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Utilization pattern of antihypertensive drugs in Chinese diabetics.

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Abstract

Purpose: To assess blood pressure control and to evaluate and compare the utilization pattern of antihypertensive therapies in Chinese patients with diabetes.
Design: Cross-sectional study.
Setting: Tertiary care centre.
Methods: Prescription/drug usage and clinical data were collected from medical records of patients with coexistent uncomplicated hypertension and type-2 diabetes from July 2014 to August 2015. Univariate analysis with Chi-square and t- test was performed followed by logistic regression to evaluate independent predictors.
Results: Out of 1166 diabetics, 968 (83%) had coexistent hypertension (57.75% men; 42.25% women). In total, controlled blood pressure was noted in 337 (34.81%) patients (18.9% isolated systolic hypertension, 4.44% isolated diastolic hypertension, and 41.83% both). Nearly 42.98% patients were on monotherapy and 57.02% on polytherapy. Overall, calcium channel blockers (CCBs) were prescribed mostly (58.47%) (monotherapy or polytherapy), secondly angiotensin receptor blockers (ARBs) (45.45%) and then angiotensin converting enzyme inhibitors (ACEIs) (25.93%), diuretics (DIs) (24.9%) and beta-blockers (BBs) (18.9%).
Conclusion: The majority of diabetic outpatients with hypertension received polytherapy achieving BP target in accordance with recommendations. The most often used antihypertensives were CCBs, followed by ARBs, ACEIs, BBs and DIs, suggesting the non-optimized treatment of hypertension. Continued efforts are needed in order to improve antihypertensive drug usage.

Keywords: Antihypertensive, Diabetes, Drug utilization.

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Introduction

Diabetes is a metabolic disease with diverse etiology distinguished by persistent hyperglycaemia along with defects in insulin secretion and/or action leading to carbohydrate, fat and protein metabolism disturbances. The consequences of diabetes include dysfunction, damage, and failure of the body's systems on long-term [1]. The incidence as well as prevalence of diabetes is increasing [2,3]. A study conducted by Klein et al projected the rise in the number of diabetics to 366 million by 2030 from 171 million in 2000 [4]. In 2014, there were 9% of adult diabetics of age 18 years and older. Diabetes leads to the death of 1.5 million people in 2012. Hypertension is predicted to rise in adult population by nearly 60% by 2025 to an aggregate of 1.56 billion people. Nearly 70% of diabetics are affected by hypertension which is approximately twice as common in diabetics vs. non-diabetics [1,4]. As per 2014 Diabetes Atlas, the number of diabetics (20 to 79 years) in China presently is about 96.3 million with 1 in 11 adults suffering from diabetes [5]. The prevalence of hypertension is rising continuously [6].

Coexistent diabetes and hypertension prevalence differs with respect to various social, ethnic, and racial classes. Additionally, hypertension in diabetics leads to a rise in the vascular complications risk significantly, thereby leading to predisposition to chronic kidney disease [7,8]. Also the coexistent diabetes and hypertension raises the risk of several complications like retinopathy, ischemic cerebrovascular disease, and sexual dysfunction substantially [9].

A study conducted by Kostis et al. demonstrated that the lowering blood pressure (BP) is the most cost efficient method than strict control of blood glucose in patients with diabetes mellitus with beneficial results that are apparent earlier [10]. There is a constant rise in the number of approvals every year in regards to treatment options for hypertensive patients, although the selection of antihypertensives is directed by diverse factors particularly comorbidities. According to the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) 7th report, the chief treatment regimen for control of blood pressure in diabetics is the combination of angiotensin

converting enzyme inhibitors and angiotensin receptor blockers (ACEI/ARB) [11].

As far as our knowledge is concerned, there is no study conducted specifically in order to determine the utilization pattern of antihypertensives in diabetics of China. The objective of the study was to assess blood pressure control in addition to evaluation and comparison of the utilization pattern of antihypertensive therapies in patients with diabetes.

Methods

Setting and subjects

This cross-sectional study was performed in diabetics attending the outpatient department of Internal Medicine at a tertiary care setting, China (patients are majorly from central urban region) over a period of a year from July 2014 to August 2015.

Participants were patients with coexistent uncomplicated hypertension and type-2 diabetes, 18 years of age and more attending the Internal Medicine during the study period. Exclusion criteria included type 1 diabetics with hypertension and breastfeeding/pregnant women. All the included participants provided the informed and written consent after complete explanation of involved procedure. The institutional ethics committee has provided the study approval, and patient confidentiality was maintained strictly. All the relevant patient medical records were examined for demographic, clinical and prescription/drug usage information.

Measurement blood pressure

Measurement of Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was done twice with three minutes interval in the sitting position after resting for 15 minutes, and the average was considered. The following criteria were used for the confirmation of hypertension: a) diagnosis of hypertension for minimum of two times during outpatient visits or b) minimum of one antihypertensive agent prescription and diagnosis of hypertension for minimum of one time during outpatient visit or c) minimum of two measurements of elevated BP (as per JNC 7 report, ≥ 130/80 mmHg) along with one outpatient hypertension diagnosis or d) minimum of two measurements of elevated BP.

Statistical analysis

Values are expressed as numbers and percentage, mean with standard deviation (SD) as well as median along with inter quartile range (IQR). The various predictor variables considered are age group, gender, and duration of blood pressure, duration of diabetes, SBP, DBP, and type of therapy. For analysis of prescription pattern, single antihypertensive drug of any frequency was considered as monotherapy whereas polytherapy was considered to be blend of two or more antihypertensives of distinct classes at any frequency and dose. Utilization pattern of antihypertensives in regards to controlled as well as uncontrolled hypertension was also analyzed. All data collected were analyzed using Statistical Package for Social Science (SPSS) of version 18.0 (Chicago IL, USA). Univariate analysis with Chi-square and t- test was performed followed by logistic regression to compute independent predictors. Multiple logistic regression analysis was used to evaluate the relationship between prescription of a particular class of drug and predictor variables. Results are expressed as odds ratio (OR) with 95% confidence interval (CI). P value ≤ 0.05 was considered statistically significant.

Results

Study characteristics

During the study period, 968 (83%) patients from 1166 diabetics had coexistent hypertension. The mean age of type 2 diabetics with hypertension was 54.41 (5.37 [SD]) yrs comprising 559 (57.75%) male and 409 (42.25%) female patients. There were 793 (81.9%) patients aged less than 61 yrs and 175 (18.1%) patients aged above 60 yrs. The mean (SD) duration of diabetes (DOD) was 11.13 (4.38) yrs whereas the mean (SD) duration of hypertension (DOHT) was 6.47 (3.28) yrs. Higher DOD and DOHT were observed in male compared to female (P<0.05). The clinical and demographic characteristics of diabetics with hypertension are presented in Table 1.

Table 1. *Clinical/ Demographic Characteristics of Diabetics with Hypertension (n=968).*

Characteristics	Total (n=968)	Men (n=559)	Women (n=409)	P value
Age, yrs				
Mean (SD)*	54.41 (5.37)	55.2 (5.29)	53.32 (5.3)	<0.001
Median (IQR)	55 (49-58)	55 (51-58)	52 (48-59)	
Age group				
40-60 years, n (%)†	793 (81.9)	430 (76.9)	363 (88.8)	<0.001
>60 years, n (%)	175 (18.1)	129 (23.1)	46 (11.2)	

Duration of Diabetes, yrs				
Mean (SD)*	11.13 (4.38)	12.7 (4.19)	8.99 (3.65)	<0.001
Median (IQR)	11.5 (7.5-16)	13.5 (10-16.5)	7.5 (6-12)	
Duration of Hypertension, yrs				
Mean (SD)*	6.47 (3.28)	7.71 (3.07)	4.77 (2.76)	<0.001
Median (IQR)	7 (3-9.5)	8 (5.5-10.5	3 (3-7)	
SBP, mmHg				
Mean (SD)*	143.04 (11.64)	142.61 (12.17)	143.64 (10.86)	0.169
Median (IQR)	145 (130-155)	145 (128-155)	145 (136-148)	
DBP, mmHg				
Mean (SD)*	87.98 (5.37)	88.69 (5.4)	87 (5.18)	<0.001
Median (IQR)	88 (85-92)	87 (85-94)	88 (85-90)	

DBP, Diastolic blood pressure; IQR, Inter quartile range; SBP, Systolic blood pressure; SD, Standard deviation;

* Compared using student t test; † compared using chi square test

Blood pressure control

In total, controlled blood pressure was noted in 337 (34.81%) patients, including 121 (29.09%) patients on monotherapy and 631 (65.19%) patients on polytherapy. Uncontrolled SBP or isolated systolic hypertension (≥ 140 mmHg) was noted in 183 (18.9%) patients and uncontrolled DBP or isolated diastolic hypertension (≥ 90 mmHg) was noted in 43 (4.44%) patients whereas both uncontrolled SBP and DBP were observed in 405 (41.83%) patients. Utilization pattern of antihypertensive drugs with respect to controlled and uncontrolled hypertension were demonstrated in Table 3.

Utilization pattern of antihypertensive drugs

Overall, 416 (42.98%) patients were on monotherapy (one drug) and 552 (57.02%) on polytherapy (more than one drugs). Among the patients on polytherapy, 409 (42.25%) patients were on combination of two drugs, 126 (13.02%) on combination of 3 drugs, and 17 (1.75%) were on blend of greater than three drugs. In monotherapy, majority of the patients were on calcium channel blockers (CCBs) (52.4%), followed by angiotensin receptor blockers (ARBs) (23.56%), angiotensin converting enzyme inhibitors (ACEIs) (17.31%), beta-blockers (BBs) (5.05%) and diuretics (DIs) (1.68%). In polytherapy, the most common treatment regimen is of two drug combination. Out of 409 patients on two drug combination regimen, the ARBs+DIs combination (31.05%) was prescribed often, followed by BBs+CCBs (20.05%), ARBs+CCBs (18.83%), ACEIs+CCBs (15.4%), ACEIs+ARBs (9.54%) and ACEIs+diuretics (5.13%). For the 126 patients on combination of three drugs regimen, 6 distinct combinations were observed. The most often prescribed three drug combinations were ARBs+CCBs+DIs (27.78%), ARBs+BBs +CCBs (21.43%), ACEIs+BBs+CCBs (17.46%), ACEIs +CCBs+DIs and ARBs+BBs+DIs (13.49% each) and ACEIs +ARBs+CCBs (6.35%). In 4 or more drug combinations, ARBs+BBs+CCBs+DIs (47.06%) were commonly prescribed (Tables 2 and 3).

CCBs were prescribed mostly 566 (58.47%) either as monotherapy or polytherapy, secondly ARBs 440 (45.45%) and then ACEIs 251 (25.93%), DIs 241 (24.9%) and BBs 183 (18.9%) (Table 2).

Table 2. Pattern of antihypertensive drug therapy.

	n (%)
Antihypertensive drug treatment regimen	
Monotherapy	416 (42.98)
Polytherapy	
Two-drug combination	409 (42.25)
Three-drug combination	126 (13.02)
≥ Four-drug combination	17 (1.75)
Antihypertensives received both as Monotherapy and Polytherapy	
CCBs	
ARBs	566 (58.47)
ACEIs	440 (45.45)
BBs	251 (25.93)
DIs	183 (18.9)
	241 (24.9)

ACEIs: Angiotensin Converting Enzyme Inhibitors; ARBs: Angiotensin Receptor Blockers; BBs: Beta Blockers; CCBs: Calcium Channel Blockers; DIs, Diuretics

Table 3. Utilization pattern of antihypertensive drugs in controlled vs uncontrolled hypertension.

Drugs n (%)	Total (968 [100])	Controlled BP (337 [34.81])	Uncontrolled BP (631 [65.19])		
			SBP (183 [18.9])	DBP (43 [4.44])	Both (405 [41.83]
Monotherapy	416 (42.98)	121 (29.09)	86 (20.67)	20 (4.81)	189 (45.43)
CCBs	218 (52.4)	68 (56.20)	44 (51.16)	16 (80)	90 (47.62)
ARBs	98 (23.56)	25 (20.66)	19 (22.09)	3 (15)	51 (26.98)
ACEIs	72 (17.31)	19 (15.70)	18 (20.93)	1 (5)	34 (17.99)
BBs	21 (5.05)	6 (4.96)	5 (5.81)	0	10 (5.29)
DIs	7 (1.68)	3 (2.48)	0	0	4 (2.12)
Polytherapy	552 (57.02)	216 (39.13)	97 (17.57)	23 (4.17)	216 (39.13)
Combination of 2 drugs	409 (74.09)	162 (75)	65 (67.01)	18 (78.26)	164 (75.93)
ARBs+DIs	127 (31.05)	71 (43.83)	13 (20)	5 (27.78)	38 (23.17)
BBs+CCBs	82 (20.05)	31 (19.14)	17 (26.15)	7 (38.89)	27 (16.46)
ARBs+CCBs	77 (18.83)	22 (13.58)	13 (20)	4 (22.22)	38 (23.17)
ACEIs+CCBs	63 (15.40)	20 (12.35)	12 (18.46)	0	31 (18.90)
ACEIs+ARBs	39 (9.54)	11 (6.79)	6 (9.23)	1 (5.56)	21 (12.80)
ACEIs+DIs	21 (5.13)	7 (4.32)	4 (6.15)	1 (5.56)	9 (5.49)
Combination of 3 drugs	126 (22.83)	46 (21.30)	30 (30.93)	3 (13.04)	47 (21.76)
ARBs+CCBs+DIs	35 (27.78)	16 (34.78)	11 (36.67)	2 (66.67)	6 (12.77)
ARBs+BBs+CCBs	27 (21.43)	7 (15.22)	5 (16.67)	0	15 (31.91)
ACEIs+BBs+CCBs	22 (17.46)	7 (15.22)	6 (20)	0	9 (19.15)
ACEIs+CCBs+DIs	17 (13.49)	6 (13.04)	4 (13.33)	0	7 (14.89)
ARBs+BBs+DIs	17 (13.49)	5 (10.87)	4 (13.33)	0	8 (17.02)
ACEIs+ARBs+CCBs	8 (6.35)	5 (10.87)	0	1 (33.33)	2 (4.26)
Combination of ≥ 4 drugs	17 (3.08)	8 (3.7)	2 (2.06)	2 (8.70)	5 (2.31)
ARBs+BBs+CCBs+DIs	8 (47.06)	3 (37.5)	2 (100)	2 (100)	1 (20)
ACEIs+BBs+CCBs+DIs	5 (29.41)	3 (37.5)	0	0	2 (40)
ACEIs+ARBs+CCBs+DIs	3 (17.65)	2 (25)	0	0	1 (20)
ACEIs+ARBs+BBs+CCBs+DIs	1 (5.88)	0	0	0	1 (20)

ACEIs: Angiotensin Converting Enzyme Inhibitors; ARBs: Angiotensin Receptor Blockers; BBs: Beta Blockers; BP: Blood Pressure; CCBs: Calcium Channel Blockers; Dis: Diuretics; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure

Choice of antihypertensives

In multiple regression analysis, age group, gender, DOD, DOHT, SBP, DBP, and type of therapy were taken as independent variables. Significant difference was found in diabetics with ≤ 60 compared to those with >60 years with respect to prescription of ACEIs (OR: 0.34, 95% CI 0.21-0.54). No association of gender with regards to antihypertensive drug prescription was noted. Significantly association of CCBs prescription with DOD, DOHT, SBP, DBP, and type of therapy (OR: 0.21, 95% CI 0.07–0.59, 7.62, 95% CI 2.62-22.09, 0.49, 95% CI 0.29-0.82, 2.28, 95% CI 1.26-4.13, 1.39, 95% CI 1.04-1.87, respectively) was observed. Prescription of ARBs was positively associated with DOHT, SBP, DBP, and type of therapy (OR: 0.24, 95% CI 0.08-0.73, 2.28, 95% CI 1.36-3.85, 0.27, 95% CI 0.14-0.5, 6.3, 95% CI 4.5-8.77, respectively). Similarly significant association was noted between ACEIs and

therapy, BBs with DOD, DOHT, SBP, DBP and therapy, and DIs with DOD, DOHT, DBP and therapy (Table 4).

Table 4. Predictors of Antihypertensive drug utilization.

Predictors	CCBs		ARBs		ACEIs		BBs		DIs	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Age group										
≤ 60 yrs	1.06 (0.72-1.57)	0.773	1.23 (0.82-1.85)	0.322	0.34 (0.21-0.54)	<0.001	1.17 (0.74-1.86)	0.509	1.16 (0.74-1.81)	0.531
>60 yrs	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Gender										
Male	1.33 (0.94-1.89)	0.111	0.84 (0.59-1.19)	0.318	0.68 (0.47-1.00)	0.683	1.15 (0.78-1.69)	0.489	0.94 (0.63-1.39)	0.76
Female	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
DOD										
≤ 9 yrs	0.21 (0.07-0.59	0.003	2.78 (0.94-8.21)	0.065	0.6 (0.21-1.69)	0.345	0.09 (0.01-0.67)	0.019	6.59 (2.04-21.31	0.002
>9 yrs	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
DOHT										
≤ 5 yrs	7.62 (2.62-22.09)	<0.001	0.24 (0.08-0.73)	0.012	1.21 (0.42-3.53)	0.725	16.55 (2.08-131.9)	0.008	0.11 (0.03-0.36)	<0.001
>5 yrs	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
SBP										
≤ 130 mmHg	0.49 (0.29-0.82)	0.007	2.28 (1.36-3.85)	0.002	1.48 (0.86-2.54)	0.154	0.43 (0.25-0.75)	0.003	1.47 (0.82-2.64)	0.201
>130 mm Hg	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
DBP										
≤ 80 mmHg	2.28 (1.26-4.13)	0.006	0.27 (0.14-0.5)	<0.001	1.43 (0.71-2.86)	0.314	3.63 (1.58-8.34)	0.002	0.33 (0.15-0.71)	0.005
>80 mmHg	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Therapy										
Monotherapy	1.39 (1.04-1.87)	0.028	6.3 (4.5-8.77)	<0.001	2.97 (2.09-4.21)	<0.001	6.57 (3.98-10.85)	<0.001	49.4 (22.29-109.4 8)	<0.001
Polytherapy	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	

ACEIs: Angiotensin Converting Enzyme Inhibitors; ARBs: Angiotensin Receptor Blockers; BBs: Beta Blockers; CCBs: Calcium Channel Blockers; CI: Confidence Interval; DBP: Diastolic Blood Pressure; DOD: Duration of Diabetes; DOHT: Duration of Hypertension; Dis: Diuretics; OR: Odds Ratio; SBP: Systolic Blood Pressure

Discussion

This study demonstrated that approximately 83% of the diabetics had a coexistent hypertension. Some vast, randomized trials showed that more than 66% of hypertensive people can't be controlled with one drug and they will need two or more antihypertensive drugs of drug classes [12]. About 70% of the diabetics with hypertension were on multiple-drug treatment regimen in a study conducted by Johnson et al. [13]. In our study 57.02 % of patients were on polytherapy.

In our study, CCBs were prescribed mostly, then ARBs, followed by ACEIs, DIs and BBs, respectively either as mono or poly therapy. In current study, dominant part of patients was on polytherapy.

In studies specific to hypertension in China revealed following findings: in 2006, two-thirds of hypertensive outpatients in Beijing general hospital were on monotherapy; in 2005, around 70.4% of hypertensive outpatients were on monotherapy in Guangzhou City general hospital; and in 2005, 68.9% in

Hangzhou City general hospital [14-16]. The utilization pattern similar to present study was observed in a study conducted by Cheng H in China [17].

Hypertension guidelines (2005) in China recommend the usage of any antihypertensive class as primary treatment option whereas the most recent guidelines suggests CCBs and DIs as first-line treatment for uncomplicated hypertension in older patients aged over 55 [18]. In current study, the most often used antihypertensives are CCBs. This result is in accordance with China national guidelines. A few studies conducted in China demonstrated similar usage pattern of antihypertensive agents [19-22]. The second most often used antihypertensives were ARBs; similar results noted in study conducted by Cheng et al. [17]. European guidelines recommend CCBs as the most cost efficient antihypertensives and BBs as least cost efficient based on sound economic modelling [23-25]. In current study, treatment options were in line with European guidelines cost-effectively. As per 2014 hypertension guidelines (JNC 8th report), it is recommended to initiate drug treatment with thiazide type DI or ACEI or ARB or CCB, alone or in combination [26]. As per 2015 NICE guidelines, the 1st line drug therapy should be ACEI or ARB. If not reduced to target, add CCB or thiazide or thiazide related DI as dual or triple therapy and then alpha blocker, BB, or potassium sparing DI [27].

The preferred antihypertensive medications for the management of hypertension in diabetics are ACEI and ARBs. However, initial choice of therapy was mostly CCBs or ARBs. In contrast with recommendations, ACEIs were prescribed lesser than CCBs and ARBs. The reason might be the non-compliance to the guidelines by internal physicians in the hospital to the benefits of usage/non-usage of ACEIs as preferred drugs in treatment of coexistent hypertension in diabetics. One more factor might be the impact of the pharmaceutical industry in drug promotion. A study by Wazana et al. demonstrated the impact on prescribing pattern of physicians (preference, rapid new drug prescription, and lesser prescription of generic drugs etc) by pharmaceutical representatives [28]. Our study results urge the need for physicians to continually educated and certified in updates and guidelines every few years.

Certain inherent limitations need to be considered during interpretation of the results of current study. As the study being a cross-sectional one, there is no way to figure out if the current therapy was the introductory/initial one (first line) or if it is switched over or amended/adjunct (added on) to the original one. The various treatment strategies/options (including complementary or alternative medicine), if any over time cannot be provided. In addition, our study allows no causality determination. Included diabetics are mostly from Chinese urban parts and hence do not mirror the entire patient population. Great differences may appear in health outcomes urban areas compared to rural areas. It's worth to note that health care in primary/secondary centers might have a different pattern of antihypertensive drug utilization and the results apply for typical tertiary care patients.

Conclusion

This study demonstrated that majority of diabetic outpatients with hypertension received polytherapy achieving BP target in accordance with recommendations. The most often used antihypertensives were CCBs, followed by ARBs, ACEIs, BBs and DIs. Thereby, suggesting the non-optimized treatment of hypertension in the Chinese Type 2 diabetic patients. Continued efforts are needed in order to improve antihypertensive drug usage and a framework for continuous prescription audit to create a database on prescribing patterns among patients with diabetes.

References

1. World Health Organization. Diabetes.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047-1053.
3. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998; 21: 1414-1431.
4. Klein R, Klein BE, Lee KE, Cruickshanks KJ, Moss SE. The incidence of hypertension in insulin-dependent diabetes. Arch Intern Med 1996; 156: 622-627.
5. International Diabetes Federation. IDF Diabetes Atlas sixth edition 2013.
6. Li L. Survey on the Status of Nutrition and Health of the Chinese People in 2002, the Fourth: Hypertension. People's Health Publication: Beijing. 2004; 49-90.
7. Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. Arch Intern Med 2005; 165: 2644-2650.
8. Adler AI, Stratton IM, Neil HA, Yudkin JS, Matthews DR, Cull CA, Wright AD, Turner RC, Holman RR. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. BMJ 2000; 321: 412-419.
9. No authors listed. National High Blood Pressure Education Program Working Group report on hypertension in diabetes. Hypertension 1994; 23: 145-158.
10. Kostis JB, Davis BR, Cutler J, Grimm RH Jr, Berge KG, Cohen JD, Lacy CR, Perry HM Jr, Blaufox MD, Wassertheil-Smoller S, Black HR, Schron E, Berkson DM, Curb JD, Smith WM, McDonald R, Applegate WB. Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. JAMA 1997; 278: 212-216.
11. Chobanian AV, Bakris GL, Black HR. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart,

Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42: 1206-1252.

12. Cushman WC, Ford CE, Cutler JA, Margolis KL, Davis BR, Grimm RH, Black HR, Hamilton BP, Holland J, Nwachuku C, Papademetriou V, Probstfield J, Wright JT Jr, Alderman MH, Weiss RJ, Piller L, Bettencourt J, Walsh SM; ALLHAT Collaborative Research Group. ALLHAT Collaborative Research Group. Success and predictors of blood pressure control in diverse North American settings: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). J Clin Hypertens (Greenwich) 2002; 4: 393-404.
13. Johnson ML, Singh H. Patterns of Antihypertensive Therapy among Patients with Diabetes. J Gen Intern Med 2005; 20: 842-846.
14. Du F. Analysis of outpatient prescriptions about antihypertensive drugs. Chin Pharm Aff 2008; 22: 254-256.
15. Deng BK. Use of antihypertensive drugs in the outpatients of our hospital. Eval Anal Drug-use Chin Hosp 2007; 7: 350-351.
16. Cheng L, Fan JJ, Liao JP. Prescribing pattern of antihypertensive drugs in a general hospital in central China. Hai Jun Yi Xue Za Zhi 2006; 27: 337-338.
17. Cheng H. Utilization of antihypertensive drugs in the outpatient in our hospital. Int J Clin Pharm 2011; 33: 215-220.
18. British Hypertension Society. Hypertension: management of hypertension in adults in primary care. 2006.
19. Du WM, Wang YM, Chen BY. Utilization of antihypertensive drugs for five year in Shanghai City. Chin J Clin Pharm 2002; 11: 76-78.
20. Feng L, Jiang YL, Sun CY. Trends in treatment for cardiovascular diseases for three years in 22 hospitals in Nanjing City. Chin J Pharmacoepidemiol 2004; 13: 22-24.
21. Zhao W. Investigation of application of antihypertensive drugs by four university hospitals during 2003-2004 in Beijing. Chin J Pharmacoepidemiol 2006; 15: 298-300.
22. Liang LM, Liao GR, Li Y. Analysis of antihypertensive drugs in Guangzhou during 2001-2003. Eval Anal Drug-use Chin Hosp 2004; 4: 219-221.
23. Mancia G, De Backer G, Dominiczak A. The task force for the management of arterial hypertension of the European Society of Hypertension, The task force for the management of arterial hypertension of the European Society of Cardiology. 2007 Guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2007; 28: 1462-1536.
24. Estacio RO, Jeffers BW, Hiatt WR. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. N Engl J Med 1998; 338: 645-652.
25. Mogensen CE, Neldam S, Tikkanen I. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and noninsulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. BMJ 2000; 321: 1440-1444.
26. James PA, Oparil S, Carter BL. 2014 evidence-based guideline 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: 507-520.
27. NICE guideline. Type 2 diabetes in adults: management. 2015.
28. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? JAMA 2000; 283: 373-380.

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