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Adherence to oral anticoagulation therapy

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ABSTRACT

Introduction: Warfarin is the most frequently prescribed anticoagulant. Clinical treatment is demanding because of the narrow therapeutic range and considerable differences between the patients. The aim of this survey is to establish adherence to warfarin in subjects who have been prescribed warfarin as a long-term therapy.

Methods: The survey included 30 subjects, and was conducted at local pharmacy store. Statistical processing was carried out using the SPSS (ver. 21.) software. Used for qualitative variables was the Chi-square test, and for quantitative ones the ANOVA test. Data were provided in the form of tables and charts. Level of significance was p=0.05.

Results: The survey included 30 subjects, 14 men and 16 women. Of the total number of polled subjects, 15 were informed by a health care professional about the specificities of warfarin use, 7 said they were not informed, while 8 said they did not know. Most compliant in terms of regularly taking their medicines were pensioners, followed by the unemployed, χ^2=13.231; p<0.05. The number of subjects within the expected therapeutic INR range was 22 (p<0.05).

Conclusion: Strict compliance with the warfarin regimen is important in order to increase its effectiveness, extend the time and strengthen the intensity of anticoagulant action in the body. That is why the target groups of patients, who use warfarin, need additional information before and during therapy, in order to avoid side effects, and at the same time maintain therapeutic efficacy of the medicine throughout the treatment.

Keywords: adherence; compliance; anticoagulation therapy

INTRODUCTION

Warfarin is the most frequently prescribed anticoagulant; it is prescribed to more than 2 million new patients every year. Warfarin is often used as a permanent therapy for prevention of embolism in patients with atrial fibrillation, heart valve disease, and for primary and secondary prevention of venous thromboembolism (1). Warfarin is also used to prevent thromboembolic attacks in patients with acute myocardial infarction and angina pectoris, in patients with biological heart valves, and after certain orthopedic surgeries. Clinical treatment is demanding because of the

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narrow therapeutic range and considerable differences between the patients. In the absence of data obtained by genetic research or clinical information to predict the necessary dose of warfarin for each individual patient (2), initial prescribed doses may be too low, which increases the risk of thrombosis, or too high, which leads to the risk of excessive anticoagulation and heavy bleeding. In the United States, there are annually up to 800 adverse events related to the use of warfarin that are encompassed by the reporting rule (3). The risk of serious warfarin-related side-effects, its narrow therapeutic range and large inter-individual dosing differences require a preparation of algorithms in order to be able to predict, as closely as possible, the dose necessary at the initial stage(s) of treatment. Because proper administration of therapy remains a clinically significant problem despite years of research (4), a new assessment of basic issues, such as the terms used in the field, may be necessary to be able to identify innovative strategies of clinical interventions and investigations (5). Adherence is defined as: "the extent to which patients follow the instructions they are given for prescribed treatments" (6). Adherence to warfarin treatment, as well to that of other medicines (7), is essential for a good health condition of elderly patients and is thus a critical health care component. Non-compliance with the recommendations for the therapy at old age has been proven to increase the likelihood of therapeutic failure (8) and is responsible for unnecessary complications leading to increased health protection costs, early functional disability and premature death (9). Poor adherence to therapy was reported in all age groups. However, a larger prevalence of cognitive and functional disorders in elderly persons increases the risk of poor adherence. Multiple concomitant diseases and a complex medical treatment may further compromise warfarin adherence. Age-related changes in pharmacokinetics and pharmacodynamics render this population even more sensitive to the problems caused by poor adherence to therapy (10).

The aim of the study was to determine the adherence to warfarin in patient's whom warfarin is a long-term therapy and to evaluate the factors that directly or indirectly reduce or increase the level of adherence.

METHODS

The survey included 30 subjects, who were undergoing an anticoagulant therapy. The survey was conducted at local pharmacy store in Sarajevo in 2013. The main inclusion criterion was continuous warfarin therapy through at least 12 months. Within the group of subjects who met inclusion criteria, 30 patients were randomly chosen. The subjects were polled, and the answers received were statistically processed. Modified Morisky questionnaire on chronic therapy adherence has been used. Subjects have had 4 measurements of INR values during the therapy course.

Statistical analysis

Statistical processing was carried out using the SPSS (ver. 21.) software. Used for qualitative variables was the Chi-square test, and for quantitative ones the ANOVA test. Data were provided in the form of tables and charts. Level of significance was p=0.05.

RESULTS

The survey included 30 subjects, 14 men and 16 women. An analysis of average age of the subjects, by applying the ANOVA test, did not find a statistically significant difference (Table 1). The average age of male subjects was 55.14±16.96 years, and that of female subjects 54.43±15.48 years, F=0.014; p=0.906.

An analysis of marital status of the subjects included in the survey found that the majority of the subjects were married (n=22), while three subjects from each group have never been married or have the status of a widow(er). One of the subjects was divorced (Figure 1).

Figure 2 shows INR values during measurement. Established with the use of the Chi-square test, there was a statistically significant difference in the frequency of findings within the expected therapeutic range ($p<0.05$). On first measurement, in 12 subjects the INR values were within the expected therapeutic range, on the second measurement 14, on the third measurement 17, and finally on the ultimate, fourth, measurement the number of subjects whose results were within the expected INR therapeutic range was 22.

TABLE 1. Age and gender of subjects

	N	Mean	SD	Std. Error	95% confidence interval for mean		Minimum	Maximum
					Lower bound	Upper bound		
Male	14	55.14	16.96	4.53	45.3473	64.9384	23.00	75.00
Female	16	54.43	15.48	3.87	46.1848	62.6902	30.00	75.00
Total	30	54.76	15.91	2.90	48.8247	60.7086	23.00	75.00

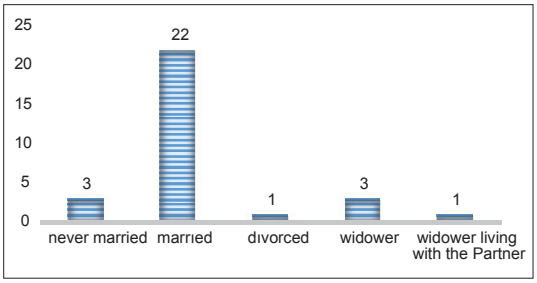

FIGURE 1. Marital status of subjects.

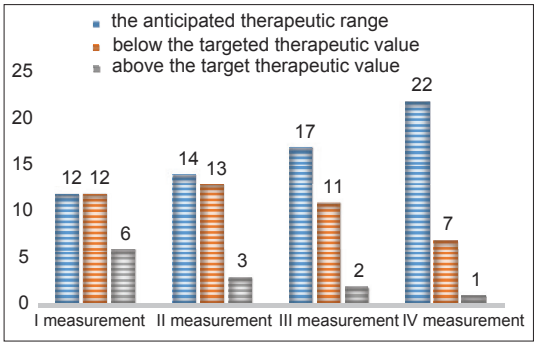

FIGURE 2. INR values during measurement period.

Of the total number of polled subjects, 15 were informed by a health care professional about the specificities of warfarin use, 7 said they were not informed, while 8 said they did not know (Table 2).

Answers to the question about the frequency of forgetting to take the medicine have produced statistically significant difference (Table 3). Most compliant in terms of regularly taking their medicines were pensioners, followed by the unemployed, χ^2=13.231; p<0.05.

Over the past two weeks, the frequency of forgetting to take medicine was the lowest in pensioners and the unemployed (Table 4), while those employed and students tend to forget to take their medicines more often, so there is a statistically significant difference

TABLE 2. Level of information concerning the specificities of warfarin use, provided by health care professional

		Frequency	Percent	Valid percent	Cumulative percent
Answer	Yes	15	50.0	50.0	50.0
	No	7	23.3	23.3	73.3
	Do not know	8	26.7	26.7	100.0
	Total	30	100.0	100.0	

in relation to the employment status, χ^2=14.948; p<0.05.

Based on the answers to the question on adherence, the subjects mostly said they did not forget to take medicines while traveling; also they never stop using medicines without prior consultation with the relevant doctor. When asked whether they feel under pressure because daily administration of medicines might be impractical, they mostly said they never felt that way, while 5 subjects said they sometimes do feel under pressure (Table 5).

DISCUSSION

Coumarine derivatives (warfarin and acenocoumarol) are vitamin K antagonists (VKA) and are used for long-term treatment of patients with venous thrombo-embolism (VTE). Warfarin therapy usually starts within 24-72 hours of the onset of parenteral heparin treatment. The usual initial dose is 5-10 mg, while lower doses are recommended to elderly patients, or those with lower body weight, or underweight patients. Warfarin doses and their monitoring have been adjusted to the INR (international normalized ratio) values (11). The survey polled 30 patients on warfarin. The average age of the subjects was 55. Most of the subjects were married. While measuring INR values during the treatment statistically significant difference in terms of the number of subjects with referent

TABLE 3. Frequency of forgetting to take medicine

	Employment status				Total
	Unemployed	Employed	Student	Pensioner	
I never forget to take medicine	9	5	0	11	25
I forget to take medicine once a week	2	2	0	0	4
I forget to take medicine 2 to 3 times a week	0	0	1	0	1
Total	11	7	1	11	30

TABLE 4. Frequency of forgetting to take medicine over the past two weeks

	Employment status				Total
	Unemployed	Employed	Student	Pensioner	
Not once	11	5	0	11	27
Once or twice	0	2	0	0	2
3 to 5 times	0	0	1	0	1
Total	11	7	1	11	30

values during 4 measurements was discovered. On first measurement, the figure was 12, and after the fourth measurement the number of subjects within the expected therapeutic INR range was 22 ($p<0.05$) (Chart 2). Randomized clinical studies during which the patients indicated for anticoagulant therapy were randomly prescribed warfarin or some other alternative anticoagulant were rather helpful by showing the risk of warfarin-related non-compliance (5,12), independently from the potentially confounding factors affecting the validity of observational studies. When it comes to patients who were prescribed warfarin or an alternative medicine, it is necessary to analyze additional factors affecting the treatment outcome due to non-compliance or improper drug administration (6,8). In such studies, regular INR testing was carried out mostly on randomized patients using warfarin. In these studies, both the side-effects and the monitoring may be factors affecting poor adherence (13). Some trials have shown that subjects using oral anticoagulants tend to discontinue their therapy more often, while some have shown no difference in terms of non-compliance with the prescribed therapy in relation to placebo (13). In the polled group, only 50% of the subjects were informed by a health care professional about the specificities of warfarin administration. The frequency of forgetting to take medicines was most often reported in those employed, while pensioners were most regular in taking their therapy. The subjects polled mostly said they did not forget to take warfarin even when they traveled. Of the total number of subjects (n=30), 28 said they never stopped taking warfarin without consulting a physician, despite good clinical picture of primary disease for which warfarin has been administered. Most of the subjects never feel pressure on account of the medicine administration regimen, while 5 subjects said they sometimes felt pressure, and 4 subjects feel pressure more often. Unemployed subjects are the ones who have most difficulties remembering to take warfarin. A study conducted in Japan analyzed warfarin adherence in subjects who took therapy for atrial fibrillation (14). Of the total number of subjects (n=330), as many as 52% did not know the therapeutic significance of warfarin. A questionnaire found that only 51% of the subjects had a basic preliminary knowledge of warfarin, atrial fibrillation and heart attack (14).

CONCLUSION

Strict compliance with the warfarin regimen is important in order to increase its effectiveness, extend the time and strengthen the intensity of anticoagulant action in the body. That is why the target groups of patients, who use warfarin, need additional information before and during therapy, and a quality interaction between the health care professional and the patient, in order to avoid side effects, and at the same time maintain therapeutic efficacy of the medicine throughout the treatment. Adherence to warfarin can be successfully monitored by determining the value of INR, however adherence itself is directly affected by patient's knowledge on warfarin's mode of action, patient's

TABLE 5. Answers to questions on compliance

	Employment status				Total
	Unemployed	Employed	Student	Pensioner	
When you travel, do you forget to take your medicines with you?					
I do not travel	5	4	1	6	16
Never	6	3	0	5	14
χ^2=1.197; p=0.754					
When you feel your health is under control, do you sometimes stop taking medicines on your own, without consulting a doctor?					
I never do it alone	11	6	0	11	28
I sometimes do it alone	0	1	0	0	1
I always do it alone	0	0	1	0	1
χ^2=11.727; p=0.068					
Taking medicines every day is impractical for many people. Do you feel under pressure because you need to follow recommendations for your treatment?					
I never feel that way	8	5	0	7	20
I sometimes feel that way	1	2	0	2	5
I often feel that way	2	0	0	2	4
I always feel that way	0	0	1	0	1
χ^2=12.006; p=0.213					
How often do you have difficulties remembering to take your medicine?					
Never	8	6	0	10	24
Sometimes	3	1	0	1	5
Often	0	0	1	0	1
χ^2=0.249; p=0.168					

daily and professional activities as well as form of the drug and therapy regimen.

COMPETING INTERESTS

Lana Lekić works as a medical representative for [1]Boehringer Ingelheim RCV GmbH&Co.KG. Alen Lekić works as a medical representative for Sanofi Aventis groupe.

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