Possibilities of pharmaceutical care in patients with increased risk for cardiovascular disease

PhD thesis

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1. Introduction

Non-infectious diseases are the leading cause of death worldwide, of which cardiovascular conditions, tumours, chronic respiratory diseases and diabetes are the most significant, all having top priority in public health. In terms of cardiovascular mortality, Hungarian findings are comparable to European data: 50 % of total mortality is due to cardiovascular diseases.

There are several conditions which themselves or when associated with an underlying disease may considerably increase the risk for cardiovascular disease. One of these is metabolic syndrome, a condition created by the co-existence of several diseases, each of which poses a great risk, making the treatment and care of these patients especially important. Either considered as a disease entity or a group of diseases associated with an increased cardiovascular risk, the tasks of caring for patients with metabolic syndrome can be clearly defined.

In the past decade, pharmaceutical care has undergone a significant development from pharmacy

screening for diabetes to advanced-level care using standards and guidelines. The high number of pharmacist-patient meetings and the role of pharmacies in health care create the basis for pharmacist involvement in public health care campaigns.

Pharmacists have the opportunity to take care of their patients in a more complex way, including assessment and improvement of adherence or even therapy management.

2. Objectives

The primary objective of my PhD dissertation was to investigate the possibilities of pharmaceutical care in patients with type 2 diabetes, involving four public pharmacies and seven GP practices in Borsod-Abaúj-Zemplén County. The study population included patients with type 2 diabetes consenting to participation and cooperating over the study period. A further objective was to study the association of repeated myocardial infarction, one of the complications of type 2 diabetes,

with the use of acetyl salicylic acid, other concomitant chronic conditions, and mortality, making use of national and regional data bases. My research was in line with my daily pharmaceutical practice as the patients included in the study suffered from diseases which had potentially severe outcome but could benefit from appropriate pharmaceutical care in terms of improvement in the quality of life and gain in life years.

1.) Aim of survey performed while dispensing pharmaceutical products containing metformin:

(a) Evaluation of drug taking habits in patients with type 2 diabetes filling up prescriptions for pharmaceutical products containing metformin

(b) Evaluation of the impact of complications and associated diseases on adherence to therapy in patients with type 2 diabetes

2.) Aim of study evaluating adherence to oral antidiabetic therapy in patients with type 2 diabetes:

(a) To investigate whether SMS messages sent on the patients' mobile phones can improve adherence

compared to controls

(b) To assess whether inclusion in the study can lead to improvement in glycated haemoglobin and blood glucose levels

3.) When analysing the data of patients with myocardial infarction my aim was:

(a) To evaluate risk factors contributing to the disease and relevant to pharmaceutical care

(b) To evaluate the patients' medication and association of such medication with medical guidelines, with a special emphasis on the effect of acetyl salicylic acid administration.

3. Methods

3.1. Study of drug safety control performed while dispensing pharmaceutical products containing metformin

3.1.1 Method of the first survey

Two surveys were conducted. The first of these was

carried out in public pharmacies between May and November 2014. Four pharmacies and a total of 102 patients took part in this survey. Participation was voluntary. Patients with type 2 diabetes filling up a prescription for a pharmaceutical product containing metformin were asked to complete a questionnaire with the help of the pharmacist.

The data were entered in a Microsoft Office Excel 2007 file, descriptive statistics were prepared of both discrete and continuous data, then cross tables were created and summations were performed. The associations and differences between the study variables were tested by the chi square test at a significance level of $p=0.05$.

3.1.2. Method of the second survey

The second survey was performed in public pharmacies between August and September 2015 and included four pharmacies and 106 patients.

The data were aggregated using Microsoft Office

Excel 2007, descriptive statistics was prepared and summations performed. Associations were evaluated by the chi square test with $p < 0.05$ considered as significant.

3.2. Method of adherence study

A prospective study covering the period between 1 March 2010 and 21 May 2011 was conducted in patients with type 2 diabetes, with the participation of seven GPs in Miskolc. The study had been planned to include a total of 140 diabetic patients.

During the study period, blood glucose levels and glycated haemoglobin levels were checked regularly. The patients taking part in the study were divided into two groups: A and B.

Patients in group A received a reminder on their mobile phones three times daily. Patients in group B received no such messages and served as controls.

A web-based application was used to create the IT basis of the research.

The results of the study were aggregated using

Microsoft Office Excel 2007 and were processed for descriptive statistics. Statistical analysis was performed by means of the two-sample t-test and variance analysis (ANOVA) (level of significance: $p < 0.05$).

3.3 Method of medical records evaluation of patients with myocardial infarction

A retrospective study was conducted by evaluating the medical records of 659 patients with myocardial infarction treated at the 1st Department of Internal Medicine and Cardiology, Borsod-Abaúj-Zemplén County Hospital and Training Hospital.

Cases diagnosed by specialists were evaluated, with patients identified on the basis of the ICD I21-I23 code.

Using the integrated Medical NetWork System, the data of patients identified by their TAJ number and ICD code were subjected to analysis.

Microsoft Office Excel 2007 was used and the analysis was performed by the chi square test.

Differences of mean values were considered significant at $p < 0.05$.

4. Results

4.1. Results of the first survey

The questionnaire was completed by 60 female and 42 male patients.

Non-adherence was reported by 31.4% of the patients. The difference between males and females was significant ($p=0.014$).

Reasons for non-adherence were also evaluated; the difference here had borderline significance ($p=0.087$), with men being more likely to forget to take their medicine than women.

Adherence was the lowest among male patients aged 60 to 70 years having secondary education.

Nearly half of the patients had their medicine substituted. No significant association was found between substitution and experienced adverse effects or

substitution and adherence.

4.2. Results of the second survey

Fifty-seven and 43% of patients taking part in the survey were males and females, respectively.

Factors influencing adherence, differences between genders and age groups, duration of diabetes, and the existence of complications and associated diseases were evaluated. No significant differences in adherence were found with regard to these factors.

Adherence was not significantly affected by the pharmaceutical form, strength, dosing frequency or concurrent medication.

The association between complications and the duration of diabetes proved to be significant ($p=0.002$).

Similarly, a significant difference was found between the complexity of OAD therapy and the duration of diabetes ($p<0.001$).

The difference between the dosing regimen and the

duration of diabetes (in years) was also significant ($p<0.001$).

A significance difference was found between the dosing regimen and the incidence of complications ($p=0.023$).

The association between pharmaceutical strength and the duration of diabetes was of borderline significance ($p=0.059$).

4.3. Results of the adherence study

Of the 131 patients, 70 were males and 61 females. The mean age was similar in the two groups.

At the end of the study, there was no significant difference between the two groups either in final glycated haemoglobin levels ($p=0.212$), or final blood glucose levels ($p=0.845$).

The absolute value of glycated haemoglobin changed, with significantly less diversity and more stable therapeutic outcome in the SMS group.

Baseline and final HbA1c values were also compared and a significant difference was found (p=0.047). No significant difference was shown in blood glucose measurements (p=0.856).

4.4. Results of evaluation of medical records of patients with acute myocardial infarction

Of the 659 patients whose records were evaluated in the study 411 were males and 248 females. In this patient population, a significant difference was found with regard to gender (p=0.004).

Evaluating the association between chronic conditions (asthma, type 2 diabetes, hypertension, dyslipidaemia, obesity) and reinfarction, two important observations were made: the prevalence of reinfarction was significantly higher in patients with diabetes (p=0.063). The presence of diabetes was associated with a nearly one-and-a-half-time increase in the risk of reinfarction (RR:1.4255001; CI-0.0595213-0.7685667).

A significant, although reverse, association was

found between dyslipidaemia and mortality (p=0.0001): fewer infarction patients with dyslipidaemia died.

Evaluation of chronic cases produced two important findings. The rate of reinfarction was shown to be significantly higher (p=0.047) in hypertensive patients with diabetes. Simultaneous presence of these two condition resulted in a more than one-and-a-half-time increase in the risk of reinfarction (RR:1.5470563; CI 0.021-0.8516).

The result pertaining to hypertension, dyslipidaemia and reinfarction also proved to be statistically significant (p=0.03).

Use of acetyl salicylic acid in patients with acute myocardial infarction/ reinfarction was evaluated. The rate of reinfarction was significantly higher (p=0.0001) in patients who received acetyl salicylic acid.

5. Conclusions

Several findings of our research complement or support earlier observations published in the literature.

In our studies, the following were found:

a.) The patients with type 2 diabetes included in our research had better adherence compared to the findings of similar studies. Adherence was found to be lower in male patients.

b.) In accordance with findings in several other studies, forgetfulness was the most common cause of non-adherence; in the present research, it was most typical of middle-aged men.

c.) In line with findings in the literature, hypertension was the most common condition associated with type 2 diabetes and several patients had more than two associated diseases.

d.) Our research confirmed earlier findings that with the progression of type 2 diabetes complications are more likely to occur and therapy becomes more and more complicated.

e.) The rate of reinfarction was higher in patients with myocardial infarction who also suffered from diabetes and hypertension or dyslipidaemia and

hypertension.

The novel findings of our research are as follows:

a.) The adherence study in patients with type 2 diabetes revealed that the therapy was more successful in patients who received SMS reminders, as reflected by the lower diversity of HbA1c values. Overall, it is concluded that this method failed to produce the expected improvement in glycated haemoglobin levels, is not effective enough, and too expensive.

b.) The adherence study demonstrated that active involvement of patients in pharmaceutical care could improve, by way of better patient cooperation, glycated haemoglobin levels.

c.) The evaluation of medical records revealed that acetyl salicylic acid was not included in the therapeutic regimen of a number of patients with multiple risk factors. In such cases, controlled recommendation of pharmaceutical products containing acetyl salicylic acid may play an important role in prevention.

Practical applicability of the study results:

A special attention should be paid to the pharmaceutical care of patients with cardiovascular conditions, as these patients are often exposed to multiple risk factors. Of these factors, the most important are diabetes, hypertension, dyslipidaemia and, in many cases, an unhealthy lifestyle, smoking and alcohol abuse.

Results of the present research showed that the burdens incurred by a disease, such as the cost of medication, significantly increase with the progression of the disease.

In accordance with the current guidelines, pharmacists can assist patients by introducing specifically designed care, by educating patients on self-check, and by involving them in health care programmes.

The data collected in these studies can help identify the patient groups that require special attention.

6. Bibliography of the candidate's publications

Argay M, Koós I, Takács I, Dormaeva I, Meskó A, Zelkó R, Hankó B. (2013) Pharmaceutical care for patients with acute myocardial infarction in Hungary. INTERNATIONAL JOURNAL OF CLINICAL PHARMACOLOGY AND THERAPEUTICS, 51:(2) pp. 91-95.

Márton Argay, Andrea Meskó, Romána Zelkó, Balázs Hankó (2015) Therapy reminder message for hungarian patients with type 2 diabetes. ACTA POLONIAE PHARMACEUTICA, 72:(6) pp. 1289-1293.