Peer reviewed article

Patient self-management of long-term oral anticoagulation in Switzerland[1]

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Summary

Indications for oral anticoagulation (OAC) have increased in recent years. OAC requires frequent monitoring of the prothrombin time to keep the intensity within the therapeutic range and to minimise the risk for complications. Patient self-management (PSM) has been found to improve the quality of OAC.

The present study aimed to investigate the first 330 patients performing PSM in Switzerland. A questionnaire was sent to all patients who followed a teaching program for PSM of OAC between 1998 and 2003. Moreover, family physicians were contacted and/or discharge letters were obtained from the hospitals or the treating physicians.

During the study period 13 patients died. Out of the 300 patients providing information 254 (85%) still perform PSM. At least one INR determination per two weeks was done by 74% of the patients and 25% performed at least one INR measurement every 15–30 days. The median time spent within the individual INR target range was 72%. No thromboembolic complications occurred, however, among the 13 patients who died, 1 had myocardial infarction and 6 died of heart failure. When counting these events as arterial thromboembolic complications the frequency was 0.6 (95% CI: 0.3–1.3) per 100 patient-years. The frequency of major bleeding was 0.6 (95% CI: 0.2–1.3) per 100 patient-years.

We conclude from this study investigating a real-world patient collective that PSM is suitable and save for the patients identified by their family physicians and successfully trained by our training centre.

Key words: oral anticoagulation; patient self-management; patient education; time within target range; thromboembolic complications

Introduction

Indications for oral anticoagulant therapy (OAT) have increased in recent years. OAT is performed using vitamin-K antagonists, such as the coumarin derivatives. In Switzerland Phenprocoumon and Acenocoumarol are used [1, 2]. Patients eg with mechanical heart valves, atrial fibrillation or recurrent venous thromboembolism need to be treated for a long period, even life-long. OAT requires frequent monitoring of the prothrombin time to determine the correct dose of the coumarin used. This is necessary to keep the intensity, measured as international normalised ratio (INR), within the therapeutic range in order to reach an optimal protection against thromboembolic events as well as to minimise the risk for bleeding [3]. The management of OAT in Switzerland is routinely performed by family physicians.

In the treatment of diabetes mellitus, self-monitoring and self-adjustment of insulin dosage combined with a structured patient teaching have resulted in major improvements [4]. Based on this experience, a structured teaching and self-management program for patients with oral anticoagulation (OAC) had been successfully introduced in Germany [5]. Patient self-management (PSM) includes self-testing of the patients' own INR as well as self-dosing of the anticoagulation drug, whereas in patient self-testing patients only test their INR and call the result to their physician, who then makes any dosing decision [6, 7]. Both, self-testing and PSM had been made possible by the development of coagulation monitors. These instruments measure the prothrombin time from a capillary sample of whole blood and provide an INR result

Abbreviations

INR	International normalised ratio
ISI	International sensitivity index
OAC	Oral anticoagulation
OAT	Oral anticoagulant therapy
PSM	Patient self-management

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within minutes. They have been successfully tested for their accuracy, reliability and ease of handling [8–13].

In Switzerland, self-management of OAC was introduced in 1996 [14]. Since then several studies compared patient self-management of OAC with treatment by practitioners [5, 15, 16] or with specialised anticoagulation clinics [6, 17–19]. Overall, self-management achieved a higher level of OAT control [20] and major complications and minor haemorrhages were found to be less common among patients performing self-management [21]. A recent systematic review and meta-analysis on self-monitoring and self-management of oral anticoagulation confirmed the advantages of this method [22].

In the present study we report on the results of a retrospective analysis of the first 330 patients who followed a structured teaching program for self-management of OAT in Switzerland between 1998 and 2003.

Patients and methods

We enrolled all patients which had been trained for PSM of OAC between 1998 and 2003 at our centre in Switzerland. More than 90% of all patients performing patient self-management of OAT in the German-speaking part of Switzerland were trained by this centre. The patients were selected by their family physicians for the PSM program and admitted to the teaching centre. Patient characteristics were collected from the patient records at the teaching centre and were completed with the information of the questionnaire. The study had been approved by the local ethic committee.

A structured educational program similar to the German program [5] was developed [14] and is applied since then. This program is in accordance with recently published guidelines on PSM [23]. Briefly, the program involves two training sessions. All patients participate in a one-day training course in groups of up to eight patients. A specialised team consisting of a physician and paramedical personnel is responsible for the training courses. The program includes theoretical and practical aspects of OAT involving the use of the coagulation monitor, quality control issues, interpretation of INR results, dosing algorithm and dosage adjustment of the anticoagulant, interaction with other medication, influence of nutrition, intercurrent illness and travel on INR results, as well as documentation of INR results and adverse events. This first course is followed by a training phase of several weeks with at least one parallel INR determination by the patient and family physician. Thereafter, each patient returns to the training centre for a one-hour repetition and control. The patients are advised to check the INR at least every two weeks depending on the INR result. Moreover, they are advised to get parallel measurements done by the family physician twice a year. A 24-hour hot-line exists in case of problems.

In August 2004 a questionnaire was sent to all patients who had been trained between 1998 and 2003 at our centre. The questionnaire contained four main questions with a maximum of twelve secondary questions. The questions concerned patient data, treatment modalities, and experience with the coagulation monitor and oral anticoagulation, problems with PSM and adverse events. In case we did not receive the questionnaire back within a certain time period, the patients, the relatives and/or the family physician was contacted by a phone call. Discharge letters or respective reports were obtained from the hospitals or the treating physicians.

Adverse events were classified as clinically overt episodes of minor or major bleeding as well as thromboembolic events. Major bleedings were either bleedings requiring transfusion or hospitalisation or intracranial bleedings. Minor bleedings were epistaxis, haematoma or bleedings from any site not requiring hospitalisation.

From 1998 up to 2000, the portable coagulation monitor CoaguChek, and since 2000 the newer version, the CoaguChek S, were used (Roche Diagnostics, Rotkreuz, Switzerland) for INR determination. Both are hand-held, battery powered reflectance photometers with single use test strips. The surface of the test strip is coated with a mixture of iron oxide particles and rabbit brain thromboplastin (ISI 1.6–1.8). The test strip is inserted into the meter and prewarmed to 37 °C. After pricking the tip of a finger, a drop of capillary blood applied to the "application field" comes into contact with the thromboplastin, triggering the coagulation cascade. The meter measures the time interval between first contact of the blood sample with the thromboplastin and the time point of coagulation and calculates this value into an INR with the aid of a calibration curve.

The questionnaires were analysed by two persons and the data were collected in an excel file. The individual percentage of time within either the individual INR target range or within a general INR range of 2.0 to 4.5 was calculated based on the written INR-protocols of the patients using linear interpolation between successive INR measurements, calculating the portion of time during each interval that was spent in-range, summing across all intervals, and then dividing by the total duration of therapy [24]. The Poisson confidence intervals (CI) for event rates were calculated at the 95% level. All statistics were done using MedCalc.

Results

From 1998 to 2003 330 patients with an indication for long-term OAC were trained for PSM at our centre. Patient characteristics are given in table 1. A questionnaire was sent to all patients. The questionnaire was returned by 296 (90%), whereas 34 (10%) did not. From 30 patients out of the latter group, information could be received by contacting them by phone and/or contacting their relatives and treating physicians. Four patients could not be contacted since they left the country without a new address. The total observation time of the 326 patients was 1119 years.

Table 1

Characteristics of the 330 patients trained for patient self-management of oral anticoagulant therapy (PSM).

Sex	
Men	206 (62%)
Women	124 (38%)
Age at the training course	
years, median [range]	52 [3–85]
Indication for oral anticoagulant therapy	
Mechanical heart valve prosthesis	127 (38%)
Atrial fibrillation	31 (10%)
Venous thromboembolism	136 (41%)
Arterial thromboembolism	36 (11%)
Duration of oral anticoagulant therapy before training for PSM	
months, median [range]	10 [1–192]
Drug used for oral anticoagulant therapy	
Phenprocoumon	304 (92%)
Acenocoumarol	26 (8%)

Table 2

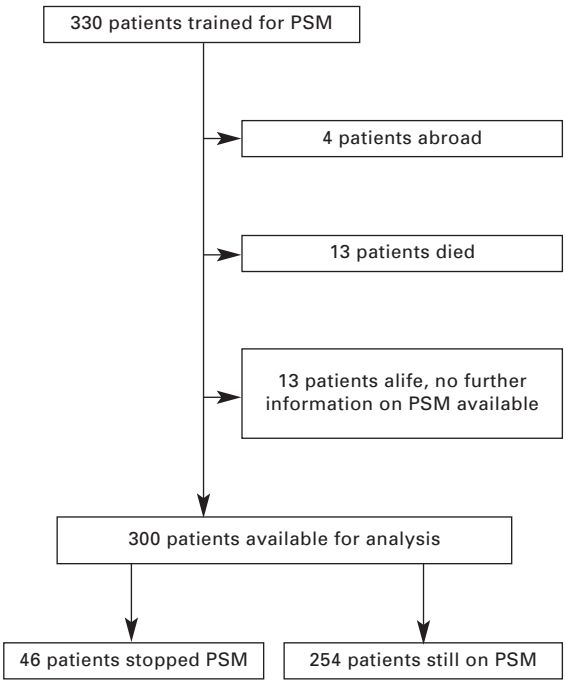
Analysis of adverse events among the 300 patients with the respective information available.

Observation interval (months)	39 [0–75]
Total observation time (years)	1012
Minor bleeding events§	
Patients (n)	46
Episodes (n)	57
Frequency (per 100 patient-years)	7.1 (5.4–9.2)
Major bleeding events	
Patients (n)	6
Episodes (n)	6
Frequency (per 100 patient years)	0.6 (0.2–1.3)
Thromboembolic complication	
Events	0 (0–0.4)

Values are presented as median and [range] or percentage and (95% confidence interval).
§ Analysis based on 258 patients (78%) who provided detailed information to that question (total observation time of 804 years).
INR, International Normalised Ratio

Figure 1

Flow of the 330 patients who had been trained for patient self-management (PSM) of OAC between 1998 and 2003.



Adverse events

Since no information was available of the 4 patients who left the country, analysis of adverse events was based on 326 patients. During the study period 13 patients died. Causes of death were myocardial infarction, aortic rupture (Marfan syndrome), suicide, carcinoma of the pancreas, carcinoma of the lung, carcinoma of the urine bladder (each n = 1) and in 6 patients heart failure. One patient died during mechanical valve replacement. The responsible physicians judged causes of death among the 13 patients not to be attributed to OAC. Bleeding events and thromboembolic complications are summarised in table 2. In total 6 major bleeding events were recorded: two patients had haematuria, one with prostate disease and one with nephrolithisis, both requiring hospitalisation. Two patients suffered from gastrointestinal bleeding and one patient suffered from intra-abdominal bleeding following rupture of an ovarian cyst. These five patients had an INR within their individual therapeutic target range (INR values between 2.7 and 4.1) at the time of bleeding. One patient had bowel wall bleeding at an INR of 7.0. During the observation period, no thromboembolic complications occurred. However, among the thirteen patients who died, one had myocardial infarction and six died of heart failure. When counting these events as arterial thromboembolic complications, the frequency would be 0.6 (95% CI: 0.3–1.3) per 100 patient-years. Not all patients were willing to give detailed information on minor bleeding events. Therefore, minor bleeding analysis (table 2) was based on 258 patients (78%) with a total observation time of 804 years.

Patients who stopped PSM

To the question whether they still perform PSM or not 13 patients (6 women and 7 men, median age 32 years, range 24 to 61 years) were not willing to provide information. Therefore, 300 patients could be analysed with respect to PSM (table 3). 254 patients (85%) still performed PSM, whereas 46 patients (15%) stopped PSM (figure 1). 252 patients out of 254 responding to the respective question indicated their satisfaction with PSM to be good or very good (99.2%).

Median duration of PSM among the 46 patients who stopped PSM was 9 months [range 0–66]. Six patients out of the 330 which were trained (1.8%), decided not to start PSM at the end of the training course. Five patients were involved in the study on PSM in Switzerland [14] and stopped PSM after the scheduled duration of 6 months of that study. Seven patients provided no information on why they stopped PSM. The remaining 28 patients named the following reasons for stopping PSM: no indication for OAT anymore (n = 10), contraindication for OAT (n = 5), financial reasons as the insurances did not pay the strips for the coagulation monitor (n = 5), problems with the technical aspects of INR determination (n = 10), frequent controls at the general physician due

Table 3

Characteristics of the 254 patients still performing patient self-management of oral anticoagulant therapy (PSM) and the 46 patients who stopped with PSM.

	On PSM n = 254	PSM stopped n = 46
Sex		
Men	158 (62%)	28 (61%)
Women	96 (38%)	18 (39%)
Age years, median [range]	52 [3–85]	53 [22–80]
Indication for oral anticoagulant therapy		
Mechanical heart valve prosthesis	105 (41%)	8 (17%)
Atrial fibrillation	26 (10%)	5 (11%)
Venous thromboembolism	99 (39%)	26 (57%)
Arterial thromboembolism	24 (10%)	7 (15%)
Drug used for oral anticoagulant therapy		
Phenprocoumon	231 (91%)	44 (96%)
Acenocoumarol	23 (9%)	2 (4%)

Table 4

Analysis of INR determinations.

Patients (n)	188
Follow-up (months)	33 [3–75]
Number of INR Tests per patient (n)	65 [3–351]
Median interval* between two INR determinations (days)	7 [2–52]
Individual target range	
INR determinations in target range (%)	66.8 [9.5–100]
Time within target range (%)	72.0 [11.5–100]
Target range of 2.0–4.5 (n = 184)§	
INR determinations in target range (%)	91.4 [17.6–100]
Time within target range (%)	95.2 [11.5–100]

Values are presented as median and [range]. INR, International Normalised Ratio.
* The median interval between the INR determinations was calculated for each patient.
§ Patients with an individual target range including INR <2.0 (n = 4) and/or INR >4.5 (n = 0) were excluded from this analysis. 109 patients had an individual INR target range with the upper limit >3.0 INR units.

to other reasons (n = 2) and problems in finding the correct dose of the anticoagulant (n = 1).

Analysis of INR determination

Regarding the frequency of INR self-testing 249 patients provided information. At least one INR determination per week was done by 34% of the patients; 40% measured their INR at least every 8–14 days, 25% at least every 15–30 days and 1% had INR estimates rarer than once per month. 188 patients provided their INR protocols from which the percentage of INR determinations and the percentage of time spent within the individual therapeutic INR range and within the INR range of 2.0 to 4.5, respectively, could be calculated. The results are presented in table 4. The median time spent within the individual INR target range was 72%. During the rest of the time, the INR was twice as often below the target range as compared to the time above the target range. The median deviation from the lower or higher value of the INR target range was 0.2 INR units [range 0.1–0.8] and 0.3 INR units [range 0.1–1.4], respectively. There was no obvious indication that age, sex or median interval between two INR determinations influenced the time spent within the individual target range.

Discussion

In the past 20 years, patient self-testing and patient self-management (PSM) has emerged as management option for patients with an indication for long-term oral anticoagulant therapy (OAT). Of the millions of patients worldwide being treated with OAT, only up to 150000 practise PSM, most of them in Germany [25, 26]. In Switzerland, PSM had been introduced in 1998 [14]. Up to 2003, 330 patients had been trained and since then another 350 patients. Our training centre is responsible for about 90% of all patients trained in Switzerland.

PSM had been studied in controlled clinical trials [6, 15–21] and recently analysed in a meta-analysis [22]. These studies found PSM to be asso-

ciated with better efficacy of INR testing and with fewer thromboembolic events and lower mortality. However, it had been stressed that PSM is not feasible for all patients and requires identification and education of suitable candidates. Accordingly, respective guidelines had been published [23]. We, therefore, decided to retrospectively evaluate the quality of the OAT among all the patients who had been trained for PSM in Switzerland between 1998 and 2003. We found that patients selected by their family physicians and trained at our centre had a high percentage of INR time spent within the target range and a low frequency of major haemorrhages and thromboembolic events, comparable to what has been found by others in controlled clinical trials [22].

Our study provides results on patients performing PSM over a median period of 42 months [range: 0–75 months] with a total observation time of 1119 years. Such long-term data on patients performing PSM are rare. Most studies had an observation period of less than one year [22]. There is only one non-randomised study investigating PSM over five years [27].

In our study, six patients (1.8%) decided not to start with PSM after the training course. This low early "dropout rate" indicates rigorous selection of motivated patients by the family physicians. Of the 317 patients being alive, at least 254 continued with PSM (80%) after a median follow-up of 37 months [range 8–75 months]. Ten patients stopped due to problems with the technical aspects of INR determination. Those patients might have had a profit of an additional training. Only one patient stopped PSM due to problems in finding the correct dose of the anticoagulant.

The percentage of INR determinations and the percentage of time spent within the individual therapeutic INR range are the methods which have been used to assess efficacy of INR testing most commonly [17, 24] and which had been found to be important predictors of clinical outcome [28]. In our study, the patients achieved a high degree of that efficacy, the median time spent within the individual INR target range and within the range of 2.0 to 4.5 were 72% and 95.2%, respectively, and the percentage of INR determinations in target range and in the range of 2.0 to 4.5 was 66.8% and 91.4%, respectively. It should be mentioned, that episodes where patients temporally interrupted OAC and used bridging therapy with heparins for invasive procedures were not eliminated from the current analysis. This results in a bias for the worse of the efficacy of the OAT. Nevertheless, the results of the present study are favourably compared to those found by others: a recent systematic review found the mean time spent within the INR target range to be 56% to 76.5% for patients performing PSM and 32% to 77% for patients managed by an anticoagulation clinic or by the family physician [22]. It has been discussed that a higher frequency of INR testing results in a higher percentage of the INR spent within the target range [29], with an (unrealistic) optimum of test frequency of once every 2 to 4 days. In our study, 74% of the patients performed INR testing at least every 2 weeks and only 1% tested fewer than once per month. It may be speculated whether more frequent testing, eg once every week, would have resulted in a better therapeutic efficacy. However, whether more frequent testing indeed results in clinical important endpoints remains to be shown in prospective studies.

We found a frequency of 7.1 and 0.6 per 100 patient years for minor and major bleedings, respectively, and, when counting the one patient who died of myocardial infarction and the six who died of heart failure as arterial thromboembolic events, a frequency of 0.6 per 100 patient years of thromboembolic complications. The latter represents a "worst case" scenario and it is very likely that oral anticoagulation was not associated with death in those seven patients. However, we decided do include these patients in the analysis in order not to underestimate the rate of complications. The study by Menéndez-Jándula et al. was the first to demonstrate in a randomised controlled setting PSM to be superior in terms of reduction of major complications [21]. The recent meta-analysis by Heneghan et al. showed PSM to be associated with fewer thromboembolic events and with lower mortality as compared to routine care [22]. The frequency of major complications found in our study is difficult to compare with the results of other studies. This is mostly due to the fact that most of them lasted no longer than 12 months and reported the total amount of complications during the study period and did not provide risks per 100 patient years. However, our results are comparable to what has been found by others. Sawicki et al. reported from a non-randomised 5-year study a frequency of bleeding complications of 0.62 per 100 patient years and 1.1 per 100 patient years for thromboembolic complications [27].

There are several possible reasons that PSM resulted in better therapeutic control and better outcome compared with usual care or anticoagulation clinic care. Testing at home allows not only an increased frequency of testing, but also improved timeliness, providing the ability to test when it is needed. PSM might allow better management of patients who need to stop anticoagulants for invasive procedures. Finally, patient self-management may have a substantial impact on patient motivation, empowerment, compliance and satisfaction that may be important elements in achieving better outcomes [30].

Patient satisfaction with PSM was high, as demonstrated not only in the present study (>99%), but in others as well [15]. Moreover, positive effects of PSM on quality of life have been reported recently [31]. Satisfaction and quality of life aspects could lead to improved patient motivation and compliance which might further explain the good results obtained with PSM [32]. Interestingly, education with or without self-monitoring

(without self-dosing) among patients with unstable control of OAC produced an improvement in the INR time within the therapeutic range [33]. Moreover, other investigators found insufficient education on OAC to be the major factor predicting bleeding [34].

Although PSM has been introduced years ago and benefit has been shown, the issue of quality control remains largely unresolved, although attempts to perform an external quality control assessment program have been done [35]. The coagulation monitors used for PSM in Switzerland are indeed equipped with quality control solutions. However, the responsibility is left with the patient and his or her family physician to perform parallel INR measurements with capillary blood of the patients and with venous blood performed by the family physician every six months. In the present study, 84% of the patients indicated to perform parallel measurements at least every six months by the family physician (data not shown). The patients performing PSM in Switzerland reached a high percentage of agreement (>90%) when compared with parallel INR measurement in the training centre [13].

Funding of PSM is not guaranteed in Switzerland. Insurers pay PSM on an individual basis in about 50–75% after application for each patient by the respective insurer. The situation is better in Germany, where insurers fund PSM once the competence of a patient to perform PSM has been established. Cost-effectiveness analysis have been done with conflicting results showing PSM to be a cost-effective strategy in a Canadian study [36] and not to be cost-effective in a UK study [37]. The results of such analyses are highly dependent on the model and the included variables as well as of the cost of the respective medical services in a given country. For Switzerland, no formal cost-effectiveness analysis exists.

The present study has limitations. As already discussed, the patients performing PSM are highly selected and do not represent the general population of patients with oral anticoagulation. This selection influences the rates of adverse events as well as the quality of OAT. The latter is, in addition, influenced by the fact that we were able to analyse the INR protocols of only 188 of the 256 patients still performing PSM. This may result in a bias for the better of the quality of OAT. However, the major limitation of the present study is its retrospective design with comparison with historical controls. Therefore, the results should be interpreted with caution. However, other studies found that PSM improves the quality of OAT with fewer thromboembolic events and a lower mortality [22]. Our intention was not to confirm this, however, to analyse the quality of PSM in Switzerland. The contribution of this study is to provide data from a real-world patient collective.

In conclusion, we retrospectively analysed all the patients who had been trained for PSM in Switzerland between 1998 and 2003. We found that the efficacy of OAC as well as the frequency of adverse events to be in the range of what has been published for patients performing PSM in controlled trials. The median time spent within the individual INR target range was 72%. The frequency of arterial thromboembolic complications was 0.6 (95% CI: 0.3–1.3) per 100 patient-years and that of major bleeding events 0.6 (95% CI: 0.2–1.3) per 100 patient-years. We conclude that PSM is suitable for the patients identified by their family physicians and successfully trained by our training centre.

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