

11. SUMMARY

Introduction

Increasing prevalence of chronic forms of cardiovascular diseases, their treatment is lifelong in majority of patients, causes considerable increase of the utilisation of cardiovascular drugs.

Considering the fact that healthcare financial resources are restricted, it is necessary to use the drugs effectively and rationally. That is why it is important to study the trends in pharmacotherapy and drug prescribing in the real practice and consequently evaluate the drug use from the epidemiological, economic or social point of view.

Objectives

The objective of this work was to evaluate several aspects of the cardiovascular drug utilization on the basis of use of several large drug databases and different pharmacoepidemiologic attitudes.

Specific issues were addressed in four independent studies:

- 1) A comparison of cardiovascular drug utilization in selected districts of the Czech Republic and Great Britain.
- 2) Cardiovascular drug utilisation, mortality and socio-economic inequalities: An ecological study in 20 districts of the Czech Republic.
- 3) An analysis of the hypertension treatment in general practitioners in the Czech Republic in the 90's.
- 4) Pleiotropic effects of statins and prevention of diabetes mellitus type 2.

1) A comparison of cardiovascular drug utilization in selected districts of the Czech Republic and Great Britain.

In many studies that analyse the quality and cost-effectiveness of pharmacotherapy was found that the percentage of inappropriate or unproven therapies is unexpectedly high. The international comparative studies of drug utilisation that include data from the Czech Republic are sporadic, despite they are interesting for example as a basis for discussion of the drug policy.

The objective of this study was to compare the utilisation of selected cardiovascular drug groups and to describe utilisation trends of these drugs in years 1997 to 2000 in selected districts of the Czech Republic and Great Britain.

Methods and results

In this drug utilisation review we analysed the prescription data of five districts in central Moravia and Silesia using the General Health Insurance Company database and the prescription data of five districts in the South Wales in Great Britain using the data from PIAS database.

The average total utilisation of the evaluated drugs was considerably higher in Czech districts compared to districts of Great Britain (478,1 DID and 287,9 DID in Czech and Wales districts respectively in II.00). In the Welsh districts there was higher utilisation in nifedipine, AT₁ blockers and statins.

Certain drugs that belonged among the most prescribed drugs in the Czech districts have only very limited data of the effectiveness (vasoprotectives and peripheral vasodilatants). The prescription data of the Czech republic showed that certain obsolete drugs, as reserpine, were still used and significantly higher utilisation of digoxine has been found (14,4 DID and 5,8 DID in Czech and Welsh districts respectively in v II.00) compared to the Welsh districts. Utilisation of these drugs, however, was significantly decreasing during the study period.

Much more pronounced differences in the drug utilisation have been observed amongst Czech districts compared to the districts of Wales.

In both counties the common trends toward the increase in use of the drugs from newer cardiovascular drug classes, such as calcium channel blockers, ACE inhibitors and cardio-selective beta-blockers, has been observed.

2) Cardiovascular drug utilisation, mortality and socioeconomic inequalities: An ecological study in 20 districts of the Czech Republic.

Social and economic factors are one of the basic determinants that influence cardiovascular mortality and morbidity. It has been proven that factors of socio-economic deprivation also influence the drug utilisation on both individual and local level.

The objective of this ecologic study was to evaluate the equity of the drug use on the district level and to evaluate the influence of several parameters of the socio-economic deprivation of the inhabitants on the drug utilisation.

Methods and results

In this drug utilisation evaluation we used aggregated data from 20 districts of the Czech Republic that were supplied by General Health Insurance Company and five parameters of the social and economic deprivation of the individual districts in year 2000. This data has been obtained from Czech statistic office and Ministry of labour and social affairs.

Results of the study show up to tenfold difference in the cardiovascular drug utilisation on the district level in certain drug groups.

Variability of the utilisation of certain drugs was influenced by the socio-economic characteristic of the districts. Our study shows that the most sensitive to the differences of the socio-economic deprivation of the inhabitants of the districts is the utilisation of the newer drug groups such as dihydropyridine calcium channel blockers, verapamil and diltiazem, ACE

inhibitors and statins, where the five socio-economic parameters explained more than 60% of the variability of the drug utilisation in these districts.

The highest influence on the differences on the drug utilisation was observed for percentage of the university-educated inhabitants, number of ambulatory practitioners and percentage of single member households.

3) An analysis of the hypertension treatment in general practitioners in the Czech Republic in the 90's.

Hypertension control in the population depends on the knowledge and therapeutic approach of the general practitioner by whom the majority of the hypertensive patients is treated. During the 90's a considerable changes in the approach to hypertension treatment have been introduced. It is therefore important to study their impact on the blood pressure compensation and a type of antihypertensives used.

The objective of this study was to describe trends in the hypertension treatment by general practitioners in the Czech Republic in the 90's, to characterise patients with hypertension, the level of blood pressure compensation and type of prescribed antihypertensives.

Methods and results

In this retrospective cross-sectional analysis we evaluated the hypertension therapy in patients of 12 randomly chosen general practitioners from different regions of the Czech Republic. Routinely recorded data from years 1992,1996 and 1999 were collected from the medical records of the patients.

We included 862 hypertensive patients, 47,6% men and 52,4% women, with average age $62,5 \pm 11,0$ years.

The results show that despite partial increase over the study period, the blood pressure compensation has remained low (36,2% in 1999). This finding represents a challenge for general practitioners towards the increased effort to reach recommended values of blood pressure in their patients and also towards decreasing risk factors, such as obesity and hypercholesterolemia, theirs average values were found high over the normal values.

The choice of antihypertensive drugs was found to be positive. The most often used drugs were diuretics and beta-blockers (54,0% and 63,2 % of patients respectively in 1999). We observed considerable increase of the use of ACE inhibitors (from 1,7% in 1992 up to 35,2% in 1999), which was significantly higher in patients with diabetes mellitus and ischemic heart disease history (OR 2,59 [1,78; 3,79] and OR 2,27 [1,57; 3,28] respectively) compared to the other patients in the study. During the study period a decrease in use of central antihypertensives, such as reserpine, and decrease in use of nifedipine has been observed which was also considered positive.

4) Pleiotropic effects of statins and prevention of diabetes mellitus type 2.

Experimental and clinical experience with statins over last years shows that, apart from antihyperlipidemic effect, statins might have also other effects independent on cholesterol lowering. One of these beneficial effects of statins is their ability to influence different pathophysiological processes of the development of diabetes mellitus type 2 and so contribute to delay or prevention of the onset of the disease. Pravastatin has been proven to have the impact on the new onset of diabetes mellitus type 2. It is not known, however, whether similar effect can be found in other statins and non-statin antihyperlipidemics.

The objective of this study was to find whether development of the diabetes mellitus can be influenced also by other statins and non-statin antihyperlipidemics. Second objective was to determine the dose and time dependency of the statin use and development of diabetes.

Methods and results

In this case-control study we used the data from the PHARMO RLS database. From the cohort of 12 510 patients, who were users of antihyperlipidemics, we included 757 cases, who during the study period were prescribed antidiabetics for the first time, and 2259 controls. Average age was 62,6 years (SD 10,2) and 39,6% were women.

Results show that ever-users of statins had the same risk of the onset of antidiabetic treatment as ever-users of pravastatin (OR 1,10 [0,87; 1,40]), whilst ever-users of non-statin antihyperlipidemics had this risk significantly increased (OR 2,68 [1,81; 3,97]).

Dose and time dependence analysis showed that statins probably might delay the onset of antidiabetic therapy with higher probability than to prevent it completely.

This study was a generation of the hypothesis (signal) that all statins might have beneficial effects on diabetes mellitus development. That is why these results need to be further confirmed in randomised clinical study.

Conclusion

Total utilisation of cardiovascular drugs included into the study in the Czech Republic was significantly higher than in Great Britain, which in some cases requires rigorous revision. Among the Czech districts dramatic differences in the drug utilisation have been found, what was not observed in such a magnitude in Welsh districts.

The differences in the drug utilisation among Czech districts can be in part explained by the difference at the level of socio-economic deprivation of the inhabitants of the districts, particularly for the newer drug groups.

During 90's we observed only modest increase in blood pressure compensation in hypertensive patients. Mainly patients with history of stroke and diabetes mellitus would require much more rigorous blood pressure control.

Statin antihyperlipidemics might delay the new onset of diabetes mellitus type 2 similarly as pravastatin.