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A project to improve the management of patients on warfarin in a primary care setting through the introduction of a POC analysis

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ABSTRACT

When noticed that patients commonly misunderstood their warfarin prescriptions when they were given by telephone. We found that the average TIR (time in range) (the relative time period the patients PT-INR value was in the therapeutic range) for patients decreased, and we noticed that the numbers of incidents increased. We made several interventions over a period of close to three years (2010-2012) to improve the quality of care, increase patients' TIRs, and decrease incidents.

The interventions included; taking extra care when speaking to patients about their warfarin prescriptions on the phone and using an express mail delivery system to make sure patients got their letters in time. However, these changes made little difference to the measured results.

In 2012, we introduced a point of care analysis. Through these simple actions TIR figures increased from 55 % to 75-80 % and fewer non-conformance reports were filed. Medical incidents, leading to costly hospitalizations, after the introduction of POC (point of care analysis) fell from six to two to three instances a year. The number of patients undergoing treatment and included in the study increased from 200 in 2008 to 250 in 2015.

We found that these changes improved the quality of the care given without causing extra work for the staff. Patients were satisfied and the method has spread to other primary care centres.

PROBLEM

In Sweden, the numbers of patients undergoing anticoagulant treatment are increasing and approximately 1.8% of the population are treated with warfarin or novel oral anticoagulants (NOAC). PT-INR (prothrombin time-international normalized ratio) values are often accepted as therapeutic in the range two to three, but individuals may have other goals for treatment, e.g. in the case of mechanical heart valves.

Strict surveillance of PT-INR is needed in warfarin treatment (with tests at least every

sixth week in patients with good control, and tests several times a week when the treatment is first started) and is often regarded as tiresome for the patient and expensive for the health care system.^{1 2}

Tullinge Primary Care Centre is owned by the county council and is situated in the south of the Greater Stockholm area. Approximately 16,500 people attend this centre and about 230 of them (1.5%) have warfarin treatment. After two decades we have almost centralized the monitoring to only a few physicians.

Patients used to report to the care centre's laboratory in the morning and left after their blood sample was given. Samples were prepared, which included a time consuming centrifugation process, and were then analyzed. Results were sent to the physicians in the afternoon who either contacted the patients by phone, or by letter. There were several problems with this system. When the physician tried to contact the patient by phone, it was not uncommon that he/she was busy and did not answer. An answer-phone message was usually left by phone, however this could easily be misunderstood and incidents occurred where patients took the incorrect dose of their medication. These incidents were reported as non-conformance reports as a part of an internal quality management program.

In 2009, we had noticed that there were high rates of non conformance reports and low rates of TIR. Time in range (TIR) represents an estimate of how long patients are within the therapeutic range for their warfarin medication. This therefore acts as an indirect measurement of how well the patients' medication has been monitored. A value above 75% is regarded as 'good'.

We decided to undertake a quality improvement project with the aim of



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improving patients' PT-INR values so that they were within the therapeutic range (TIR). We also wanted to reduce the number of incident reports and medical incidents by introducing a POC analysis.

BACKGROUND

Warfarin is a widely used, relatively cheap, drug which decreases the risk of thrombosis or embolisations in patients with illnesses such as atrial fibrillation (AF), venous thrombo-embolism, and mechanical heart valves. Many patients have been treated with this drug for many years. Treatment with warfarin requires close monitoring with regular tests of PT-INR.

Recently, more expensive drugs such as NOAC have started to be used. These drugs have similar effects to warfarin but do not require the same close monitoring. Warfarin is still the most commonly used drug in Sweden. The monitoring can be performed both in a hospital setting by anticoagulant clinics or in a primary care centre. The results of this monitoring, which is measured as TIR, are high in both settings at over 75%.^{4 5} In the Stockholm area most patients are monitored by their primary care centres.

Treatment with warfarin requires surveillance due to a narrow therapeutic range which is influenced by both dietary factors and other medications.⁶ The risk of dangerous side effects such as bleeding, or insufficient treatment which leads to thrombosis risk, can be minimized by monitoring. The drug's effect can be reversed by, e.g. administration by vitamin K. The effects of some NOACs are harder to reverse if bleeding should occur and NOACs are not accepted for use in patients with mechanical heart valves in Sweden. Warfarin thus constitutes a sustainable way to reduce the risk of thrombo-embolization.

The Tullinge Primary Care Centre operates its own laboratory. During the study period, the Owren PT test was used as the test of choice to determine PT-INR values. When the Owren PT test is performed shortly after the blood sample is taken, an otherwise time consuming centrifugation step can be omitted and PT-INR results can be available within 5 minutes. Since the Owren PT test is regarded as more robust and is cheaper than other tests, such as the CoaguChek XS, we use this latter test only in cases where the medical laboratory scientists are occupied or in some instances when tests are performed in the patient's home.

Whereas Owren PT is a test that has to be performed in a laboratory by a trained medical laboratory scientist, CoaguChek XS is a mobile test using amperometric (electrochemical) determination of the PT time.

Although studies have reported high convergence between the two tests (seven to nine), some patients should not be tested with the CoaguChek XS method according to suggestions by Equalis (External Quality control in laboratory medicine in Sweden). The Owren PT test should be used in patients with hemoglobin

concentrations above 170 g/L or below 90 g/L, those who are seriously ill or having suffered massive bleeding.¹⁰

According to guidelines, all patients tested with CoaguChek XS should also be parallel tested with the Owren PT test. Before the CoaguChek XS is used by itself to test a patient, blood samples from that patient are tested three times using both methods simultaneously; if results differ more than 0.3 only Owren PT test is used thereafter. We also undertake double testing if CoaguChek values are above 5.

BASELINE MEASUREMENT

Data were compiled on all patients who were treated with warfarin in the studied time period using RAVE-m4 computer software.⁹ The individual patients were identified and data from their case-sheets were extracted. At this stage patient names were removed from the data such that all data were anonymous.

The patient case sheets were studied to identify any medical complications. Medical complications included; intracranial or retroperitoneal bleeding that led to hospitalization or blood transfusion.

Therapeutic time in range (TIR) reported incidents in the quality control system were measured. To monitor the time patients were within the TIR, the data for each patient was assessed to see the percentage of values within the target range of 2.0 to 3.0. An average for all patients over the six month period was then calculated. This figure is an indirect measure of how long the patients were within the therapeutic range.

When studying the TIR levels we chose to test them only in patients suffering from atrial fibrillation since their goal PT-INR values were the same (which was not always the case in other diagnoses).

The baseline measurement in 2009 showed that among the 200 patients treated, there were 10 reported incidents (five incidents per 100 patients) and two medical incidents leading to hospitalization (one incident per 100 patients). TIR, a measure of how well patients stayed within the therapeutic range, was 70%.

When we studied the non-conformance reports we found that vital information such as the number of pills or the date of the next INR test was sometimes not given. This was both when giving information by telephone and also sometimes with written prescriptions. These errors which are recorded in our quality control system are denoted as reported incidents or incidents. We also noticed that information given at the laboratory in the morning could be lost due to the distance between laboratory personnel and the physicians.

DESIGN

We formed a project team made up of physicians and laboratory scientists. Over the years we introduced a number of interventions.

The main intervention introduced in May 2012 was a point of care (POC) analysis where the patients came to the laboratory on a pre-arranged date at a pre-arranged time. Here, they had their samples taken and waited 10-15 minutes for a prescription which was given to them by the physician, who also booked a slot for their next test. To guarantee a smooth flow, the physicians worked in the laboratory and information could easily be exchanged between patient, medical laboratory scientists and physicians. Patients always receive a written prescription to minimise the risk of misunderstanding when the patients and physicians meet in person.

This novel method and its outcome was presented as a poster³ at the 2013 “Day of patient safety” arranged by Stockholm county council. This information was available to all employees in Stockholm county council. We felt that it was important to spread information about this new process to other health centres in the county.

STRATEGY

Improvement cycle 1, 2010: Due to the high number of non-conformance reports, we decided to show extra care when informing patients of their results by phone. We also contacted the mail services and started sending our letters out by express delivery to see if it was possible to get our letters to patients on time. With increasing numbers of patients using warfarin we also increased the number of monitoring physicians from two to five. This may have led to a decrease in the physician’s knowledge of patients treated.

We predicted that reported incidents in our internal quality control system would decrease and time in range values would increase. Repeated measurements were carried out for a total of 195 patients who were on warfarin.

Improvement cycle 2, 2011: We met as a group several times to try to find new ways to improve our care. We discussed several options tested previously at Tullinge and also other primary care centres. We did not have the time to make these changes the same year but hoped that the time spent in discussions and the focus given to this issue would inspire those of us who worked with warfarin prescriptions to be more precise and clear in our contact with patients. We hypothesised that there would be a decrease in incidents and an increase in TIR values. Repeated measurements were carried out for a total of 199 patients.

Improvement cycle 3, 2012: We deduced that a process where patients returned in the afternoon to get their prescriptions, after having left their blood samples that morning, involved too many journeys for, often elderly, patients. We found that it was often impractical for the patient to go to the physicians’ office to get the prescription after having given the blood sample. In May 2012 we introduced the point of care set-up which we have described earlier. Here, patients were tested in the laboratory, results were obtained quickly, and patients

were given a prescription by the physician who was also present at the laboratory. We predicted that this would improve our results. Repeated measurements were carried out for 220 patients. Two months after the introduction of the POC analysis, patients were asked to give their opinion in a questionnaire.

RESULTS

The number of patients undergoing treatment with warfarin and the number of patients with atrial fibrillation who were treated with warfarin are given in figure 1. A steady increase in patients treated was observed from 200 in 2008 to 250 patients in 2015. The number of patients with atrial fibrillation increased but possibly to a lesser extent after the introduction of NOAC.

In the study period we measured TIR every six months. Measurements of reported and medical incidents were made every 12 months (figure 2 to 3).

Improvement cycle 1, 2010: Following our interventions, reported incidents increased further to 19 (number of medical incidents were still two that year)

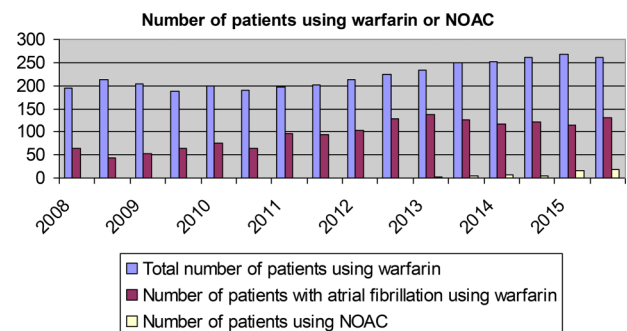


Figure 1 Number of patients treated with warfarin or NOAC at Tullinge primary care centre. Time given in a six-month basis

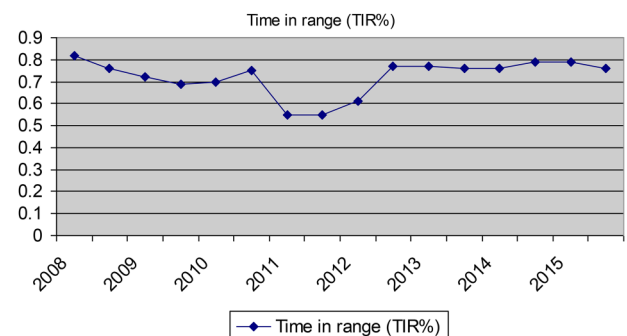


Figure 2 Time in therapeutic range in patients with atrial fibrillation treated with warfarin at Tullinge primary care centre. Time in range present an estimate on how long time the patients are within the therapeutic range of warfarin-medication and thus an indirect measurement on how well the patients medication have been monitored. A value above 0.75 is often regarded as token of good treatment. Time is given in a six-month basis

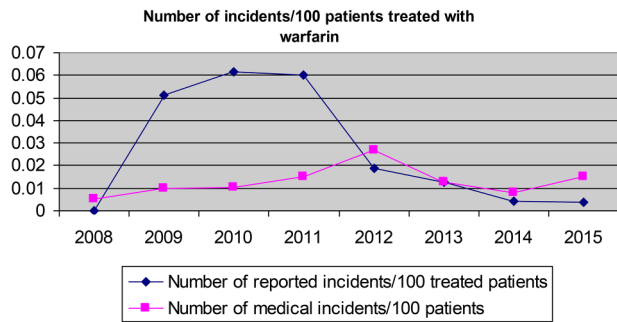


Figure 3 Relative number of incidents reported related to warfarin-medication. A reported incident is an incident where the patient or the staff has noticed a problem or something that may be harmful or even have caused an injury to the patient. Those are reported in our internal quality system. A medical incident as in unwanted effect of the treatment most commonly a haemorrhage, that have led to hospitalisation or caused a need of blood transfusion

(9.5 incidents/100 patients and one medical incident/100 patients) and TIR values remained at 70%.

Improvement cycle 2, 2011: Following our interventions, the number of reported incidents decreased slightly to 12 (three medical incidents) (six incidents/100 patients and 1.5 medical incidents/100 patients) and there was a further fall in TIR to only 55%

Improvement cycle 3, 2012: Following the introduction of the POC analysis in May 2012, measurements showed a decrease in incidents reported in our quality control system to only 4 (1.8 incidents/100 patients) and an increase in TIR values to 77%.

Medical incidents included ten patients with intracranial hemorrhage (four subdural hematomas, three intracerebral and three subarachnoidal hemorrhages). A further six patients had gastrointestinal haemorrhages. Such incidents were found both before and after the introduction of POC analysis, but numbers decreased after the introduction.

TIR values varied in the three cycles with a drop to only 55% in cycle 2. This low measurement is hard to

explain but may possibly reflect a certain rigidity in the results of warfarin prescriptions. When a patient with stable prescriptions and stable INR values starts to get out of balance, it may take several prescriptions over a period of many weeks to get back into a steady state.

Only a few patients (15 out of 200) chose to answer the questionnaire which we gave out in 2012. We got a few comments about the short waiting time and some who highlighted that they were no longer able to chose their own appointment time. Patients appreciated being able to meet with their physician for the prescription. The POC system allowed for better monitoring.

All physicians and laboratory personnel helped to introduce the POC analysis and they all found the changes beneficial. The close cooperation between physicians and laboratory staff has been inspiring.

TIR values in patients undergoing treatment due to atrial fibrillation are given in figure 2. The decrease in TIR results noted in the years prior to the introduction of POC analysis and the increased numbers of non-conformance reports changed at that time and we now have the same TIR as when only two physicians took part in the monitoring. Few non-conformance reports are now registered.

From 2010, patients were parallel tested with both Owren PT and CoaguChek XS methods. We found that results in as many as 8% of our patients differed by more than 0.3 between the two methods. These patients were, thus, unsuited to the CoaguChek XS method.

We also noted discrepancies regarding PT-INR values when the analysis was performed in the patients' homes. In these patients, parallel testing had already been successfully carried out, but despite this, differences in the PT-INR value were noticed between Owren PT and CoaguChek XS analyses. Differences were substantial and strongly influenced the prescription. Some of these differences are shown in table 1.

Use of the Owren PT analysis is cheaper than the use of the CoaguChek XP by a difference of 1.5 €. By using this more robust test as our standard test we saved 7000 € annually.

Table 1

Patient	CoaguChek XS result PK-INR	Owren XP result PK-INR	Disease leading to treatment with anticoagulants	Notice
Male 83 years old	4,8	3,8	Atrial fibrillation	Under treatment with antibiotics due to bacterial osteitis in foot.
Male 83 years old (same as above but a different analysis)	4,8	3,7	Atrial fibrillation	Under treatment with antibiotics due to bacterial osteitis in foot.
Female 80 years old	4,9	4,2	Atrial fibrillation	–
Male 88 years old	2,9	2,3	Atrial fibrillation	Newly home from hospital treatment after falling
Male 88 years old (same as above but a different analysis)	5,2	3,4	Atrial fibrillation	Newly home from hospital treatment after falling
Female 85 years old	4,2	3,0	Atrial fibrillation	
Female 96 years old	3,0	2,5	Atrial fibrillation	

LESSONS AND LIMITATIONS

This study is based on an actual primary care centre and thus the number of patients is limited to those who receive their care here. After the introduction of POC care, the number of medical incidents leading to hospitalization decreased. Reasonably we could hypothesise that this would lead to lower health care costs and better clinical outcomes, however further studies would be required to fully establish this.

We did not measure whether the patient's quality of life was affected by these changes. The new system does mean that the patient has to wait for their prescription. This may take up to half an hour, however it means they don't have to be accessible by phone in the afternoon, as was required with the previous system.

If this study was to be done again, we would consider using a different methodology which tests interventions on a few patients first (small scale) before scaling them up if successful. We would also want to collect more data on a more frequent basis; this would allow us to see how each intervention impacts on the data and also to ensure sustainability over time.

CONCLUSION

POC analysis of PT-INR levels using the Owren PT system was introduced in May 2012 in Tullinge primary care centre. This led to an increase in time in therapeutic range values and a decrease in non-conformance reports. However, in the years to come there was no further increase in TIR values above values found already some years ahead of the introduction. This may indicate that POC analysis helps to prevent the risks of patient misunderstanding rather than increasing TIR values and the quality of prescriptions.

Patients were pleased with the introduction of the POC analysis as it led to faster communications between the laboratory staff and physicians.

The use of the Owren PT system as the primary test, with CoaguChek used only in special cases, seems efficient. Each analysis takes 5-10 minutes extra. We do not have to transfer patients to more expensive treatments such as NOAC and we have an alternative analysis ready when there are confusing results with CoaguChek. To rely only on the latter method would make it hard to resolve situations when its results are outside its range of reliability and in situations where there are questions about its usability. We have found several such situations in the period of time studied (table 1).

Although it would be possible to send samples to a larger laboratory, we would not be able to get the results until the next day. Without the Owren PT system in the care centre, one would also have to send analyses away when performing parallel testing for patients who are starting warfarin. Waiting for the results the next day would cause concern to the patients and extra work to the physician prescribing.

The number of medical complications, as well as TIR values, after the introduction of POC analysis are now in

line with, or even better than, figures given in other studies.^{4 12} Numbers are stable indicating that the increase seen after the introduction are sustainable. We have noticed that this method presented have already spread to other care centres.¹³

We hope that this method can be used also in other settings where a patient must have regular laboratory tests.

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Declaration of interests Nothing to declare.

Ethical approval The study is an improvement study and thereby not requiring ethical approval in accordance to Swedish law. Patients were informed about the POC analysis and could decline to participate with no consequences to their treatment.

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