

SUPPLY OF ANTIHYPERTENSIVE DRUGS AND CARDIOVASCULAR MORTALITY IN POLAND IN 2000–2010

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Background and objective. *In Poland, the sale of antihypertensive drugs has significantly increased since 2000. According to that fact, the aim of our study was to determine if the increased use of antihypertensive drugs correlates with the decreasing mortality due to cardiovascular diseases (CVD) including hypertension (HT).*

Methods. *The analysis is based on data on annual national sales (million units) of four types of antihypertensive drugs in 2000–2010. For the same period standardized mortality rates were calculated based on the data available from the Central Statistical Office in Poland. Data analysis involved correlation analysis between annual mortality rates due CVD and HT and country-wide annual sales of antihypertensive drugs (2000–2010).*

Results. *In the period 2000–2010, standardized mortality rates of CVD in the whole population followed a decreasing trend. Analysis of correlation of CVD with specific drug provided the following findings: diuretics ($r=-0.97$; $p<0.0001$) beta-blockers ($r=-1.0$; $p<0.0001$) renin-angiotensin system (RAS) inhibitors ($r=-0.72$ $p=0.01$) calcium-channel blockers ($r=-0.82$; $p=0.001$) Standardized mortality rates for the HT showed fluctuating trend. Correlations of that mortality with global sale of these drugs were no longer negative: $r=0.54$; $p=0.08$, $r=0.56$; $p=0.08$ $r=0.55$; $p=0.07$; $r=0.63$; $p=0.03$, respectively.*

Conclusions. *In Poland, in 2000–2010, an improved access to pharmacological control of HT was associated with an apparent reduction in mortality from CVD but not from HT. The latter findings might reflect imprecise definition of HT as a cause of death or the fact that HT leads to other cardiologic events usually reported as a cause of death.*

KEY WORDS: antihypertensive drug therapy, cardiovascular disease, hypertension.

Introduction

Standardized mortality rates caused by cardiovascular diseases (CVD) have been decreasing in developed countries since 1980 [1]. In Poland, in the last 20 years, CVD mortality decreased twice and the dynamics was strong between 1990 and 2000 [2]. Many hypotheses have addressed the issue, including changes of lifestyle and diet, improved access to modern medical technologies [3]. Another potential factor could be related to better pharmacological control of hypertension (HT) [4]. Such an explanation can be explored in ecological manner through analysis of correlation between the nation-wide sale of hypertensive drugs and CVD/HT mortality, over a period of time.

The major classes of antihypertensive drugs include beta-blockers (BB), renin-angiotensin system inhibitors (RES), diuretics (D) and calcium channel blockers (CCB). Clinical studies confirm that those drugs used in the treatment

of HT are effective in preventing heart attack and stroke [5]. Less is known about population-based impact of the increased supply of the above drugs on ultimate outcome of HT, such as CVD mortality. In Poland, increased sales of and access to modern antihypertensive drugs has occurred over the two last decades and annual whole-country sales are available for a recent period (2000–2010), thus making such analysis possible.

The principal aim of our study was to determine if the increased use of antihypertensive drugs correlates with the decreasing mortality due to cardiovascular diseases (CVD) including hypertension (HT), in general population of Poland. The secondary aim of the study was to explore the hypothesized correlation in three age groups: 0–44 years, 45–64 years, above 64 years.

Materials and Methods

The analysis is based on data on annual sales (million units) of four types of antihypertensive drugs in 2000–2010: beta-blockers (BB), renin-angiotensin system inhibitors (RES),

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diuretics (D) and calcium channel blockers (CCB). Annual standardized mortality rates due to CVD and HT were calculated from raw data provided by the reports of the Central Statistical Office in Poland, using direct method (reference population: WHO European Standard Population [6]. Correlation analysis of CVD and HR with drug sales (Spearman method) was performed for the entire population and for three age groups (0 to 44, 45 to 64 and over 64 years of age). Statistical significance was assumed at $p=0.05$. All calculations were performed in SAS software (version 9.20, SAS Institute, Cary, N.C.).

Results

Standardized mortality rates due to CVD (n/100 000) in Polish population between 2000-2010 were: 439, 428, 412, 412, 391, 377, 365, 358, 350, 350, 331, respectively. In the same period the annual sales of all antihypertensive drugs (mln units globally) were: 100, 97, 96, 100, 105, 117, 123, 134, 143, 154, 158. Figure 1 shows

annual antihypertensive drugs supply in each defined category and annual mortality rates due to CVD, over the same period.

Correlation analysis of CVD mortality with the defined classes of drugs showed negative and statistically significant coefficients: BB ($r=-1.0$ $p<0.001$), RES ($r=-0.72$ $p=0.01$), D ($r=-0.97$; $p<0.001$), CCB ($r=-0.82$ $p=0.001$). Additional analyses involving stratification for age showed larger coefficients of correlation in older segments of the population (Table 1).

Standardized mortality rates due to HT (n/100 000) in Polish population between 2000-2010 were: 11,73; 10,82; 10,44; 11,30; 11,36; 12,53; 13,02; 12,60; 11,53; 12,38; 12,0; 10,24, respectively. Figure 1 shows annual antihypertensive drugs supply in each defined category and annual mortality rates due to HT, over the same period.

Trends of antihypertensive drugs supply with standardized mortality rate caused with HT are shown in Figure 2.

Table 1. Correlation of the supply of selected antihypertensive drugs (BB, RES, D, CCB) with CVD standardized mortality rate in polish population between 2000-2010

Specified group age	Type of antihypertensive drug			
	BB	RES	D	CCB
0-44 years	$r=-0.82$ $p<0.05$	$r=-0.46$ NS*	$r=-0.756$ $p<0.05$	$r=-0.52$ NS*
45-64 years	$r=-0.99$ $p<0.05$	$r=-0.71$ $p<0.05$	$r=-0.96$ $p<0.05$	$r=-0.82$ $p<0.05$
>64 years	$r=-0.98$ $p<0.05$	$r=-0.72$ $p<0.05$	$r=-0.96$ $p<0.05$	$r=-0.82$ $p<0.05$

Legends: NS - not significant, BB - beta-blockers, RES - renin angiotensin system inhibitors, D - diuretics, CCB - calcium channel blockers.

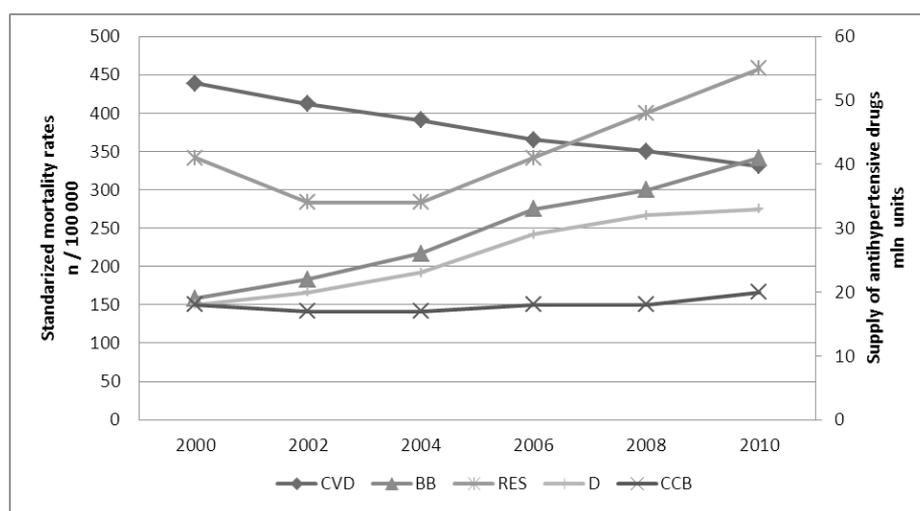


Fig. 1 Annual sales of antihypertensive drugs and CVD standardized mortality rate in 2000-2010 in polish population. Legends: CVD - cardiovascular diseases, BB - beta-blockers, RES - renin angiotensin system inhibitors, D - diuretics, CCB - calcium channel blockers.

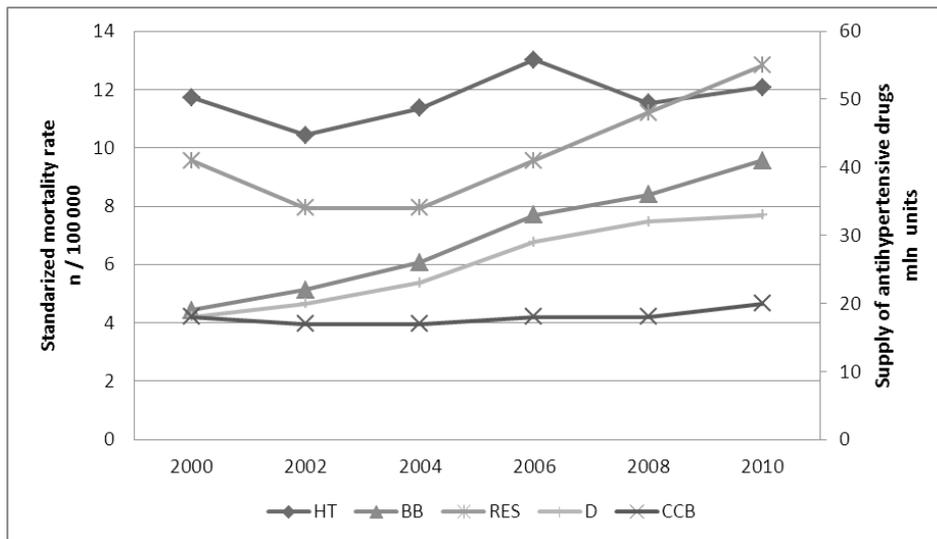


Fig. 2 Annual sales of antihypertensive drugs and HT standardized mortality rate in 2000-2010 in Polish population. Legends: HT - hypertension, BB - beta-blockers, RES - renin angiotensin system inhibitors, D - diuretics, CCB - calcium channel blockers.

Correlation analysis of HT mortality with the defined classes of drugs showed negative and statistically significant coefficients: Beta-Blockers ($r=0.56$ $p=0.07$), RES ($r=0.55$ $p=0.07$), Diuretics ($r=0.54$; $p=0.08$), CCB ($r=0.63$ $p=0.03$). Additional analyses involving stratification for age showed larger coefficients of correlation in older segments of the population (Table 2).

Discussion

High mortality due to cardiovascular diseases, seen for decades in the XX century in Poland, declined rapidly in 1991-1994. Since then the pace of decline is slower, but apparent. For example, CVD standardized mortality rates significantly decreased from 431 in 2000 to 339 in 2010. The observed phenomenon is attributed to a number of factors, including change of lifestyle with particular focus on healthy diet. Some estimates suggest that the reduction of dietary cholesterol intake in the analyzed period has explained a 39% reduction in general mortality due to coronary heart disease (CHD),

in Poland [7]. Other factors include reduced smoking and increased physical activity with the estimated contribution to decreased CHD mortality at the levels of 11% and 10%, respectively [8]. Other studies suggest an important role of tobacco smoking cessation (as most important cause), followed by blood pressure control (10%) and cholesterol (10%) [9]. The role of smoking habit together with high density lipoprotein cholesterol concentrations, triglyceride concentrations, diabetes, body mass index, height, alcohol intake, physical activity, and level of education have been also confirmed by ecological findings in the Polish population [10].

Interest in the impact of environmental factors on CVD mortality is justified by given socioeconomic changes in Poland, in recent decades. However, the role of clinical control of CVD cannot be neglected. After 1990 the Polish population has an increasing access to modern therapeutical measures, including effective medical technologies and effective

Table 2. Correlation of the supply of selected antihypertensive drugs (BB, RES, D, CCB) with HT standardized mortality rate in Polish population between 2000-2010

Specified group age	Type of antihypertensive drug			
	BB	RES	D	CCB
0-44 years	$r=-0.58$ NS*	$r=-0.29$ NS*	$r=-0.52$ NS*	$r=-0.31$ NS*
45-64 years	$r=0.79$ $p<0.05$	$r=0.70$ $p<0.05$	$r=0.78$ $p<0.05$	$r=0.75$ $p<0.05$
>64 years	$r=0.92$ $p<0.05$	$r=0.76$ $p<0.05$	$r=0.87$ $p<0.05$	$r=0.83$ $p<0.05$

Legends: NS - not significant, BB - beta-blockers, RES - renin angiotensin system inhibitors, D - diuretics, CCB - calcium channel blockers.

medicaments used in the treatment of CVD. In Poland, the contribution of those factors to the diminished CHD mortality could be as large as 37% [8]. The effect is likely to reflect not only a better access to modern pharmacological managements but also could be attributed to some changes in health care organization including physician-patient interactions. Social aspects could play a role and result in improved compliance of patients thus leading to stronger preventive outcomes in patients with chronic CVD [11].

Our findings showed a negative correlation between country-wide sale of antihypertensive drugs and CHD mortality, particularly in older segment of the Polish population. The result corresponds with a view concerning beneficial effect of pharmacological prevention of CHD mortality. Such effect was also seen in other study that addressed a risk of so called composite CVD events, stroke and all-cause mortality [12]. A large meta-analysis covering more than 40000 patients with hypertension provided interesting evidence concerning cardiovascular events and mortality: antihypertensive therapy was associated with the reduction of all-cause mortality rate by 13%, the risk of death from all-cardiac causes by 18%, CV events by 21, and stroke by 30%, including fatal stroke by 39% [13]. With regard to our findings it is of relevance that the gain is much larger in older patients than in young patients with hypertension [14]. It remains unknown to what extent the age-related difference reflects age-related duration of disease and, consequently, age-related duration of the treatment. Such explanation cannot be ignored when discussing no apparent

effect of the treatment of hypertension on CHD mortality over the period of 4-5 years [15].

Our findings did not show major differences between correlations provided by different groups of antihypertensive drugs analyzed in the study. The study protocol hampers a more detailed discussion of that point. The ecological approach used in our analysis has well-known limitations but a general conclusion about a beneficial impact of increased access of the population to modern antihypertensive therapy on a risk of CVD mortality in that population seems to be convincing. We did not see a similar effect in relation to HT mortality. A lack of such effect could be explained by a relatively infrequent occurrence of HT as a reported cause of death in Poland. Death certificates usually include fatal complication of HT thus making this diagnosis an unreliable index of cause-specific mortality, with a very limited pertinence to conclusive statistical analyses.

Conclusions

In Poland, an improved access of the population to pharmacological control of HT, as suggested by increased country-wide sale of modern antihypertensive drugs, is associated with an apparent reduction in mortality from CVD but not from HT. The latter finding might reflect imprecise definition of HT as a cause of death or the fact that HT leads to other cardiologic events usually reported as a cause of death. The findings seem to confirm an important contribution of pharmacological measures in prevention of CVD mortality, in addition to the well explored role of socio-economic and life-style factors, in Poland.

References:

1. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, Cowan MJ, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet* 2011; 377: 568-577.
2. Barański K, Zejda JE.: Nadciśnienie tętnicze jako główna przyczyna zgonów w Polsce w latach 1990-2010. *Nadciśnienie tętnicze*, 2014; 18(2): 74.
3. Cheng A, Braunstein JB, Dennison C, Nass C, Blumenthal RS. Reducing global risk for cardiovascular disease: using lifestyle changes and pharmacotherapy. *Clin Cardiol*. 2002; 25(5): 205-12.
4. Gudmundsson LS, Johannsson M, Thorgeirsson G, Sigfusson N, Sigvaldason H, Witteman JC. Hypertension control as predictor of mortality in treated men and women, followed for up to 30 years. *Cardiovasc Drugs Ther*. 2005; 19(3): 227-35.
5. White WB.: Update on the drug treatment of hypertension in patients with cardiovascular disease. *Am J Med*. 2005; 118(7): 695-705.
6. WHO age standardization of rates: a new who standard: Ahmad OB, Boschi-Pinto C, Lopez AD, Murray C, Lozano R, Inoue M.: GPE Discussion Paper Series: No.31 EIP/GPE/EBD World Health Organization 2001.

7. Zatonski WA, Willett W.: Changes in dietary fat and declining coronary heart disease in Poland: population based study *BMJ* 2005; 331:187.
8. Bandosz P, O'Flaherty M, Drygas W, Koziarek J, Wyrzykowski B, Rutkowski M, et al.: Explaining the decline in coronary heart disease mortality in Poland between 1991 and 2005 ESC Congress, Stockholm, Sweden (2010 28 Aug–01 Sep) Abstract 1119.
9. Unal B, Critchley JA, Capewell S.: Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. *Circulation*, 109 (2004): 1101–1107.
10. Zatonski WA, McMichael AJ, Powles JW, Ecological study of reasons for sharp decline in mortality from ischaemic heart disease in Poland since 1991 *BMJ*. 1998 Apr 4; 316(7137): 1047–105.
11. Papp R, Csaszar A, Paulik E, Balogh S.: Correlations between prescription of anti-hypertensive medication and mortality due to stroke. *BMC Cardiovascular Disorders* 2012, 12: 1.
12. Thompson AM, Hu T, Eshelbrenner CL, Reynolds K, He J, Bazzano LA.: Antihypertensive treatment and secondary prevention of cardiovascular disease events among persons without hypertension: a meta-analysis. *JAMA*. 2011; 305(9): 913–22.
13. Ostrowski M, Zanchetti A, Nikfar S, Muntner P, Aronow WS, Howard VJ, Wong ND, Howard G, Abdollahi M, Banach M.: The effect of hypertension pharmacotherapy in older adults. The results of a meta-analysis of 11 randomized control trials with 40325 patients. *European Heart Journal* (2014) 35 (Abstract Supplement), 1192.
14. Perez MI, Musini VM, Wright JM.: Effect of early treatment with anti-hypertensive drugs on short and long-term mortality in patients with an acute cardiovascular event. *Cochrane Database Syst Rev*. 2009 Oct 7;(4):CD006743.
15. Diao D, Wright JM, Cundiff DK, Gueyffier F. Pharmacotherapy for mild hypertension. *Cochrane Database of Systematic Reviews* 2012, Issue 8.

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