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Long-Term Results of Patients' Self-Management of Oral Anticoagulation

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Objective: Control of oral anticoagulation therapy has been reported to be often inadequate. Prospective controlled randomised short-term investigations suggest that patients' self-management of oral anticoagulation may lead to improved control. Prospective long-term studies of this intervention are not available. **Design:** Prospective, multicenter, follow-up study of a randomised interventional trial. **Setting and subjects:** A structured teaching and treatment programme for self-management of oral anticoagulation was offered to 178 patients. Follow-up was until death or for a period of five years resulting in 809 patient years (py). **Main outcome measures:** Accuracy of anticoagulation control, measures of treatment-related quality of life, bleeding and thromboembolic complications. **Results:** 134 Patients (89 %) of the 150 patients, available for the final 5-years examination performed self-monitoring, 116 (77 %) performed self-adaptation of coumarin dosage. At baseline 32 % of patients were within the INR target range; during the final year of the follow-up period, 62 % of INR self-measurements were within the target range. On self-monitoring the mean squared deviation from the mean of the individual INR target range was 0.44 (standard deviation [SD] in parentheses) (0.77). The mean time within the target range was 225 days per year (d/y) and 80 d/y below and 60 d/y above the target range. During the follow-up period, 5 major bleeding complications (0.62 per 100 py) and 9 thromboembolic events (1.1 per 100 py) occurred. When compared to baseline, parameters of quality of life improved. **Conclusions:** We conclude that after participation in a structured teaching and treatment programme, compliance with self-management of oral anticoagulation persists in the long-term, results in an improvement of accuracy of anticoagulation control and quality of life and is associated with a relatively low risk of bleeding and thromboembolism. *J Clin Basic Cardiol 2003; 6: 59–62.*

Key Words: oral anticoagulation, self-management, bleeding, thromboembolism, teaching and treatment programme, quality of life

The increasing number of indications for oral anticoagulation has raised concerns how this therapy should be undertaken. There is good evidence that an exponential rise in the risk of both thromboembolism and bleeding in patients occurs outside the therapeutic international normalised ratio (INR) range [1]. However, this therapeutic range is rather small and consequently, over- and under-dosing of therapy is frequent [2, 3]. Patients' empowerment, including self-management of therapy has been proposed for an improvement of the results of oral anticoagulation [4]. A number of prospective, controlled, randomised trials have shown that self-management of oral anticoagulation is effective and improves control of anticoagulation and quality of life as compared to standard management [5–8]. However, recently it has been rightly pointed out that prospective data is lacking on the long-term practicability, efficacy and safety of patients' self-management of oral anticoagulation [4, 9]. We have performed a prospective follow-up study to assess the long-term compliance, quality of control, quality of life and the risk of complications in patients who were offered a participation in an anticoagulation teaching and self-management programme.

Methods

Patients

The methods of this study were reported elsewhere [5]. In short: Five departments, specialized in the treatment of patients with oral anticoagulation therapy participated in this multicenter study. The centres were advised to screen all consecutive patients with oral anticoagulant treatment appearing at the respective centre. No other pre-selection was

done. The ethical committees of all participating centres approved the study protocol. All patients gave their written informed consent to participation in the study. The oral anticoagulant was phenprocoumon. Before the enrolment the international normalized ratio (INR) therapeutic target range was defined individually by the treating physicians and reported to all patients. In the first part of the study, patients were randomised to an intervention group and a control group. Patients of the intervention group could immediately participate in the teaching and treatment programme while this programme was offered to the control group patients six months after. The results of the first part of this study were reported elsewhere [5]. In the second part of the study, after participation in the teaching and treatment programme, all patients were followed prospectively until death or for a period of five years. According to the German health care structure, patients were treated during this follow-up period by general practitioners including referral to consultants when necessary.

Teaching and Treatment Programme for Patients' Self-Management of Oral Anticoagulation

A structured educational programme was developed and all teaching-nurses and physicians, responsible for patients' education in the intervention group, participated in a 2-day training course. The oral anticoagulation teaching and self-management programme was aiming at increased responsibility for disease management by the patients based on systematic INR self-monitoring and self-management of the anticoagulant dosage. It consisted of three consecutive weekly teaching sessions of 60–90 minutes for groups of three to six patients.

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During the first session, patients are informed about anticoagulation in general. Using a whole blood PT-INR monitor (CoaguChek®, Roche Diagnostics, Germany), they receive an extensive training in INR self-monitoring [5]. During the first week, patients are encouraged to measure INR values daily and to record the results and the anticoagulant dosages in their logbook. The topics of the second session include instructions to prevent bleeding and thromboembolic complications and the effect of diet and additional medication on anticoagulation control. During the second and the third session, patients are instructed about indications and models of reducing or increasing the anticoagulant dosages in order to achieve INR values within the target range. Several examples of adapting drug dosage are discussed, patients complete practice exercises. In addition, any problems that might be encountered including operations, illness, exercise, pregnancy, and travelling are discussed. The quality of INR self-monitoring is checked by the teaching nurse at the end of the first and at the beginning of the following two sessions. After participation in the programme, patients have to estimate their INR value with an absolute deviation of less than 0.4 from the reference value, otherwise the training has to be repeated. At the end of the training, all patients who participated in the study, achieve an INR deviation of less than 0.4 from the reference INR measurement in parallel INR measurements. After participation in the programme, patients are encouraged to control the INR values by self-monitoring once per week and to adjust their anticoagulant dosage accordingly.

Outcome Measures

Patients, treating physicians and relatives were contacted for a structured telephone interview five years after the final examination of the study's first part. In addition, patients were asked to complete a questionnaire, which was sent to them, and to send their anticoagulation logbooks to the study centre. Additional information about complications and hospital admissions including discharge letters and autopsy reports were collected from the hospitals and from general practitioners' archives.

The quality of anticoagulation control during the final follow-up year was assessed by evaluating all documented INR values from the respective patient with regard to the frequency of values and the time spent within and outside the target range [1]. To evaluate positive and negative differences between the target INR range and INR values, the squared INR deviation was assessed:

$$\text{Squared INR deviation} = [\text{INR} - \frac{1}{2}(\text{upper value of target INR range} + \text{lower value of target INR range})]^2$$

At baseline and the final follow-up, treatment-related quality of life was assessed using a structured questionnaire containing 32 items (available on request from authors). This questionnaire was developed with the help of the national self-help group for patients with oral anticoagulation. The members of the patients' self-help group formulated sentences describing their feelings with regard to their treatment, of which 40 were combined into a questionnaire. After the first evaluation of this questionnaire [5], 40 items were reduced to a list of 32 items. The study patients estimated the impact of every item on their self-perceived treatment-related quality of life by a graded scale ranging from a minimum of "1" (total disagreement) to a maximum of "6" (total agreement). The 32 items covered 5 treatment-related topics: general treatment satisfaction, self-efficacy, strained social network, daily hassles, and distress. The total score for each topic and the in-

ternal reliability coefficient of the questionnaire (Cronbach's α) was assessed according to Todd and Bradley [11].

Bleeding complications were classified as minor or major according to Landefeld [12]. Thromboembolic events were defined as ischaemic cerebral infarction confirmed by a computer tomographic scan, valve thrombosis, peripheral or pulmonary embolism or myocardial infarction.

Analysis

179 patients were enrolled in the first part of the study. One patient died in the control group during the first 6 months before he had been offered a participation in the self-management programme. Hence, 178 patients were included in the second part of the five-year follow-up study resulting in 809 patient-years available for evaluation.

Data are presented as means and standard deviations or proportions. Wilcoxon rank sum tests were used to evaluate the changes in quality of life. For interpretation, an effect size of 0.5 is considered moderate, 0.8 is considered large [13]. The evaluation was performed on an intention-to-treat basis. Statistical computations were performed with SAS version 8.0 [14]. P-values below 5 % were regarded as significant.

Results

Participation in a teaching and treatment programme for self-management of oral anticoagulation was offered to 178 patients, who were enrolled in the study; the baseline characteristics are given in Table 1. No patient was lost to follow-up. 161 decided to participate in all three sessions of the programme. During the 5-year follow-up period 19 patients died. Autopsy protocols and medical records of three patients who died were lacking or inconclusive, hence the causes of death remained unidentified in these three cases. From the remaining 16 fatal events, one patient had a fatal bleeding, three had fatal thromboembolic events, four died due to malignant diseases, four from cardiac failure, two had fatal arrhythmia, one patient died during an aortic valve operation, one died during an operation of an abdominal aortic aneurysm. During the follow-up, five severe bleeding complications and nine fatal or non-fatal thromboembolic events occurred, resulting in a mean risk of severe bleeding of 0.62 per 100 py and a mean thromboembolic risk of 1.1 per 100 py. A total of 215 hospital admissions with a total of 2973 inpatient treatment days occurred resulting in mean hospital treatment duration of 3.5 days per patient per year.

Long-term compliance and structure of oral anticoagulation self-management was assessed five years after baseline investigation. Before the final five-year follow-up, 19 patients had died, in 4 coumarin therapy had been stopped and 5 patients had refused to participate in the final examination, leaving 150 patients available for the final examination. The characteristics of these patients are given in Table 1. After five years, 134 patients reported regular INR self-monitoring and in 16 patients INR measurements were done in a laboratory only. These 134 patients reported 6173 self-monitoring INR values during the last year of follow-up resulting in a mean of 46.1 (25.2) self-measurements of INR per patient per year. On self-monitoring, the mean squared INR deviation from the mean of the therapeutic range was 0.44 (0.77). 93 % of patients correctly indicated their individual therapeutic INR range. During the final year of follow-up, 62 % of INR self-measurements were within, 23 % below and 15 % above the target range. Of the 16 patients who decided to measure their INR values in a laboratory, 281 INR values were reported, 17.6 (5.4) per patient per year. In total, during the last year of

the study, 767 laboratory INR measurements were done, 486 in 103 patients with self-monitoring and 281 in 16 patients without self-monitoring (31 patients with self-monitoring had no laboratory INR measurements at all). The mean time within the target range was 225 (85) days per year (d/y) and 80 (74) d/y below and 60 (68) d/y above the target range. 124 patients performed regular self-adaptation of the phenprocoumon dosage on a routine basis, while 10 patients changed the dosage only after consultation with a physician. The mean number of self-management dosage adaptations was 22.7 (24.4) per year, while the mean number of physician-led dosage adaptation was 6.6 (5.1) per year.

The treatment-related 32-items-questionnaire was completed by 119 patients both at baseline and at 5-years follow-up. The internal reliability was acceptable as indicated by the Cronbach's α values between 0.66 and 0.82. All investigated aspects of treatment-related quality of life improved after participation in the self-management programme (Table 2). The most pronounced improvement was in general treatment satisfaction and self-efficacy scores.

Discussion

In the initial randomised controlled part of this study [5] we have shown that self-management of oral anticoagulation can be reliably performed by patients and improves quality of anticoagulation control and treatment-related quality of life. In the second part of this study we have demonstrated patients' compliance to this form of therapy in the long-term and we have shown that it is associated with an improvement of the quality of anticoagulation control, which is maintained during the follow-up of five years. Before participation in the self-management programme, the squared INR deviation in the intervention group was 1.32, only 29 % of INR measurements were within the target range. At the end of the randomised controlled part of this study, the squared INR deviation from the mean of the target range in the intervention group was 0.65 with 53 % of INR values being within the target range. After five years, the squared INR deviation was even lower at 0.44 and the percentage of INR values within target range increased to 62 %. Hence, not only the improvement in the quality of anticoagulation control after participation in the self-management programme is long lasting, but it may even improve further with the duration of patients' self-management. Our prospective study confirms previous uncontrolled retrospective data [15–18] and con-

trolled study results [6–8, 19], indicating that this form of anticoagulation treatment improves both quality of care and quality of life and supports patients' demand for a better access to this form of treatment [20].

Numerous studies have shown a clear association between the deviation of INR values from the therapeutic range and the risk of bleeding and thromboembolic complications [1, 21–23]. Previously, the risk of major bleeding in patients with mechanical heart valves was described as high as 2.7 per 100 py [1], 6.0 per 100 py [24] and 4.7 before and 1.0 after attending an anticoagulant clinic [2]. Thromboembolic complications have been described at a frequency of 0.71 per 100 py [1] and 6.6 per 100 py before and 0.6 per 100 py after attending an anticoagulant clinic [2]. Because in this study the control-group patients have also participated in the self-management programme after six months, it is not possible to evaluate the risk of complications in a randomised controlled way. However, when compared with the previously published risk evaluations [1, 2, 24], in this prospective study self-management of oral anticoagulation was associated with a relatively low risk of major bleeding (0.62 per 100 py), while the risk of thromboembolic complications (1.1 per 100 py) was comparable to results in an anticoagulation clinic.

Life-long oral anticoagulation is bound to result in a decrease in quality of life. Patients with oral anticoagulation therapy often report fear of complications and complain about dietary limitations, less freedom when travelling and regular time-consuming visits to physicians and laboratories [5, 6, 8]. In the first randomised controlled part of this study [5], we have shown that, if anticoagulant therapy is based on self-monitoring and self-management, most aspects of treatment-related quality of life improve. In this study, we could demonstrate, that this positive change in the aspect of quality of life lasts long. The improvement in patients' satisfaction and in quality of life in this study is in accordance with results of other investigations [6, 8] and may contribute to the long-term patients' acceptance of this form of anticoagulation management.

In conclusion, self-management of anticoagulation therapy is feasible and accepted on the long-term by the majority of patients who are offered this form of therapy. It results in an improvement in the quality of anticoagulation control, which occurs immediately after initiation of this therapy and is long lasting. The long-term patients' compliance to this form of an-

Table 1. Baseline characteristics of patients who were enrolled into the long term follow-up study and patients who were available for the final five year follow-up examination. Data are frequencies or means with standard deviations in parentheses.

Variable	Patients enrolled n = 178	Patients evaluated at the final follow-up n = 150
Gender (n; male/female)	125/53	104/46
Age (years)	55.1 (11.9)	54.4 (12.2)
Weight (kg)	75.5 (13.6)	75.8 (13.4)
Smoker/ex-smoker/non-smoker (n)	15/86/77	9/74/67
Heart valve replacement (n)	150	132
Atrial fibrillation (n)	9	6
History of minor bleeding (n)	20	19
History of major bleeding (n)	2	1
Duration of prior anticoagulant use (years)	2.1 (4.7)	2.0 (4.3)
Phenprocoumon dosage (mg/week)	18.2 (6.1)	18.1 (6.1)

Table 2. Assessment of treatment-related quality of life scores at baseline and five years after participation in the programme in 119 patients for whom complete data on quality of life assessment were available both at baseline and at the five year follow-up. Evaluation was based on a modified structured questionnaire containing 32 items covering five treatment related topics. Decrease in the scores for strained social network, daily hassles and distress indicate improvement, in the general treatment satisfaction and self-efficacy improvement is indicated by an increase in scores. Maximum score is 6 and minimum 1. Some items had missing values, e.g. in the "daily hassles" subscale, which contains some job-specific items (e.g. problems at work). Data are means (standard deviations in parentheses), p-values are given for the differences between baseline and follow-up.

	Baseline	Follow-up	Effect size	p-value
General treatment satisfaction	2.84 (1.41)	5.35 (0.70)	2.11	< 0.001
Self-efficacy	4.70 (0.98)	5.48 (0.58)	1.07	< 0.001
Strained social network	2.19 (1.04)	1.72 (0.78)	-0.61	< 0.001
Daily hassles	2.05 (0.75)	1.70 (0.59)	-0.67	< 0.001
Distress	2.97 (1.11)	2.56 (1.06)	-0.53	< 0.001

ticoagulation treatment may be due to the concomitant major improvement in quality of life measures. The incidence of bleeding complications may be lower with this form of treatment and the risk of thromboembolic complications is comparable to the results in an anticoagulation clinic.

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