO; 2009.
- [2] M. Ezzati, A.D. Lopez, A. Rodgers, S. Vander Hoorn, C.J. Murray. Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet*, 360 (9343) (2002), pp. 1347-1360
- [3] C.M. Lawes, D.A. Bennett, S. Lewington, A. Rodgers. Blood pressure and coronary heart disease: a review of the evidence. *SeminVasc Med*, 2 (4) (2002), pp. 355-368
- [4] C.M. Lawes, D.A. Bennett, V.L. Feigin, A. Rodgers. Blood pressure and stroke: an overview of published reviews. *Stroke*, 35 (3) (2004), pp. 776-785
- [5] P.D. Sloane, L.M. Slatt, M.H. Ebell, L.B. Jacques, M.A. Smith (Eds.), Introduction to common problems Essentials of family medicine (5th ed.), Lippincott Williams & Wilkins, Hagerstown, MD (2007), pp. 119-130
- [6] Canberra: National Heart Foundation of Australia; 2012. National Heart Foundation of Australia. High blood pressure statistics.
- [7] Briganti E, McNeil J, Shaw J, Zimmet P, Chadban S, Atkins R, et al. Untreated hypertension among Australian adults: The 1999-2000 Australian diabetes, obesity and lifestyle study. *Med J Aust*. 2003;179:135-9.
- [8] Tu K, Zhongliang C, Lipscome L. Prevalence and incidence of hypertension from 1995 to 2005: A population-based study. *Can Med Assoc J*. 2008;178(11):1429-35.
- [9] Anonymous. Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. *Arch Intern Med* 1997; 157: 2413-2446.
- [10] WHO. Guidelines Subcommittee. International Society of Hypertension Guidelines for the management of hypertension. *J Hypertens* 1999; 17: 151-183.
- [11] P. Primatesta, M. Brookers, N.R. Poulter. Improved hypertension management and control. Results from the health survey for England 1998. *Hypertension*, 38 (2001), pp. 827-832.
- [12] B. Chamontin, L. Poggi, T. Lang, et al. Prevalence, treatment and control of hypertension in the French population. Data from a survey on high blood pressure in general practice. *Am J Hypertens*, 11 (1998), pp. 759-762
- [13] R.H. Fagard, Van der Enden, M. Leeman, X. Warling. Survey on treatment of hypertension and implementation of WHO/ISH risk stratification in primary care in Belgium. *J Hypertens*, 20 (2002), pp. 1297-1302
- [14] Sega R, Facchetti R, Bombelli M, Cesana G, Corrao G, Grassi G, et al. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. *Circulation*. 2005;111(14):1777-83.
- [15] Krousel-Wood M, Thomas S, Muntner P, Morisky D. Medication adherence: a key factor in achieving blood pressure control and good clinical outcomes in hypertensive patients. *Curr Opin Cardiol*. 2004;19(4):357-62.
- [16] Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA*. 2003;290(2):199-206.

- [17] Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. *Hypertension*. 2007;49(1):69-75.
- [18] Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet*. 2002;360(9343):1347-60.
- [19] World Health Organization. The world health report 2002. Geneva, Switz: World Health Organization; 2002.
- [20] James P, Oparil S, Carter B, Cushman W, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guidelines for the management of high blood pressure in adults; report from the panel members appointed to the eighth joint national committee (JNC 8) *JAMA*. 2014;311:507-20.
- [21] Canberra: National Heart Foundation of Australia; 2010. National Heart Foundation of Australia. Guide to management of hypertension 2008.
- [22] Pimenta E, Calhoun D. Treatment of resistant hypertension. *J Hypertension*. 2010;28:2194-5.
- [23] Calhoun D, Jones D, Textor S, Goff D, Murphy T, Toto R, et al. Resistant hypertension: A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Hypertension*. 2008;51:1403-19.
- [24] London: National Institute for Health and Clinical Excellence; 2011. National Institute for Health and Clinical Excellence. Hypertension: Clinical management of primary hypertension in adults.
- [25] Frank J. Managing hypertension using combination therapy. *Am Fam Phys*. 2008;77:1279-86.
- [26] Kholza N, Chua D, Elliot W, Bakris G. Are chlorthalidone and hydrochlorothiazide equivalent blood-pressure-lowering medications? *J Clin Hypertens*. 2005;7:354.
- [27] Kaplan N. The choice of thiazide diuretics: Why chlorthalidone may replace hydrochlorothiazide. *Hypertension*. 2009; 54:951.
- [28] Kumar N, Calhoun D, Dudenbostel T. Management of patients with resistant hypertension: Current treatment options. *Integr Blood Press Control*. 2013; 6:139-51.
- [29] Carter B, Ernst M, Cohen J. Hydrochlorothiazide versus chlorthalidone: Evidence supporting their interchangeability. *Hypertension*. 2004; 43:4.
- [30] Chlorthalidone. 50th ed. Sydney: MIMS Australia; 2013. Monthly Index of Medical Specialties; p. 57.
- [31] Madkour H, Gadallah M, Riveline B, Plante GE, Massry SG. Indapamide is superior to thiazide in the preservation of renal function in patients with renal insufficiency and systemic hypertension. *Am J Cardiol*. 1996;77:23-25.
- [32] Viera A. Resistant hypertension. *J Am Board Fam Med*. 2012; 25:487-95.
- [33] Friedman O, Logan A. Can nocturnal hypertension predict cardiovascular risk? *Integr Blood Press Control*. 2009; 2:25-37.
- [34] Okamoto L, Gamboa A, Shibao C, Black B, Diedrich A, Raj S, et al. Nocturnal blood pressure dipping in the hypertension of autonomic failure. *Hypertension*. 2009; 52:363-9.
- [35] Ayala DE, Hermida RC, Mojón A, Fernández JR. Cardiovascular risk of resistant hypertension: Dependence on treatment-time regimen of blood pressure-lowering medications. *Chronobiol Int*. 2013; 30:340-52.
- [36] Carter B, Chrischilles E, Rosenthal G, Gryzlak B, Eisenstein E, Vander Weg M. Efficacy and safety of nighttime dosing of antihypertensives: Review of the literature and design of a pragmatic clinical trial. *J Clin Hypertens*. 2014;16(2):115-21.
- [37] Chapman N, Dobson J, Wilson S, Dahlhoef B, Sever P, Wedel H, et al. Effect of spironolactone on blood pressure in subjects with resistant hypertension. *Hypertension*. 2007;49:839.
- [38] Myat A, Redwood S, Qureshi A, Spertus J, Williams B. Resistant Hypertension. *BMJ*. 2012; 345:7473-70.

- [39] Mann J, Schmeider R, McQueen M, Dyal L, Schumacher H, Pogue J, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): A multicenter, randomised, double-blind, controlled trial. *Lancet*. 2008;372:547.
- [40] Persell SD. Prevalence of resistant hypertension in the United States, 2003-2008. *Hypertension*. 2011;57:1076–80.
- [41] Yaxley JP, Thambar SV. Resistant hypertension: an approach to management in primary care. *Journal of Family Medicine and Primary Care*. 2015;4(2):193-199. doi:10.4103/2249-4863.154630.
- [42] Black H, Elliot W, Grandits G, Grambasch P, Lucente T, White W, et al. Principal results of the Controlled Onset INvestigation of Cardiovascular Endpoints (CONVINCE) Trial. *JAMA*. 2003;289:2073.
- [43] Du X, Cruickshank K, McNamee R, et al. Case-control study of stroke and the quality of hypertension control in north west England. *BMJ*. 1997;314:272–276.
- [44] Payne JN, Milner PC, Saul C, et al. Local confidential inquiry into avoidable factors in deaths from stroke and hypertensive disease. *BMJ*. 1993;307:1027–1030.
- [45] Shea S, Misra D, Ehrlich M, et al. Predisposing factors for severe, uncontrolled hypertension in an inner-city minority population. *N Engl J Med*. 1992;327:776–781.
- [46] Berlowitz D, Ash A, Hickey E, et al. Inadequate management of blood pressure in a hypertensive population. *N Engl J Med*. 1998;339:1957–1963.
- [47] Frijling B, Spies T, Lobo C, et al. Blood pressure control in treated hypertensive patients: clinical performance of general practitioners. *Br J Gen Pract*. 2001;51:9–14.
- [48] Fahey T, Schroeder K, Ebrahim S. Educational and organisational interventions used to improve the management of hypertension in primary care: a systematic review. *The British Journal of General Practice*. 2005;55(520):875-882.
- [49] Hypertension Detection and Follow-up Program Cooperative Group. Five year findings of the Hypertension Detection and Follow-up Program. I. reduction in mortality of persons of high blood pressure, including mild hypertension. *JAMA*. 1979;242:2562–2571.
- [50] Hypertension Detection & Follow-up Program. Therapeutic control of blood pressure in the Hypertension Detection and Follow-up Program. Hypertension Detection and Follow-up Program Cooperative Group. *Prev Med*. 1979;8:2–13.
- [51] Davis B, Ford C. The Hypertension Detection and Follow up Program. In: Black HR, editor. *Clinical trials in Hypertension*. New York: Marcel Dekker Inc; 2001. pp. 27–60.
- [52] Oliveria SA, Lapuerta P, McCarthy BD, et al. Physician-related barriers to the effective management of uncontrolled hypertension. *Arch Intern Med*. 2002;162:413–420.