Patient education and oral anticoagulant therapy

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Background and Objectives. The stability of oral anticoagulant therapy is affected by an irregular intake of vegetables, interactions with other drugs, intercurrent disease, and compliance. With the aim of investigating whether educating patients could affect anticoagulation stability, we prepared a questionnaire on the basis of some fundamental information given by us to our patients during their first attendance to our clinic. Moreover we sought to determine whether administering the questionnaire would be useful in improving the anticoagulation stability of patients whose anticoagulation was poorly controlled.

Design and Methods. The questionnaire was administered to a group of 219 anticoagulated patients attending our Thrombosis Center. All patients were invited to fill in the questionnaire, which was handed out by a nurse, while they were waiting for their blood sampling results. None of the patients refused to fill in the questionnaire, which was completed at once and independently. The answers to the questionnaire were correlated with the time spent by the patients in the therapeutic range.

Results. A significant difference was found between the time spent in the therapeutic range by patients who declared a regular intake of their therapy (91%, 14-100%) and that spent in the range by those who answered they sometimes forgot to take it (75%, 9-100%). The percentage of time spent in the therapeutic range was significantly longer (92%, 36%-100%) in patients who reported regular vegetable intake and in those that never ate vegetables than that observed in patients who admitted occasional intake of vegetables (86%, 5%-100%). In the group of patients below 65 years of age, a significant difference in the time spent in the therapeutic range was observed in the case of regular assumption of oral anticoagulant drugs (95% vs 68%, $p<0.01$) and in that of regular daily vegetable intake (95% vs 86%, $p=0.03$). The difference in time spent in the range between patients who knew why they were taking the oral anticoagulant and those who did not was statistically significant only in the older group (89% vs 76%, $p=0.04$). In women, the time spent in the therapeutic range depended on regular vegetable intake (92% vs 74%, $p=0.02$), assumption of other drugs (91% vs 72%, $p=0.02$), and intercurrent disease (92% vs 76%, $p=0.04$). In men a significant difference was observed in favor of those who knew why they were taking oral anticoagulants (93% vs 83%, $p<0.01$). Logistic regression analysis showed that the risk of being below the chosen cut-off of the time in range (90%) was 6.0 (C.I. 95%: 2.2-16.3) in those patients who sometimes forgot their daily dose even though they knew why they were taking the oral anticoagulant. Moreover, the risk of being below the cut-off was 3.0 (C.I. 95%: 1.3-6.5) in those who never forgot to take their therapy, but did not know the reason why they were taking oral anticoagulants. Finally we observed a significant improvement in the time spent in the range by patients with poor anticoagulation control when we included the three months before and after the questionnaire in our analysis.

Interpretation and Conclusions. In conclusion we believe: 1) that greater emphasis should be given to educational courses for anticoagulated patients especially in consideration of age and gender differences; and 2) on its own, administration of the questionnaire leads to a significant improvement in the time spent by patients in the therapeutic range.
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Oral anticoagulants are recommended in the prevention of thromboembolic events, and in the past ten years indications for their use have increased dramatically.[1]

To maintain anticoagulated patients in their therapeutic range, regular monitoring of the prothrombin time (PT), expressed as the international normalized ratio (INR), and related dosage changes are necessary.[2] In fact the risk of hemorrhage or recurrent thrombotic episodes is increased by marked fluctuations in the level of anticoagulation. However, periodic checks of the PT and contextual therapy adjustments are not enough to avoid anticoagulation instability, since various factors, such as intercurrent disease, interactions with other drugs,[3] irregular vegetable intake,[4,5] seasonal variations,[6] and the doctor's experience in handling oral anticoagulants,[7] may affect anticoagulation therapy.

Although oral anticoagulant therapy does not limit the life-style of the patients,[8] poor compli-

ance is another important factor that may be responsible for bad anticoagulation control,[9,10] given that many patients require long-term therapy and their collaboration is fundamental. In general, when patients are on chronic therapy, they omit about 40% of their daily medications,[11] and 10 to 26% of those on chronic oral anticoagulant treatment are not compliant.[12]

At the beginning of oral anticoagulant therapy doctors should give their patients a short educational course on how to manage the therapy correctly. In particular, in our Thrombosis Center this course covers the indications, risks and benefits of oral anticoagulants, modality of administration, dietary behavior, and importance of the influence of other drugs and intercurrent diseases.

To our knowledge the influence of patients' education on oral anticoagulant stability has never been dealt with in a scientific paper before. With the aim of investigating whether a patients' education may potentially affect anticoagulation stability, we prepared a questionnaire based on the information given to our patients during their first clinic attendance. We then administered the questionnaire to a group of 219 consecutive anticoagulated patients attending our Thrombosis Center. In particular, we concentrated mainly on the patients' understanding of the reason why they were taking oral anticoagulants, on the mechanism of the therapy through its regular assumption, and the possible improvement of anticoagulation stability after the questionnaire. The questionnaire also covered aspects of dietary behavior, intercurrent diseases that did not require hospitalization, and assumption of other drugs.

Design and Methods

Patients

We enrolled 219 consecutive patients (108 males, 111 females, mean age 60±12 years), attending our Thrombosis Center, who had started oral anticoagulant treatment six months earlier. The questionnaire, which was handed out by a nurse, was completed by the patients at once and independently, while they were waiting for their blood sampling results. With the aim of evaluating whether there was a difference between signed and anonymously filled in questionnaires, on one of four consecutive days of questionnaire administration the patients were asked to answer the questionnaire anonymously. Therefore, we obtained two subgroups of patients: 54 anonymous patients (27 m, 27 f, mean age 60±13 years), and another 165 patients (81 m, 84 f, mean age 60±12 years) who signed the ques-

tionnaire. One hundred and sixteen of the latter subgroup were being treated with acenocoumarol, while the remaining 49 were being treated with warfarin. The diagnoses of the latter group of patients were as follows: deep vein thrombosis and/or pulmonary embolism (n=60), atrial fibrillation (n=67), biological valve prosthesis (n=10), mechanical valve prosthesis (n=13), stroke (n=5), acute myocardial infarction (n=8), and cardiomyopathy (n=2). Since the questionnaire did not contain general questions about diagnosis but only about age and gender, we obviously lack the indications for therapy in those patients who filled in the questionnaire anonymously.

Methods

At the beginning of the study we administered a pilot questionnaire to a group of 16 anticoagulated patients (8 m, 8 f, mean age 61 ± 12 years) in order to evaluate how well they understood the questions. This allowed to obtain a final version which was then validated. All 16 patients were excluded from the group of 219 patients of the study. The main issues touched upon by the final questionnaire were the following: regular assumption of therapy (A, B), vegetable intake (C), intercurrent disease (D), interactions with other drugs (E), and patients' understanding of why they were taking oral anticoagulants (F) (Table 1). The questionnaire contained six main questions that elicited a maximum of eight closed answers, which were arranged in increasing levels of irregular intake. This method is generally used when a questionnaire analyses negative behavior, as the patients must be able to select a less serious level of negative behavior, as expressed in our questionnaire with the answer options: *never, exceptionally, sometimes, once a week, a few times a week, many times a week, almost every day, and every day*.[13,14] On that basis and in order to simplify data reading, the answers to questions A to C were processed into two classes: namely never and sometimes. Moreover, in question B, in which the patients were asked if they ever took the therapy late, we only evaluated the answers of those who said they had never forgotten to take their therapy. This was because the aim of this question was to assess the sole effect of the therapy taken late, without the interference of other variables. The answers *never* and *always* to question C were included in the same class, i.e. *never*, because both cases resulted in a regular daily vitamin K intake. Finally, questions D and E elicited two answers: *yes* and *no*, while question F elicited six answers, which were divid-

Table 1. Questionnaire administered to the group of 219 patients on oral anticoagulant (O.A.) therapy.

A) During your O.A. treatment, how many times did you forget to take the O.A. drug?
Never, exceptionally, sometimes, once a week, a few times a week, many times a week, almost every day, every day.

B) During your O.A. treatment, how many times did you take the O.A. drug later?
Never, exceptionally, sometimes, once a week, a few times a week, many times a week, almost every day, every day.

C) How often do you eat vegetables?
Every day, almost every day, a few times a week, once a week, rarely, never.

D) Have you ever been ill in the past month?
       yes   *no*

E) Have you taken any drugs in the past month?
       yes   *no*

F) Why are you taking O.A. therapy?
To prevent a new thrombotic episode, to prevent an embolic episode, to improve the valve function, to improve blood circulation, to improve memory and concentration.

ed into two classes: i.e. *right* and *wrong*. The data were analyzed in their entirety, and in relation to age (<65 and >65 years) and gender.

PTs were measured by an automatic coagulometer (ACL Futura, Milan, Italy) with a commercial thromboplastin (Thromboplastin, Milan, Italy) with an ISI of 1.08. The criteria employed in our Thrombosis Center for dose-adjustment have been published elsewhere.[15]

Statistical analysis

Since the distribution was non-parametric, the data were expressed as median and range. The percentage time spent in the therapeutic range was calculated using the INR Day Program by Rosendaal.[16] To show a statistically significant association between the two different classes of answers to the questionnaire and the percentage time spent in the therapeutic range, the Mann-Whitney U test was carried out. To compare the time spent in the therapeutic range before and after the questionnaire, the Wilcoxon matched pairs test was used. Finally logistic regression was employed to evaluate the interactions among the variables considered in the univariate analysis (Mann-Whitney test). To this purpose the variable *percentage of time spent in the therapeutic range* was divided into >90% and <90%. We chose this cut-off because we noticed that the time spent in the therapeutic range by some of our patients was very long (100%), while in others it was much shorter, though they attended the Center regularly and were themselves surprised that their levels fluctuated. The cut-off was also

chosen to point out the differences between the two sub-groups and because we considered that the fluctuations might have been due to the fact that the patients might have misinterpreted parts of the starting recommendations.

Results

The results showed that there was no difference between anonymously filled in and signed questionnaires. The average time spent in the therapeutic range was significantly different in those patients who answered *never* vs those who answered *sometimes* to question A while it was not significantly correlated to different responses to question B. In the patients who answered *never* to question C, the percentage time spent in the therapeutic range was significantly longer than the time spent by the patients who answered *sometimes.* Responses to questions D and E did not lead to statistically significant results. Question F elicited a trend towards statistical significance between patients who answered *right* and those who answered *wrong* (Table 2). Logistic regression analysis showed that the risk of being below the chosen cut-off (90%) was 6.0 (C.I. 95% 2.2-16.3) for those patients who answered *sometimes* to question A, though they knew why they were taking the oral anticoagulants. Moreover, the risk of being below the cut-off was 3.0 (C.I. 95% 1.3-6.5) for the patients who answered *never* to question A, but did not know the reason why they were taking the oral anticoagulants. The risk was 1.86 (C.I. 95% 0.96-3.6) for patients who had an irregular vegetable intake. Finally we observed a significant improvement in the time spent in the therapeutic range by patients with poor anticoagulation control when we considered the three months before and after the questionnaire, while patients with good anticoagulation control showed a slight, statistically significant, decrease in their therapy stability, which had no clinical significance (Table 3).

Age differences

In the group of patients below 65 years of age, a significant difference in the time spent in the therapeutic range was observed in patients who took their oral anticoagulant drugs regularly (95% vs 68%, $p<0.01$) and in those who had a regular daily vegetable intake (95% vs 86%, $p= 0.03$). In the older group these differences were not significant and the medians observed were very similar. The difference between patients who knew why they were taking oral anticoagulants and those who did not was only statistically significant in the older group (89% vs 76%, $p= 0.04$).

Gender differences

In women, the time spent in the therapeutic range depended on regular vegetable intake (92% vs 74%, *p* =0.02), assumption of other drugs (91% vs 72%, *p*= 0.02), and intercurrent disease (92% vs 76%, *p*=0.04). In men, non-significant differences were observed for all questions, except for those asking why they were taking oral anticoagulants (93% vs 83%, *p*<0.01), while in the women this difference did not reach statistical significance.

Discussion

The lack of statistical difference between the signed and anonymously filled in questionnaires showed that the results were not affected by signing. Forty patients (40/165, 24%) who stated that they missed a daily dose, though only sometimes, spent less time in the therapeutic range than those who stated they never did. This could be because they did not perfectly understand the need to take the therapy every single day. The average time spent in the therapeutic range of patients (75/125, 60%) who took their therapy late, i.e. a few hours after the recommended time (5-6 PM), was similar to that in patients who always took their therapy on time. This suggests that to improve adherence to the therapy, the patients should be given the opportunity of taking oral anticoagulants at the time they prefer, and that a time recommendation is unnecessary. Patients with an irregular daily vegetable intake (95/165, 57%) spent a significantly shorter time in the therapeutic range, suggesting that the doctor at the Center should know the patient's dietary behavior through a questionnaire on food intake and thus be able to tailor his advice about the patient's daily food intake.

Concerning the question about intercurrent diseases and assumption of other drugs, there was no difference between the two subgroups of answers. This was an expected result since we only considered illnesses that did not require the patient's admission and analgesic drugs currently recommended for pain relief in anticoagulated patients. A trend towards a statistically significant difference was observed in the time spent in the therapeutic range by patients who knew why they were taking their therapy and those who did not, but in logistic regression it emerged that this was an important factor that could affect anticoagulation stability. In fact the risk of being below the chosen cut-off (90%) for the time spent in the range was 3 in the patients who never forgot to take the therapy but did not know why they were taking it. This suggests that these patients should be given a new dedicated course with clear and easy explanations about the indications for and safety of the therapy, especially as primary prevention of thromboembolic events.

The results were different depending on whether we considered the patients divided by gender or the group as a whole. In the women, some variables, such as intercurrent disease, the assumption

Table 2. Time spent in the therapeutic range by the patients who answered questions A, B, C, D, E, and F.

	never n	sometimes n	time in range (never)	time in range (sometimes)	p
A	125	40	91%, 14-100%	75%, 9-100%	<0.01
B	50	75	92%, 14-100%	90%, 27-100%	0.29
C	70	95	92%, 36-100%	86%, 9-100%	0.04

Question A: During your O.A. period, how many times did you forget to take O.A.T. ?
Question B: During your O.A. treatment, how many times did you take O.A. later ?
Question C: How often do you eat vegetables ?

	yes (n)	no (n)	time in range (yes)	time in range (no)	p
D	124	41	90%, 14-100%	79%, 9-100%	0.16
E	114	51	90%, 14-100%	84%, 9-100%	0.11

Question D: Have you ever been ill in the past month?
Question E: Have you taken any drugs in the past month?

	right (n)	time in range	wrong (n)	time in range	p
F	113	90%, 9-100%	52	84%, 14-100%	0.05

Question F: Why are you taking O.A.T.?

Table 3. Time spent in the therapeutic range three months before and after the questionnaire.

	n	before	after	p
<70%	34	55%, 9-69%	67.5%, 27-100%	0.0004
>70%	83	95%, 71-100%	91%, 56-100%	0.038

of other recommended drugs, and an irregular intake of vegetables, affected the time spent in the therapeutic range. Since women are more affected by pain due to arthrosis, menstruation, headache, or osteoporosis, they usually take more drugs (and not only recommended ones), probably reducing their adherence to the therapy. This is confirmed by our results. In fact women who had been ill (22% vs 14%) and those who took other drugs (28% vs 11%) were more likely to forget to take their therapy and have a more irregular vegetable intake (67% vs 51%) than women who had not been ill. On the other hand, intercurrent diseases, assumption of other drugs, and irregular vegetable intake was different in men. Ill men were more likely to take oral anticoagulants (15%) than men who had not been ill (7%), while the percentage of those who forgot to take the therapy was similar (14% vs 14%) when they also took other drugs. Finally, the men who had been ill had a more regular daily vegetable intake (61% vs 50%). A possible explanation for these findings could lie within the local family model, considering also the median age of the studied patients. Intercurrent diseases and assumption of other drugs in women may mean further stress added to daily housework and family care, and may cause a reduction in therapy adherence, while in ill men adherence could be improved by the care and attention from their wives.

The analysis of age differences showed that forgetting to take therapy and having an irregular vegetable intake affect the time spent in the therapeutic range in patients below 65 years of age more than in the older patients. Moreover in the patients over 65 years old, knowing the reason for taking oral anticoagulants was fundamental to maintaining the PT value in the therapeutic range, which shows that older patients perhaps need an easier and clearer explanation about the advantages of taking oral anticoagulants as primary prophylaxis.

An interesting finding of this work was that, by itself, the questionnaire's administration brought about a significant improvement in the time spent in the therapeutic range by patients with poorly controlled anticoagulation, when considered three months later. The questionnaire may have reminded them of the recommendations given at the start of the therapy and focused their attention on the fundamental concepts of oral anticoagulants. Although a significant difference was found in the time spent in the therapeutic range before and after the questionnaire in patients who showed

good anticoagulation control, this result appears far less important and casual, since the reduction in the time spent in the therapeutic range was slight and above the 90% cut-off. The experience presented here has been useful to us in the context of a critical review of the management of our patients. In particular more care should be dedicated to the educational course for anticoagulated patients, especially in consideration of age and gender differences. Such a questionnaire may be periodically integrated into the daily practice of a Thrombosis Center.

Disclosures

Conflict of interest: none.
Redundant publications: no substantial overlapping with previous papers.

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What is already known on this topic

There are some data about the different factors that may affect anticoagulation therapy. For example, intercurrent diseases, irregular vegetable intake, experience of doctors, etc. However, there is very little information about the influence of a patient's education on oral anticoagulation stability.

What this study adds

This study confirms the importance and need of educational courses for patients under anticoagulaton therapy.

Potential implications for clinical practice

If the patients are given adequate education concerning anticoagulation therapy, the treatment will clearly be more effective and stable.

Jordi Fontcuberta, Associate Editor (Barcelona, Spain)