Acta Poloniae Pharmaceutica – Drug Research, Vol. 72 No. 6 pp. 1289–1293, 2015 ISSN 0001-6837
Polish Pharmaceutical Society

GENERAL

THERAPY REMINDER MESSAGE FOR HUNGARIAN PATIENTS WITH TYPE 2 DIABETES

MÁRTON ARGAY[1], ANDREA MESKÓ[2], ROMÁNA ZELKÓ[2]* and BALÁZS HANKÓ[2]

[1]Semmelweis University, School of PhD Studies, Budapest, Hungary
[2]Semmelweis University, University Pharmacy Department of Pharmacy Administration, H-1092 Budapest, 7-9 Hogyes E Street, Hungary

Abstract: Adherence is an essential element for the optimal treatment while it is closely related to the outcome of chronic diseases. Non-adherence rate is really high; increasing the adherence is an important task for health-care professionals in order to treat the morbidity and co-morbidity and to prevent complication. The object of this study was to find a method which can improve patients' adherence in type 2 diabetes. A one year long prospective study was carried out from 2013 March. One hundred thirty one diabetic patients joined the survey, 66 in the control and 65 in the intervention group. Patients in the intervention group received a reminder SMS three times a day to take their medicine. Glycated hemoglobin and blood glucose level was measured regularly. The patients' parameters and the difference of the values were examined. No significant difference was found between the control and intervention groups. In the survey significant results was found in the final glycated hemoglobin values. During the time of the research, the patients became active participants of their therapy. Due to this active co-operation, positive results could be achieved. Based on the results, a decision making support module should be implemented to the existing medical information system to improve the therapeutic adherence of wide range of patients.

Keywords: chronic diseases, adherence, pharmaceutical care, glycosylated hemoglobin, reminder SMS

Chronic diseases are the leading mortality cause with more than 60% of all death, according to the WHO (World Health Organisation). Patients with chronic diseases generally suffer in polymorbidity. The success of the complex therapy highly depends on how the patients adhere their medication. To achieve good adherence is the main goal of health-care professionals in order to decrease mortality in patients with chronic diseases. Pharmacist can influence many factors which improve adherence. Besides guidance, adherence must be followed up because in chronic diseases the poor adherence increases with long duration and the complexity of the treatment. The highly prevalent diabetes mellitus and its co-morbidity with complications is becoming a major public health problem worldwide. In Hungary the prevalence of diabetes is 5-5.5%, this means 500.000 patients. Approximately 90% of all cases belong to type 2 diabetes. Achieving optimal blood glucose level and preventing the chronic complications are the goals of the medical therapy. Complexity of this heterogeneous disease needs a complex approach and treatment in which the patient is an active participant, too. The result is greatly influenced by how the patients take their medicine, so the adherence is an important factor which has to be examined for the successful therapy. In developed countries the adherence to medical therapy is approximately 50%, in long-term medication this rate is considered to be low (1). There are several statistics showing this result and the adherence is far from optimal, therefore reducing effectiveness of the medical therapy and treatment results (2, 3). A Hungarian study from 2007 published adherence results to diet (76.8%), physical activity (33.8%), self-monitoring of blood glucose (81%), drug purchasing (20.4%) and drug taking 52.1% (4). Further research found adherence rate between 47.9% and 49.2% to oral antihyperglycemic drugs. There was significant difference between male and female patients, women had a significantly better ($p < 0.001$) adherence rate than men, 51.3% *vs*. 45.5% (5).

In diabetic patients the HbA1C (glycated hemoglobin) measurement is a basic test in

* Corresponding author: e-mail: zelko.romana@pharma.semmelweis-univ.hu; fax/phone: +36-1270927

glycemic control, while it represents average blood glucose over three months. The duration of diabetes and the complications are significantly associated with the glycated hemoglobin. In T2DM (type 2 diabetes) 1% increase of HbA1C poses 15-18% relative risk of cardiovascular disease (6). In the case of AMI (acute myocardial infarction) 14% reduction was found in association with 1% reduction of HbA1C 1% in UKPDS (United Kingdom Prospective Diabetes Study).

Correlation is observed between adherence and HbA1C: 10% increase of adherence decreases HbA1c with 0.1% (7), good adherence to drug therapy is associated with decreased mortality and with positive health outcomes. Therefore, the primary aim of this study was to study the effectiveness of therapy reminder message on the patients' adherence in type 2 diabetes and the consequent specific disease parameters.

EXPERIMENTAL

A prospective study was carried out in patients with T2DM from March 1, 2013 to May 31, 2014 in Miskolc, Borsod-Abaúj-Zemplén county. Seven general practitioners took part in the survey. Patient recruitment was performed 2 months long with the help of their general practitioners. The following criteria had to be fulfilled for the patients who took part in the survey:

– diagnosed type 2 diabetes
– oral antidiabetic therapy
– cell phone user
– regular medial check (monthly)
– age (30-65 ages)

Each patient had a personal file containing: name, age, medication, and blood glucose and glycated hemoglobin. During the survey, regular glycemic controls were made. The blood glucose level measurement was performed monthly by the general practitioner in each visit. The glycated hemoglobin was measured among laboratory conditions every three months. The participants were divided into two groups: A and B. To divide the participants into the intervention and control groups we used the RAND() formula of Microsoft Excel. The participants were put into an Excel worksheet and with the RAND() formula a random numbers to each one of them were assigned. They were sorted in ascending order based on the random numbers assigned to them and chose the first half of them to be in the intervention group, and the second half of them to be in the control group.

Patients belonging to group A got a reminder message on their cell phone three times a day (08 a.m., 02 p.m. and 08 p.m.) to take their medicine. Descriptive statistics for the groups are summarized in Table 1.

Patients belonging to group B did not get any reminder SMS. Glycated hemoglobin levels were compared between the above groups. The aim of the study is to improve adherence by reminding patients to take their medicine regularly, in order to achieve optimal Hba1C level.

The study was authorized by the Regional Ethics Committee (RKEB:01-01-2010). All patients gave written consent to participate.

Table 1. Descriptive statistics for groups A and B.

Patients	Number	Minimum age	Maximum age	Mean	S.D.
SMS group (A)	65	40.00	82.00	59.9385	8.71937
Control group (B)	66	40.00	75.00	60.2154	7.89084

Table 2. The summarized group statistics.

	Adherence group	N	Mean	S.D.	S.E. Mean
HBAFIN	SMS	65	6.7015	1.06778	0.13244
	control	66	6.6561	1.19062	0.14656
BLODGLU-	SMS	65	7.4200	1.79463	0.22260
FIN	control	66	7.4821	1.82328	0.22443

S.D. = standard deviation, S.E. = standard error

Table 3. Deviation values of the glycated hemoglobin difference.

	N	Mean	S.D.	S.E.	95% confidence interval for the mean		Minimum	Maximum
					Lower bound	Upper bound		
SMS	65	-0.0585	0.84167	0.10440	-0.2670	0.1501	-2.30	2.40
Control	66	-0.4045	1.11265	0.13696	-0.6781	-0.1310	-3.40	3.10
Total	131	-0.2328	0.99896	0.08728	-0.4055	-0.0602	-3.40	3.10

S.D. = standard deviation, S.E. = standard error

Table 4. Initial and final glycated hemoglobin values.

SMS (A) group	Initial HbA1C	Final HbA1C
Male	6.69	6.765
Female	6.851	6.677
Control (B) group		
Male	7.019	6.644
Female	7.100	6.668

Statistical comparisons were performed with two sample t-test and ANOVA.

The figures/results were aggregated with Excel.

Technical information

A web based application was used to provide the research with IT support. The application is able to send SMS to the patients to remind them to take their medicine used in the diabetes therapy. Administration of the patients' data included in the research could be worked out on the web based user interface of the application. It can be customized which patients should get a reminder SMS in the morning, at noon and in the evening. Also the text of the messages can be customized. Doctors can log in to the system and enter diabetes related data of their patients; the system stores this data historically. This feature enables us to handle research data effectively when creating statistics and drawing conclusions.

RESULTS

The study was designed with 140 diabetic patients, after one year, 9 patients dropped out. From the 131 patients 70 were male and 61 were female, average of 60 years. The average age was 59 years in the intervention group, 60 years in the control group. There were 38 male and 27 female patients in the intervention group. In the control group, there were 32 male and 34 female patients.

Oral antidiabetic therapy was a recruitment criterion. The OAD medication was recorded during the study; 45.67% of the patients had OAD monotherapy: 27.1% biguanid (metformin), 12.3% sulfonylurea, 4.9% thiazolidindion and 1.2% a-glucosidase inhibitor.

Combination therapies:

Biguanid (metformin) + sulfonylurea: 43.2%

Biguanid (metformin) + thiazolidindion: 3.7%

Sulfonylurea + thiazolidindion: 2.4%

Biguanid (metformin) + sulfonylurea + thiazolidindion: 3.7%

Biguanid (metformin) + sulfonylurea + α glucosidase inhibitor:1.2%

The two groups were intervention group A (initial HbA1C value 6.76%) and control group B (initial HbA1C value 7.06%).

During the survey the glycated hemoglobin and the blood glucose levels were measured.

There was no significant difference in the final value of glycated hemoglobin (HBAFIN) between the groups ($p = 0.212$).

Neither were there significant differences in view of final blood glucose value (BLODGLUFIN) ($p = 0.845$) as it can be seen in Table 2.

Table 2 shows the final glycated hemoglobin (HBAFIN) and final blood glucose (BLODGLUFIN) values.

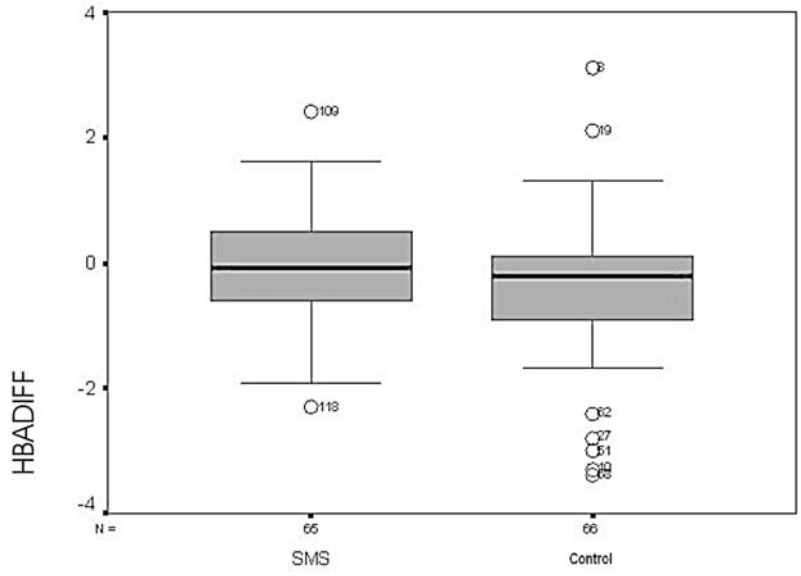

Figure 1. Difference in glycated hemoglobin levels of the SMS (adherence group) and control group

Similarly to other studies in these topic, no statistical differences were noticed between patients receiving messaging interventions compared to those who received only the usual medical care (8).

In spite of the fact that in the SMS group the HbA1c reduction was significantly lower, the deviation was lower, too, and the therapy result became more stable than in the control group (Fig. 1).

The box plot giving median, quartiles and outliers can be seen in Figure 1.

Table 3 includes deviation values of the glycated hemoglobin difference (HBADIFF).

The initial and final values of glycated hemoglobin were also examined (HBADIFF). Significant difference was found ($p = 0.047$) between the initial and the final values of glycated hemoglobin levels.

The measured blood glucose level did not show (BLODGLUDIFF) significant results ($p = 0.856$). There was no difference between the results found in the case of male and female patients. Table 4 summarizes the initial and final glycated hemoglobin values.

Improving adherence especially in patients with chronic diseases is a great challenge for the healthcare professional. Normoglycemia is the key to achieve in patients with type 2 diabetes reduction of complications and co-morbidity. The benefit of the control of glycemic parameters is evident (9, 10). While glycated hemoglobin and medical adherence are associated (11), the healthcare professionals have to find a way to solve the problem of non-adherence for the successful long-duration therapy. Web and phone based technology designed by experts can be the solution and a theme for adherence-improving researchers (12-16), because it was found that patients taking part in the message reminder program have a much higher adherence concerning their medication, than those patients who do not take part in the message reminder program (17, 18). In spite of that, this study did not confirm the benefit of reminder messages; further research is needed with larger number of patients and performed for a longer term.

DISCUSSION AND CONCLUSION

Reduction of HbA1c could be achieved after 1 year in both groups and this was the goal. The reason for this result was that the patients were active participants in their treatment.

The task of pharmacists and pharmaceutical care is to find the proper way to cooperate more closely with patients concerning education, therapy monitoring control, adverse effects and adherence to achieve a successful medical therapy. This study shows that with proper attention the healthcare professionals can influence the patients' healthcare out-

comes when the patients are ready to cooperate with them.

In Hungary, the codified pharmaceutical care provides the patients who have chronic diseases the opportunity to learn about their disease, medication, measuring and controlling their blood glucose and lipid levels and getting answers for their questions. Practice implications of the above study is that the applied therapy reminder message was effective in a way that the deviations of the key parameters (glucose level and glycated hemoglobin) were lower in the test group compared to the control group, although their absolute values did not change significantly. The latter indicates that the cost-effectiveness ratio of the method is not sufficient enough in the case of patients showing acceptable therapeutic adherence. Based on the results, a decision making support module should be implemented to the existing medical information system to improve the therapeutic adherence of wide range of patients.

REFERENCES

1. Sabaté E.: Adherence to Long-term Therapies. Evidence for Action. World Health Organization, Geneva 2003.
2. Simpson S.H., Eurich D.T., Majumdar S.R., Padwal R.S., Tsuyuki R.T. et al.: BMJ 333, 15 (2006).
3. Roebuck M.C., Liberman J.N., Gemmill-Toyama M., Brennan T.A.: Health Aff. (Millwood) 30, 91 (2011).
4. Hankó B., Kázmér M., Kumli P., Hrágyel Z., Samu A. et al.: Pharm. World Sci. 2, 58 (2007).
5. Doró P., Benkő R., Kosik E., Matuz M., Tóth K., Soós G.: Eur. J. Clin. Pharmacol. 61, 893 (2005).
6. Syed I.A., Khan W.A.: J. Pak. Med. Assoc. 61, 690 (2011).
7. Rozenfeld Y., Hunt J.S., Plauschinat C., Wong K.S.: Am. J. Manag. Care 14, 71 (2008).
8. de Jongh T., Gurol-Urganci I., Vodopivec-Jamsek V., Car J., Atun R.: Cochrane Database Syst. Rev. 12, CD007459 (2012).
9. Ohkubo Y., Kishikawa H., Araki E., Miyata T., Isami S. et al.: Diabetes Res. Clin. Pract. 28, 103 (1995).
10. The Diabetes Control, Complications Trial Research Group: N. Engl. J. Med. 329, 977 (1993).
11. Krapek K., King K., Warren S.S., George K.G., Caputo D.A. et al.: Ann. Pharmacother. 38, 1357 (2004).
12. Nundy S., Dick J.J., Solomon M.C., Peek M.E.: Patient Educ. Couns. 90, 125 (2013).
13. Yoon K.H., Kim H.S.: Diabetes Res. Clin. Pract. 79, 256 (2008).
14. Hussein W.I., Hasan K., Jaradat A.A.: Diabetes Res. Clin. Pract. 94, e24 (2011).
15. Vervloet M., van Dijk L., Santen-Reestman J., van Vlijmen B., van Wingerden P. et al.: Int. J. Med. Inform. 81, 594 (2012).
16. Vodopivec-Jamsek V., de Jongh T., Gurol-Urganci I., Atun R., Car J.: Cochrane Database Syst. Rev. 12, CD007457 (2012).
17. Foreman K.F., Stockl K.M., Le L.B., Fisk E., Shah S.M. et al.: Clin. Ther. 34, 1084 (2012).
18. Vervloet M., Linn A.J., van Weert J.C., de Bakker D.H., Bouvy M.L., van Dijk L.J.: Am. Med. Inform. Assoc. 19, 696 (2012).

Received: 7. 08. 2014