The effect of nurse-led care on stability time in therapeutic range of INR in ischemic stroke patients receiving warfarin

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ABSTRACT

Purpose: The current study is designed in order to investigate the effect of nurse-led care (the supportive and educational measurements by nurses) on stability time in therapeutic range of INR in ischemic stroke patients receiving Warfarin.

Method: In this quasi-experimental study, 80 ischemic stroke patients were investigated, 40 patients in experimental group and 40 in the control group referred to the nurse-based warfarin clinics affiliated to Shiraz University of Medical Sciences. The mean ± SD duration of the intervention was 144 ± 84 days. The patients based on the percentage stability time in the therapeutic range of INR were classified into 3 groups of good control (>75%), medium control (60–75%), and poor control groups (<60%). The results were analyzed using chi-square and independent t-test according to these categories.

Results: 38 patients in the experimental group and 39 in the control group had the therapeutic range of INR 2–3. The percentage of the stability time in the therapeutic range of INR (mean ± SD) in the experimental group was 64.08% ± 18.7 and in the control group it was 44.58% ± 25.12 (P < 0.001). The percentage of total INRs within the therapeutic range was 52.5% in the experimental group and 40.6% in the control group (P = 0.001).

Conclusions: In conclusion, using the stroke prevention guidelines, thrombotic therapy protocols and familiarity with patients’ diagnosis and risk factors in the experimental group led to more patients’ stability time (The time that patients could remain stable within the INR therapeutic range) in their therapeutic range of INR as the best indicator of clinical performance.

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1. Introduction

Stroke is defined as an “acute neurologic dysfunction of vascular origin due to impaired blood perfusion to the brain” (Sacco et al., 2013). Ischemic and hemorrhagic are the two main types of stroke, accounting for 85% and 15%, respectively. Stroke is the first neuro-vascular impairment in the world and the third leading cause of mortality after coronary heart disease and cancer. In Iran the annual stroke incidence of various ages ranged from 23 to 103 per 100,000 population (Hosseini, Sobhani-Rad, Ghandehari, & Benamer, 2010). Strokes can cause long-lasting disability in the United States and its direct and indirect expenses are about 65.5 billion dollars per year (Brunner, Smeltzer, Bare, Hinkle, & Cheever, 2010; Wann et al., 2011).

Uncontrollable stroke risk factors include age, sex, heredity, history of stroke or earlier transient ischemic attack. The uncontrollable factors include high blood pressure, atrial fibrillation, high blood cholesterol levels, obesity, smoking, excessive alcohol consumption, diabetes, asymptomatic carotid stenosis, valvular heart disease such as endocarditis or prosthetic valves, use of oral contraceptive pills, etc. (Bradley, Daroff, Fenichel, & Jankovic, 2008; Furie et al., 2011; Hinkle & Guanci, 2010). Knowing the signs and symptoms of strokes and control of modifiable risk factors can be lifesaving (Furie et al., 2011). After treatment of ischemic stroke, physicians often, in the acute phase of the disease, prescribe anti-platelet and anti-coagulant agents in order to prevent a recurrent stroke which is called secondary stroke prevention (Caplan, 2015).

Warfarin (Coumadin) is the most common oral anticoagulant used to prevent recurrent stroke. The patients in this therapy should be...
under careful monitoring of coagulation in order to control INR and food and drug interactions of warfarin (Pirmohamed, 2006).

INR below the therapeutic range may increase the risk of stroke; on the other hand, a high level of INR can cause severe bleeding, particularly intracranial bleeding especially in patients older than 65 years. About 15.3% of these bleedings are fatal (Gladstone et al., 2009).

Therefore, the patients' accurate knowledge of nutrition, medication, co-infection diseases (Gurwitz et al., 2007), level of relevant education and social status on one hand (Kaganovsky, Knobler, Rimon, Ozer, & Levy, 2004), and on the other hand necessary trainings associated with drug instruction, drug interactions, food and drug interactions, its precautions and proscriptions and also sustained, systematic and patient-centered control of INR testing, and the appropriate change of dose using the standard international guidelines for the control of the disease, and prevention of common drug complications including bleeding and thromboembolism in different parts of the body are essential for disease control (Ansell et al., 2004).

Moreover, with the loss of communication with the health care system, the chain of handling and control of patient’s drug is broken (Gordon et al., 2012). Based on the experiments and studies, for example, in the study of Hendriks et al. in 2012 aiming at comparing nurse-centered clinics and routine (monitored by cardiologists) care of patients with atrial fibrillation, it has been demonstrated that mortality or hospitalization due to cardiovascular events are fewer (Hendriks et al., 2012). So in order to eliminate the need for follow-up care of these patients, preventing the frequent referral to specialists' offices and hospitalization of these patients and also in order to prevent the patients' financial loss, in Iran and other parts of the world, anticoagulation clinics are run and managed by qualified nurses and physicians.

2. Materials and method

This is an interventional study (quasi-experimental) aiming at determining the effect of nurse-led care on stability time in therapeutic range of INR in ischemic stroke patients receiving Warfarin 2013.

The sample size for the present study was determined 40 for each group and 80 in total and by considering 20% loss of, 50 individuals were considered for each group and in total 100 individuals were included in the study. From 133 patients included 68 were related to the intervention group and 65 were related to the control group. From 68 patients of the intervention group, 28 patients were excluded due to failing to comply with the study rules, completion of treatment before the end of the study, and the disconnection with the clinic because of distance. In the control group 25 patients were excluded due to death, the disconnection with the clinic, and the completion of the treatment. Finally, 40 patients participated in each group. The sampling used was purposive simple sampling. The inclusion criteria were suffering from ischemic stroke, age younger than 76 years, residing in Shiraz or suburbs, one month of taking warfarin, and commitment to be checked by a fixed laboratory. Also, the exclusion criteria were discontinuation of warfarin intake, death, and lack of commitment to the study principles. Moreover, the mean and SD of intervention duration was 144 ± 84 days.

The research centers include Shiraz nurse-centered Warfarin neurology clinic in the clinic of Imam Reza (P.B.U.H.) and other warfarin clinics located in Ali Asghar (P.B.U.H.) hospital, Shahid-Faghihi Hospital and Imam Reza (P.B.U.H) in Shiraz. The study population consisted of two groups. The experimental group consisted of ischemic stroke patients who after the acute phase of disease needed receiving warfarin and by having the referral form from the neurologist referred to warfarin neurology research clinic. The control group were the patients with the same situation but referred to other nurse-based warfarin clinics.

From the total of 133 patients who participated in the study, 68 patients belonged to the experimental group and 65 to the control group. From the total number of 68 patients in the experimental group, 28 were excluded due to lack of compliance (9 patients), completion of treatment before completion of the study (12 patients), and lack of referring to the clinics due to long distance (7 patients). In the control group, 25 individuals were excluded due to: death (3 patients due to severity of disease and old age after getting recruited and enrolled into the study), lack of communication with the clinic (14 patients), or completion of treatment period (8 patients). Finally, 40 patients in each group and a total of 80 patients remained in the study.

Methods of warfarin neurology clinic for patients undergoing intervention were shown in Table 1.

If the patient for any reason at any time had to discontinue warfarin, he/she was excluded from the study and after initiation of warfarin and reaching the desired therapeutic range was included again. Concomitant use of aspirin less than 100 mg daily was allowed during the study. If a specific test had been requested in the previous presentation due to any problems, the result was recorded and compared with the previous tests. In case of any need for education in any area, necessary measures were taken and the trainings were recorded in the patient’s chart. The patient's skin surface was checked for small bleeding, incidence of hematoma or necrosis and the patient was asked about the possibility of bleeding in any different parts of the body, both internal and external.

Nurses play important roles in these clinics, for example checking medical history of the patient and controlling the drug dose according to the INR, consulting with patient and referring him/her to physicians based on the needs of the patient, setting the next appointments, educating regarding the correct instruction of the medication, providing the patient with information regarding the benefits and harms of the drug, making a file for the patient and recording the tests and interacting with the patient's referring physician when necessary.

But despite the existence of warfarin clinics in Iran, few studies have been conducted on proving the quality performance of these clinics in relation to patient care. On the other hand, according to surveys conducted in these clinics, international guidelines of thrombotic therapy and standards of the measurement scales in order to estimate the chances of stroke and bleeding have not been used and also monitoring the anticoagulant medication related risk factors such as thromboembolism and recurrent bleeding has not been performed. Therefore, due to the urgent need of the elderly patients, especially their tracking and continuous care, we decided to identify the high-risk individuals using the guidelines and available scores. And also by relying on the identification of the patients, adjusting INR levels commensurate with risk factors, providing educational services consistent with the need for regular, and frequent follow-up of patients we could keep the patients stable for a longer time within the INR therapeutic range and minimize the medication side effects.

Nurse led care can be usefully viewed as a continuum with, at one end, nurses undertaking highly protocol driven, focused tasks (cardioversion,2 colposcopy, smoking cessation) and, at the other end, responding to far more diverse challenges in terms of clinical decision making, such as first contact care and rehabilitation (Cullum, Spilsbury, & Richardson, 2005).

The main objectives of this study were to determine and compare stability time in therapeutic range of INR and also the change in the index of INR in two groups.
In case of any bleeding, the patient was asked to stop daily intake of warfarin immediately and contact the clinic to take necessary measures with regard to the location and extent of the bleeding. If for any reason the patient needed to be referred to a particular ward in the hospital, he/she was tracked and supported. The researcher’s phone number was provided to the patients, so in case of any doubt/question they could call the researcher.

It should be noted that the average study duration was 4 months and frequency of presentation to the clinic according to the tests results, scores and risk factors have been different for them. It means that for the patients with lower risk factors for stroke or hemorrhage, the INR in the therapeutic range was stable and needed no change in the medication dose; thus, they were asked to be co-operative, take the trainings and refer to the clinic frequently. These patients should refer to the clinic once every 2–4 weeks; otherwise, especially when the patient dose needed change up to more than 20%, he/she was required to refer to the clinic once every 1–2 weeks or even earlier.

In the control group these patients were subjected to clinical intervention routinely in this way that in the first visit by an examination a warfarin dose based on the therapeutic range of INR was prescribed and the clinic protocols began. After the initial adjustment of medication, the patient was in contact with the consultants physically or over phone and the dose was adjusted according to the INR ratio.

It should be noted that the patients of these clinics were individually or collectively trained. These trainings were more relevant to the drug instruction. Warfarin interactions with other medications, a diet tailored to the drug use and drug use in special situations such as pregnancy, lactation or menstruation in women and also informing the patients of warfarin intake risks and the surgical procedures and if the patient INR was unstable, the presentation intervals were close.

But the control group, unlike the experimental group, had no complete records and files; the risk factors associated with the incidence of recurrent stroke and bleeding were not extracted, the provided trainings were not done individually or patient-centered and were not performed in each session frequently and were not based on the extracted risk factors. Also they were not recorded in the patient charts. They were not trained for prevention of recurrent stroke based on the recurrent stroke prevention guideline; also their names and next appointment were not recorded in the patient charts. They were not trained for warfarin and bleeding risk factors given in the preventive guidelines of further strokes in patients with ischemic stroke.

In case of consultation, a call was made to the physician and recommendations were applied. In the case of consultation, a call was made to the physician and recommendations were applied. The blood pressure, pulse and weight of the patient were checked and after being recorded they were compared to the previous levels. PT ratio and new INR of the patient were compared with the previous levels and the therapeutic range of INR (INR 2–3) and if the dose of medication for any reason needed changing, the change was made based on the clinic’s protocol.

The method of calculating the percentage of patients’ stability within the INR therapeutic range is shown in Fig. 1. In this figure, the X-axis shows the time of INR test by the patient and the Y-axis shows the INR therapeutic ranges which are marked by two cross lines on the diagram. After identifying the points on the diagram based on the INR value and the date of testing, the distances between these points are connected by lines and a diagram based on the above measures was obtained. At the end, the stabilization period of INR for each patient in the therapeutic range was calculated using the following formula:

\[
\frac{\text{Sum of the interval in the therapeutic range (in cm)} - \text{Sum of the interval out of then therapeutic range (in cm)}}{\text{total time duration (in cm)}} \times 100
\]

Finally after calculation of the results, from the obtained values in both groups of 1 and 2, mean and standard deviation for all the patients were obtained. Data collection in experimental group included demographic data, diagnosis and appropriate INR levels, background diseases, type of

**Table 1**

Methods of warfarin neurology clinic for experimental group.

<table>
<thead>
<tr>
<th>First meeting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial filing and getting acquainted</td>
</tr>
<tr>
<td>Completing the examination forms and extract of the patient’s risk factors for</td>
</tr>
<tr>
<td>recurrent stroke and bleeding based on the preventive guidelines of further</td>
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<tr>
<td>strokes with ischemic stroke</td>
</tr>
<tr>
<td>Recording or asking tests for the patients</td>
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<tr>
<td>Providing education required in connection with the correct medication intake</td>
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<tr>
<td>Making the patient aware of extracted risk factors and helping to control</td>
</tr>
<tr>
<td>them</td>
</tr>
<tr>
<td>Adjusting the dose of medication based on the clinical protocol that has</td>
</tr>
<tr>
<td>been developed in accordance with the latest protocols for thrombotic therapy</td>
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<tr>
<td>Education regarding the importance of follow-up</td>
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<table>
<thead>
<tr>
<th>Second meeting</th>
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<tbody>
<tr>
<td>The blood pressure, pulse and weight of the patient were checked and after</td>
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<td>being recorded they were compared to the previous levels</td>
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<tr>
<td>PT ratio and new INR of the patient were compared with the previous levels</td>
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<td>and the therapeutic range of INR (INR 2–3) and if the dose of medication for</td>
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<tr>
<td>any reason needed changing, the change was made based on the clinic’s protocol</td>
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<tr>
<td>The control group, unlike the experimental group, had no complete records</td>
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<td>and files; the risk factors associated with the incidence of recurrent</td>
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<td>stroke and bleeding were not extracted, the provided trainings were not done</td>
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<td>individually or patient-centered and were not performed in each session</td>
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<td>frequently and were not based on the extracted risk factors. Also they were</td>
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<td>not recorded in the patient charts. They were not trained for prevention of</td>
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<tr>
<td>recurrent stroke based on the recurrent stroke prevention guideline; also their</td>
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<tr>
<td>names and next appointment were not recorded in the appointment book. Thus,</td>
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<tr>
<td>only the patients who presented to the clinic themselves were supported by the</td>
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<tr>
<td>clinic and those who did not refer to the clinic were not identified, so we</td>
</tr>
<tr>
<td>could not be sure whether the patient is in a healthy situation or is suffering</td>
</tr>
<tr>
<td>from dangerous complications associated with warfarin intake or died.</td>
</tr>
</tbody>
</table>

The method of calculating the percentage of patients’ stability within the INR therapeutic range is shown in Fig. 1. In this figure, the X-axis shows the time of INR test by the patient and the Y-axis shows the INR therapeutic ranges which are marked by two cross lines on the diagram. After identifying the points on the diagram based on the INR value and the date of testing, the distances between these points are connected by lines and a diagram based on the above measures was obtained. At the end, the stabilization period of INR for each patient in the therapeutic range was calculated using the following formula:
activity and movement restrictions after stroke, types of drugs, invasive interventions such as surgery or invasive diagnostic procedure performed on the patients, the flowchart showing the INR and PT tests and the intake dose of medication, the date of his/her visit, other routine tests’ flowchart and based on the clinical protocols and a part related to the provided trainings by the nurses to the patients.

The data collection in control group under the supervision of other warfarin clinics was limited to the information in the patient’s record or warfarin booklet provided to them and by a form designed by the researcher consisting of demographic data, the diagnosis and INR ratio, background diseases, the INR or PT ratio, and proper dose of proper medication. The warfarin booklet contains demographic features, the medical history of patient, the information about using warfarin, its side effects, the way of coping with side effects, how to use warfarin during pregnancy and lactation, contraindications to warfarin and necessary measures to prevent recurrent stroke.

3. Statistical analysis

For data analysis, Chi-square was used to compare the demographic data between the two groups and independent t-test was used to compare the percentage of stability time between the two groups. P was significant at less than 0.05.

4. Results

The present study was conducted on 80 patients with a mean ± SD of age 60 ± 11.2 in the experimental group and 62.8 ± 9.9 in the control group; they were in at the same age and sex distribution and most of patients were 60–74 years old. Smoking among men in the 2 groups was more prevalent (Table 2).

The details of the follow-up of patients in the two groups were so that INR was measured in the experimental group 321 times and in the control group it was 29 ± 15 days. The mean ± SD of the checked INR per patient in the experimental and control groups were 8 ± 4 and 7.8 ± 3.5 respectively. The repetition interval of INR in the experimental group was 20 ± 12 days and in the control group it was 29 ± 15 days.

At the end of the study, from the 40 studied patients in each group, 38 patients in the experimental group and 39 in the control group had the therapeutic range of INR 2–3. Moreover, 2 individuals in the experimental group and 1 in the control group due to artificial mitral valve were candidates for warfarin therapy in the range of INR 2.5–3.5 (Table 3).

The percentage of patients’ stability time in the therapeutic range of INR in the experimental group was 20% higher than the control group and the impact on the clinical care of patients in the experimental group was 45% higher than the control group. Moreover 70% of the studied patients in the control group in less than 60% of the study time had the therapeutic range of INR 2–3. Moreover, 2 individuals in the experimental and control groups were 8 ± 4 and 7.8 ± 3.5 respectively. The repetition interval of INR in the experimental group was 20 ± 12 days and in the control group it was 29 ± 15 days.

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The percentage of patients’ stability time in the therapeutic range of INR in the experimental group was 20% higher than the control group and the impact on the clinical care of patients in the experimental group was 45% higher than the control group. Moreover 70% of the studied patients in the control group in less than 60% of the study time had stabilization of INR within the therapeutic range and were in the poor clinical control group while this rate in the experimental group was 45% and about 55% of the patients in the experimental group have good and moderate clinical controls (Table 4).

The comparison of patients’ INR by separation of results obtained from the INR of the two groups showed that 52.5% of the INR results in the experimental group and 40% of the control group were in the therapeutic INR range. Seventy seven patients were in the treatment range of 2–3, and the other three individuals were in therapeutic range of 3.5–5/2. At first, there was no statistically significant difference between the two groups (P = 0.3). However, according to several studies, a certain INR therapeutic range cannot be assumed for all diseases, but the average therapeutic range of 2–3 was safe and effective for most diseases and as to the incidence of adverse drug effects such as thromboembolism and bleeding it is more secure (Ansell et al., 2004).

Only two groups of patients with prosthetic heart valves in the mitral position, or both simultaneously at the aortic and mitral valve (Ansell et al., 2004) and also patients with a history of anti-phospholipids

5. Discussion

The overall age range of the patients in both groups was between 32 and 74 years which is consistent with the age range of 23–80 years in the Po et al.’s study (Po, Lin, & Hseuh, 2009). After age 55 for every 10 year increase in age, the risk of stroke doubles (Bradley et al., 2008). And as you can see 54 patients (67.5%) were between 60 and 80 years of age in this study and that is the actual evidence for this claim. According to the results of Kagansky et al.’s study, older age, background diseases and intake of multiple drugs can cause more unwanted complications while taking it, due to affecting pharmacokinetics and pharmacodynamics of Warfarin medication (Kagansky et al., 2004). Since the majority of ischemic stroke patients are old, they need systemic and unremitting clinical care. The widespread use of warfarin clinics to coordinate the delivered cares especially in the elderly people increases the safety and effectiveness of drug therapy with anticoagulants.

Although both study groups had the same mean of sex distribution, in general, the ratio of females to that of males was 1/17 in the study. In the study of Goldstone, from the 597 patients suffering from atrial fibrillation who experienced ischemic stroke for the first time, the ratio of females to males was 1/3 (Gladstone et al., 2009). But in the study of Poe et al. in 2000, men outnumbered women by 1/7.

Risk of vascular diseases in premenopausal women due to the influence of female hormones and a high ratio of HDL to LDL is less than men, but in early postmenopausal period the chance is equal for both sexes (Brunner et al., 2010). Because most patients with ischemic stroke suffered from this disease in ages older than 40 years, perhaps the differences in the ratio of suffering in different studies are due to the age of stroke incidence and menopausal period in women. In some studies like the current one, the ratio of suffering from this complication in women in comparison with men not only is not less but also is more.

Cigarette smoking is a major independent risk factor for ischemic stroke risk (Kawachi et al., 1993). The danger is observed in all ages, both sexes and among different ethnic groups (Wolf, D’Agostino, Kannel, Bonita, & Belanger, 1988). In a meta-analysis, it was found that smoking doubles the risk of stroke (Shinton & Beevers, 1989) and it is done by changing the dynamics of the blood (Wilhelmsen et al., 1984) and CVD (Bonita, Duncan, Truelsen, Jackson, & Beaglehole, 1999).

Based on the obtained results of this study, a total of 17.5% of the patients in the two methods smoked. In the study of Poe et al. 41% of the patients and in the study of Goldstone et al. 27.1% of the patients were smokers. According to the study of Mianes et al., smoking doubles the need of warfarin (1/7) (Lim, Crowther, & Eikelboom, 2006).

In the current study, the patients were divided into two groups as to the therapeutic INR range. Seventy seven patients were in the treatment range of 2–3, and the other three individuals were in therapeutic range of 3/5–5/2. At first, there was no statistically significant difference between the two groups (P = 0.3). However, according to several studies, a certain INR therapeutic range cannot be assumed for all diseases, but the average therapeutic range of 2–3 was safe and effective for most diseases and as to the incidence of adverse drug effects such as thromboembolism and bleeding it is more secure (Ansell et al., 2004).
antibody positive who in addition to the use of warfarin in the therapeutic range still suffer from venous thrombosis (Lim et al., 2006) should inevitably use warfarin in the INR range of over 3. In our study, only 2 patients, 1 in the experimental group and 1 in the control group due to artificial heart valve at the mitral were controlled in the INR therapeutic range of 2.5–3.5 and the rest of the patients had therapeutic range of 2–3.

Optimal sequences of INR monitoring will be affected by many factors such as the ability of the patient to accept the medication, co-infection diseases and volatility of diseases during warfarin therapy, addiction, diet and drug changing, and quality of dosage control (Ansell et al., 2004).

Also, according to the studies such as that of Francavilla in 2006 (Francavilla, 2008) and Kagansky et al. in 2004 (Kagansky et al., 2004), the INR checking intervals vary for different patients but mostly the point is that if the patient at a recent appointment needs no change in the dosage of the drug, once every 4 weeks he/she should be tested; otherwise, once every two weeks the tests should be repeated.

In our study, in the experimental group which was under the supervision of the researcher, the same method was used.

On average, in one out of 20 the testing was checked, but in other clinics routinely the patients’ INR was checked monthly so the average intervals of their tests was approximately 29 days.

To monitor the quality control of the drug in the nurse-centered warfarin clinics under the supervision of the researcher and other warfarin clinics based on extensive meta-analysis, White and his colleagues used the time percentage of stability in the therapeutic INR range of 22, that includes the main objective of this study, too (White et al., 2016).

Based on the obtained results of the study, the percentage of patients’ stability in the therapeutic range of INR in the experimental group was 64.08 ± 18.7 and in the control group it was 44.58 ± 25.12. According to White's study, clinical control in general in the experimental group under the supervision of the researcher was average 25.12. According to White’s study (White et al., 2016), even with good medical care, only one third of the patients had stability in the therapeutic INR range over 75% of the studied time.

In our study, in the experimental group under the intervention of the researcher, 32.5% of the patients or exactly one third of them had therapeutic INR range stability more than 75% of the study time while in the control group, 15% or about one-seventh of the patients were in the therapeutic range.

On the other hand, according to the findings of White’s study, only 67.5% of the patients’ INR were within the therapeutic range. Based on these findings, we categorized the patients’ INR results in Table 4 and reached the conclusion that in the experimental group approximately 52.5% of the patients’ INR was in desired therapeutic range of 2–3 while in the control group about 40% of the patients were in the INR range. Most of the INRs or about 47% were in the range of less than 2; according to many researches done in this area, this range is associated with the risk of multiple thromboembolism in patients (Ansell et al., 2004; Gurwitz et al., 2007).

According to Kagansky’s study, 35.4% of total measured INRs were between 2 and 3, 48.5% were less than 2, and 16.1% were higher than 3 (Kagansky et al., 2004). So, in the Gurwitz’s study after categorizing the measured INRs, 36.5% of them were less than 2, 49.6% were between 2 and 3, 11.9% were between 3 and 4.5, and 2% were high than 4.5 (Gurwitz et al., 2007).

### 6. Conclusions

In conclusion, using the recurrent stroke prevention guidelines, thrombotic therapy protocols and familiarity with patients and risk factors for thromboembolism and bleeding in ischemic stroke patients in the experimental group led to more patients’ stability in their INR therapeutic range. This nurse-led warfarin monitoring protocol improved INR control in this clinic, and that other nurses could use this protocol to achieve better results in their own clinics.

### 7. Recommendations

Based on the obtained results, studies with larger population and longer duration and also evaluation of nutrition impact on INR control while taking warfarin; examination of relationship between patients’ stability in therapeutic range of INR and medications’ adverse effects such as recurrent thromboembolism and bleeding, the educational levels of the patients; the economic status of the patients and their family support during the treatment; examination of the impact of change in the season on INR fluctuations; and satisfaction levels of patients about the delivered cares in the nurse-centered clinics in comparison with the physician-centered are recommended. This nurse-led warfarin

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**Table 3**

INR control and follow-up of patient in the 2 groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Experimental group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Totally</td>
<td>321</td>
<td>317</td>
<td></td>
</tr>
<tr>
<td>INR goal 2–3</td>
<td>294</td>
<td>305</td>
<td></td>
</tr>
<tr>
<td>INR goal 2.5–3.5</td>
<td>23</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>INR per 1 patient, mean ± SD</td>
<td>8 ± 4</td>
<td>7.8 ± 3.5</td>
<td>0.75</td>
</tr>
<tr>
<td>Time between INR measurement, day, mean ± SD</td>
<td>20 ± 12</td>
<td>29 ± 15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>INR goal, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–3</td>
<td>38 (95)</td>
<td>39 (97.5)</td>
<td></td>
</tr>
<tr>
<td>2.5–3.5</td>
<td>2 (5)</td>
<td>1 (2.5)</td>
<td></td>
</tr>
</tbody>
</table>

P values are significant at less than 0.05.

**Table 4**

Patients’ stability in therapeutic range of INR in the 2 groups according to INR control.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Experimental group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of patient stability in therapeutic range of INR, mean ± SD</td>
<td>64.08 ± 18.7</td>
<td>44.58 ± 25.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>INR control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good control group (&gt;75%)</td>
<td>32.5</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Moderate control group (60–75%)</td>
<td>22.5</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Poor control group (&lt;60%)</td>
<td>45</td>
<td>70</td>
<td></td>
</tr>
</tbody>
</table>

P values are significant at less than 0.05.

**Table 5**

Percentage of INR according to patients’ achieved INR value in the 2 groups.

<table>
<thead>
<tr>
<th>Achieved INR value</th>
<th>Experimental group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR &lt; 2</td>
<td>31.6</td>
<td>46.8</td>
<td>0.001</td>
</tr>
<tr>
<td>2–3</td>
<td>52.5</td>
<td>40.6</td>
<td></td>
</tr>
<tr>
<td>3–4.5</td>
<td>13.1</td>
<td>11.1</td>
<td></td>
</tr>
<tr>
<td>INR &gt; 4.5</td>
<td>2.8</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>INR, mean ± SD</td>
<td>2.43 ± 0.9</td>
<td>2.1 ± 0.93</td>
<td>0.001</td>
</tr>
</tbody>
</table>

P values are significant at less than 0.05.
monitoring protocol improved INR control in this clinic, and that other nurses could use this protocol to achieve better results in their own clinics.

8. Limitation

- Inability to control complications resulted by warfarin
- Lack of coordination in the frequency of control of PT and INR in all cases because of differences in patients’ conditions
- Lack of regular referral of patients to the clinic.

Conflict of interest

The authors have no conflict of interest.

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