

Portable coagulometer for vitamin K-antagonist monitoring: the patients' point of view

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Purpose: The aim of this study was to know the patients' point of view on the monitoring of vitamin K-antagonist (VKA) therapy by means of a point of care testing (POCT), ie, using a portable coagulometer by self-testing at home. At first, patients had prothrombin time (PT) international normalized ratio (INR) monitoring at a thrombosis center; afterward, they were shifted to self-testing at home. An interview was done to evaluate the patients' point of view on the two monitoring periods.

Patients and methods: A total of 92 oral anticoagulated patients were enrolled. The questionnaire contained nine questions that elicited a maximum of five closer answers that were arranged in increasing levels of satisfaction: very little, little, enough, much and completely. Percentage of time in therapeutic range (TTR) and adverse events were compared during the two periods of conventional monitoring and self-testing.

Results: The period of conventional monitoring was shorter than that of self-testing ($p < 0.0001$), and the median TTR was satisfactory but lower than that of self-testing ($p < 0.0001$). A total of 85% of the patients were satisfied with self-testing at home. In all, 83% and 73% ($p = 0.06$) of patients felt comfortable about side effects while measuring the PT INR at both home and the thrombosis center, respectively. During the self-testing period, quality of life was improved in 87% of the patients. The cost of test strips was medium-high for 89% of the patients, and 75% of them stated that it was worth improving their quality of life. A switch from VKA to a direct oral anticoagulant (DOAC) was proposed to 24% of the patients, but 68% of them declined because they felt more comfortable monitoring their oral anticoagulant therapy by POCT.

Conclusion: VKA monitoring using POCT at home may play a role in improving the patients' quality of life and may be considered as an alternative to the use of DOAC at least in certain settings of patients.

Keywords: oral anticoagulants, self-testing, quality of life

Introduction

Vitamin K-antagonists (VKAs) are widely used for both prophylaxis and treatment of thromboembolic conditions such as atrial fibrillation, mechanical heart prosthesis and venous thromboembolism.¹

The mechanism of action of VKA is to block the enzyme epoxide reductase that brings back the vitamin K epoxide to its reduced form, avoiding the carboxylation of the GLA-protein residues of the vitamin K-dependent coagulation factors.² The anti-coagulation activity induced by VKA is monitored by a blood test: the prothrombin time (PT) that is expressed as the international normalized ratio (INR).³ Dose adjustment of VKA is necessary to maintain the percentage of time spent in the therapeutic range (TTR), ~70% or more; it has been demonstrated that a TTR of <70% can lead to adverse thrombotic or hemorrhagic events.⁴ The conventional monitoring of VKA

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therapy presupposes that patients attend a thrombosis center for INR measurement and wait for receiving a new dosage scheme and their next scheduled appointment.

Point of care testing (POCT) devices are portable coagulometers and are now widely used to monitor VKA treatment by self-testing or self-management.⁵ POCT devices are easy to use as the INR value can be obtained using a drop of capillary blood by fingerpicking. This can substantially reduce the time needed for blood sampling and can also avoid the need for patients to attend a thrombosis center in person because monitoring can be performed at home.⁶ A recently published meta-analysis has shown that self-testing and self-management are as safe as the conventional monitoring of the VKA and both can reduce thromboembolic events.⁷ POCT devices need a periodic external quality control of their performance. This could be done by checking the monitor versus a reference laboratory coagulometer or using a set of the European Concerted Action on Anticoagulation (ECAA) INR-certified plasmas with five different ranges of anticoagulation.^{8,9}

At our thrombosis center, patients may have a conventional monitoring of the VKA therapy but, from 2004, POCT devices have been implemented and selected patients may be able to check their VKA treatment by self-testing.

The aim of this study was to know the patients' point of view on the monitoring of VKA therapy both at a thrombosis center and by self-testing at home.

Patients and methods

Patients

At our thrombosis center, 92 patients (46 females and 46 males, mean age 64 ± 17 years) were followed for VKA monitoring in self-testing at home. All the patients were on long-term VKA therapy: 26 were treated with warfarin and 66 with acenocoumarol. Indications for VKA therapy were as follows: congenital heart disease ($n=1$), atrial fibrillation ($n=20$), stroke ($n=1$), acute myocardial infarction ($n=3$), mechanical heart valve prostheses ($n=23$), mitral valvulopathy ($n=1$), mesenteric vein thrombosis ($n=3$), portal vein thrombosis ($n=1$), deep vein thrombosis with or without pulmonary embolism ($n=25$), antiphospholipid syndrome ($n=10$) and relapsing superficial vein thrombosis ($n=4$). The criteria for giving them a POCT included patients confined to home because of serious physical illness, advanced age, lack of time due to working schedule, patients who live far from the thrombosis center and children.

Of the 92 patients, 82 (39 females and 43 males, median age 67 years, 4–97 years) had spent a period of time of at least 6 months at the thrombosis center. The other 10 patients

were shifted to self-testing earlier because of lack of time due to their working schedules.

The patient or his/her relative was instructed in the use of the POCT in one or more training days. The portable coagulometer was given to the patient only if he/she demonstrated a good ability in the use of the device. If a patient or his/her relative was judged unable to properly perform the procedure, a new training session was scheduled. The patients performing self-testing can rely on a bidirectional connection with the thrombosis center. They can send their clinical data and the INR value, obtained by the POCT, by filling in a preset electronic datasheet, which contained some questions about dose assumption, pharmacological variations, possible hemorrhagic or thrombotic events, surgery and diet behavior. The patients also had the possibility of sending personal comments about the reported events to doctors of the thrombosis center, and they received at home the electronic sheet with the adjusted dose regimen and the next appointment. All the patients gave their written informed consent to participate in the study. The ethics committee of the Azienda Ospedaliero-Universitaria of Cagliari had been consulted. The members considered their formal approval not necessary as the patients were regularly followed at our thrombosis center and the submitted questions were related to the monitoring of their oral anticoagulant therapy in order to evaluate the advantages and disadvantages.

In those patients who were monitored at the thrombosis center for at least 6 months and then were shifted to self-testing, we compared the TTR and the adverse events that occurred in the two periods. In other words, we conducted a pre-post study in which patients were controlling themselves.

Methods

A questionnaire was administered to each patient as an interview in a period of 15 days, by a doctor (DM) not belonging to the thrombosis center and therefore unknown to the patients.

The questionnaire contained nine questions that elicited a maximum of five closer answers that were arranged in increasing levels of satisfaction: very little, little, enough, much and completely. The questionnaire was organized in five domains: 1) patients' satisfaction (questions 1 and 2) investigated about VKA monitoring at the thrombosis center and by self-testing; 2) patients' psychological impact (questions 3 and 4) evaluated side effects of VKA therapy during the two periods of monitoring; 3) patients' limitations with treatment (question 5) investigated on patients' opinion about test strips' cost; 4) patients' quality of life (questions 6 and 7) explored a possible improvement of patients' quality

of life during the self-testing period and 5) patients' preferences (questions 8 and 9) analyzed what they believed in changing VKA with a direct oral anticoagulant (DOAC).

The quality control of the POCT assigned to each patient was performed, every 6 months, in two ways. First, all PT INRs were calculated with both an automated coagulometer (ACL Futura; Werfen, Barcelona, Spain) located in our thrombosis center using a recombinant human thromboplastin (Recombi-PlasTin; Werfen; International Sensitivity Index (ISI)=0.82) and a device (CoaguChek XS; Roche Diagnostics, Basel, Switzerland) using strips containing a human thromboplastin (ISI=1). A difference of ± 0.5 INR units between the two systems was considered clinically acceptable.^{8,10} It is worth to note that the automated coagulometer in our thrombosis center is periodically submitted to internal and external quality assessments, the latter organized twice a year by the Italian Federation of Centres for the diagnosis of thrombosis and the Surveillance of Antithrombotic drugs (FCSA).

Second, all the devices were tested using different sets of the same batch of five quality control plasmas, each with a different range of certified INRs.⁸

The TTR was calculated using the Rosendaal method; it was determined during the period of conventional monitoring and self-testing at home.¹¹ This method allows to obtain an INR-specific person-time that is calculated with the assumption of a linear increase or decrease between two consecutive INR determinations in a specific follow-up interval. Thrombotic and hemorrhagic episodes were carefully

recorded in the computerized program for the management of oral anticoagulated patients (TAOnet; EDP Progetti, Bolzano, Italy). Hemorrhages were classified according to the International Society on Thrombosis and Haemostasis (ISTH) subcommittee on control of anticoagulation.¹²

Data are expressed as mean and standard deviation if they had a Gaussian distribution, otherwise we used median and range.

To compare the patients' answers to the questionnaire and the thrombotic or hemorrhagic episodes in the two periods of VKA monitoring, the chi-square test for trend and the Fisher's exact test were carried out. The Wilcoxon matched pairs test was used to compare the TTR during the conventional monitoring and self-testing periods.

Results

The administered questionnaire and patients' answers are given in Figure 1.

Patients' satisfaction

A total of 85% and 36% ($p < 0.001$) of the patients stated that they were much or completely satisfied of the PT INR monitoring by means of the portable coagulometer and attending the thrombosis center, respectively. In all, 61% of the patients stated that they were very little, little or enough satisfied of the conventional monitoring, whereas only 8% of them chose one of these three categories of answers for the self-testing period ($p < 0.0001$).

	Very little	Little	Enough	Much	Completely	p-value
Q1. How satisfied are you monitoring the vitamin K-antagonist (VKA) therapy in self-testing at home?	0 (0%)	0 (0%)	7 (8%)	25 (27%)	60 (65%)	<0.0001
Q2. How satisfied are you monitoring the VKA therapy at the thrombosis center?	7 (8%)	23 (25%)	26 (28%)	22 (24%)	14 (15%)	<0.005
Q3. Do you feel more comfortable about side effects of your therapy having the point of care testing (POCT) available for measuring the prothrombin time (PT)?	0 (0%)	0 (0%)	9 (10%)	32 (35%)	51 (55%)	<0.0001
Q4. How calm did you feel about possible side effects of your VKA therapy by doing the PT at the thrombosis center?	2 (2%)	0 (0%)	17 (19%)	35 (38%)	38 (41%)	<0.0001
	Low	Average	High			
Q5. How do you evaluate the cost of the test strips to perform the PT?	3 (3%)	43 (47%)	46 (50%)			<0.0001
	Very little	Little	Enough	Much	Completely	
Q6. Has self-testing at home improved your quality of life?	0 (0%)	1 (1%)	16 (17%)	39 (42%)	36 (39%)	0.0001
Q7. Is the cost of the test strips worth improving your quality of life?	0 (0%)	2 (2%)	0 (0%)	75 (82%)	0 (0%)	<0.0001
	Yes	No				
Q8. Did some doctors propose to change VKA with a direct oral anticoagulant (DOAC)?	22 (24%)	70 (76%)				<0.0001
Q9. Why you did not accept to assume DOAC?	Free answer					

Figure 1 Questionnaire administered to the patients in self-testing at home.

Patients' psychological impact

A total of 83% and 73% ($p=0.06$) of the patients declared that they felt comfortable about possible side effects of VKA therapy while measuring their PT INR at home and at the thrombosis center, respectively. Moreover, 10% and 19% of the patients felt enough comfortable during the self-testing period and the conventional monitoring period, respectively ($p=0.047$). Only 2% of the patients felt very little comfortable about side effects at the thrombosis center.

Patients' limitation with treatment

In all, 89% of the patients declared that the cost of the test strips was medium–high.

Patients' quality of life

During the self-testing period, quality of life was considered much or completely improved by 87% of the patients, and 75% of them stated that test strips costs were worth improving their quality of life.

Patients' preference

A switch from VKA to DOAC was proposed to 24% of the patients; however, 68% of them declined because they felt more comfortable monitoring their oral anticoagulant therapy by PT INR.

When we considered the group of patients who were followed at the thrombosis center for a period of at least 6 months and then were shifted to self-testing, the results showed that the median time of conventional monitoring was shorter than that of self-testing at home (45 months, 6–158 vs 131 months, 6–135; $p<0.0001$). The median TTR at the thrombosis center was satisfactory but lower than that while self-testing (71%, 24%–89% vs 77%, 40%–100%; $p<0.0001$). There were no statistically significant differences in terms of thrombotic and hemorrhagic episodes during the two periods of VKA monitoring (Table 1). Only one patient experienced a minor bleeding episode on both conventional and self-testing periods.

Table 1 Thrombotic and hemorrhagic episodes during both conventional monitoring and self-testing at home

Adverse events	Thrombosis center	Self-testing	<i>p</i> -value
Minor bleeding	3	8	0.13
Major bleeding	0	3	0.24
Venous thrombosis	1	3	0.62
Arterial thrombosis	0	3	0.24

Discussion

Patients who used self-testing were more satisfied than when they did the PT INR at our thrombosis center; in fact, most of them said that they had a significant improvement in quality of life. Patients can carry out the PT INR at home or away from their home and send the result to the thrombosis center via Web and receive the therapy sheet in the same way.¹³ Therefore, if, on the one hand, they can avoid long waits for blood sampling and PT INR results, on the other hand, they are always supported by the doctors of the thrombosis center for the adjustment of the VKA dosage both under normal conditions and in emergency situations. Having the portable coagulometer available for PT INR measurement at home is a source of serenity for patients; in fact, most of them declared that they were less worried about the possible side effects of VKA therapy. In other words, patients having self-testing at home can measure the PT INR with the portable coagulometer even when they do not have an appointment at the thrombosis center if they feel that some factors may have interfered with VKA treatment or even just for their personal tranquility. Similar results in terms of satisfaction with self-testing were obtained by Jones et al¹⁴ who administered a questionnaire to 35 children and 55 parents who reported significant improvement in quality of life of their child and families' function. Our study supports the benefits of self-testing in adults too. Patients' psychological impact did not differ between the two monitoring periods, probably because the management of their anticoagulant therapy was always handled by the same doctors.

In Italy, the average cost of each test strip to measure the PT INR, if purchased at the pharmacy, is 6 euros, and it is considered by most patients as a medium–high cost. The Italian National Health System reimburses neither the costs for the purchase of the portable coagulometer, ranging from 650 to 750 euros, nor the costs of the test strips, as happens in other chronic diseases, such as diabetes mellitus. However, a study published in UK, which performed a systematic cost analysis for 10 years, showed that both self-testing and self-management are cost-effective.¹⁵ From a practical point of view, if it is true that the self-testing system is expensive, it is also true that patients do not consider what they spare, ie, time and costs for attending the thrombosis center, time consuming and waste of working days for their relatives.

An important point raised by the questionnaire is related to the decline of the majority of patients to be switched to DOAC, which offers the possibility to avoid a periodic laboratory monitoring.^{16,17} However, DOACs are not suitable for

all patients.¹⁸ These new oral anticoagulants have demonstrated to be either non-inferior or superior to warfarin in the registrative randomized clinical trials; they have shown to reduce cerebral hemorrhages but increase gastrointestinal bleeding.¹⁶ However, if VKA management is done at thrombosis centers, these advantages are less evident.¹⁹ Moreover, severe renal failure is a contraindication to their use. This may be crucial especially in elderly people. If we consider their daily costs (2 euros/day, at least in Italy) totally reimbursed by the National Health System, we think that self-testing could be cost-effective at a horizon of not more than 2 years.

TTR was higher and the adverse events were similar during the self-testing period, showing that self-testing is as effective and safe as the conventional monitoring. The highest number of thrombotic and hemorrhagic episodes recorded during the VKA monitoring by self-testing may be justified by the fact that patients were older than when they were monitored at the thrombosis center (67 years, 14–97 vs 55 years, 11–86; $p < 0.0001$), and obviously, they have had a longer period of monitoring in this way.

The first limitation of this study is the small number of patients considered. However, self-testing at home is not a widespread system for monitoring VKA, at least in Italy. To the best of our knowledge, this is the first study that has investigated the quality of life of patients followed in such a way. Second, we did not use a validated questionnaire to investigate, in general, the quality of life because we preferred to use a series of questions dedicated to a specific and particular topic such as the self-testing monitoring of oral anticoagulation. Third, we did not consider other possible side effects of VKA, such as arterial stiffness.²⁰

Conclusion

These results support patient preference for self-testing compared to conventional monitoring of VKA therapy and show excellent adherence to therapy. VKA monitoring using POCT at home may have a role in improving the patients' quality of life and may be considered as an alternative to the use of DOAC at least in certain settings of patients. We hope that our findings could be useful for offering different antithrombotic tools to as many patients as possible.

Author contributions

All the authors were involved in study design, data acquisition and data analysis/interpretation; took part in drafting the article or revising it critically for important intellectual content; and reviewed the final version and gave approval for submission.

Disclosure

The authors report no conflicts of interest in this work.

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