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Effectiveness of the telepharmacy service for frail older adults on warfarin

Avaliação da efetividade do serviço de telefarmácia para idosos frágeis usuários de varfarina

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ABSTRACT
This was a before-and-after quasi-experimental study with a single group of individuals, conducted between January 2020 and April 2022, to investigate the profile of use, effectiveness, and safety of warfarin among older adults followed up at a senior outpatient clinic and the impact of a pharmaceutical telemonitoring service. The proportion of older adults with the International Normalized Ratio (INR) within the target range was compared before and after offering the service by Pearson's chi-square test. A total of 53 older adults were included in the study. Most participants were women (66.0%), mean age of 78.1 years, and on use of warfarin for atrial fibrillation (49.0%), and a monthly average of 49.7 telemonitoring calls. After offering the service, the proportion of older adults with INR in the target range increased (from 50.9% to 64.1%; p = 0.022). The INR pharmaceutical telemonitoring service had a positive impact, evidencing the importance of following up with the older users of warfarin to achieve effective and safe pharmacotherapy.

Keywords: Anticoagulants. Pharmaceutical services. Frail elderly. Telemonitoring. Warfarin.

RESUMO
Estudo *quasi*-experimental do tipo antes e depois com grupo único de indivíduos, realizado entre janeiro/2020 e abril/2022, com objetivo de investigar o perfil de utilização, a efetividade e a segurança da varfarina entre idosos acompanhados em ambulatório de geriatria, bem como o impacto de um serviço farmacêutico de telemonitoramento. A proporção de idosos com a Razão Normalizada Internacional (RNI) dentro da faixa-alvo foi comparada antes e depois da oferta do serviço por meio do teste de qui-quadrado de Pearson. Foram incluídos 53 idosos, maioria feminina (66,0%), média de idade de 78,1 anos e média mensal de 49,7 telemonitoramentos. Identificou-se que após a oferta do serviço a proporção de idosos com RNI na faixa-alvo aumentou (de 50,9% para 64,1%; p = 0,022). O serviço farmacêutico de telemonitoramento de RNI impactou positivamente, destacando a importância do acompanhamento de idosos usuários de varfarina para obtenção de uma farmacoterapia efetiva e segura.

Palavras-chave: Anticoagulantes. Assistência farmacêutica. Idoso fragilizado. Telemonitoramento. Varfarina.

INTRODUCTION

Older people live with multiple chronic diseases, have a greater need to use health services, and require more medications. Furthermore, with the ongoing aging process and the expansion of access to medicines, the tendency is to increase their use by this population[1].

The use of medications among these individuals is associated with the development of adverse events as they undergo physiological changes that lead to changes in the pharmacokinetics and pharmacodynamics of the drugs used. These people generally have several chronic diseases and use multiple medications[2,3].

Some medications considerably increase the risk of adverse events among older adults, especially those with a low therapeutic index, and that require frequent follow-up, such as anticoagulants. This class generally serves for primary and secondary prophylaxis of thromboembolic events, one of the main causes of death in the world[4]. People over the age of 75 are at high risk for cardiovascular events, such as ischemic stroke. Although it is known that aging and multimorbidity predispose to hemorrhagic conditions, the use of this drug in this population is still relevant despite the potential risks[5].

Warfarin is an effective anticoagulant for the prevention of thromboembolic events widely used in Brazil for various indications, especially among older people, despite the introduction of direct-acting oral anticoagulants[6-9]. However, its use requires appropriate management, aiming to achieve control within the desired therapeutic range, in addition to preventing thromboembolic or hemorrhagic episodes. Factors such as individual variability in response to medication and multiple interactions with drugs and foods (especially those containing vitamin K) make warfarin management difficult[10,11].

Therefore, monitoring the use of warfarin is essential for health promotion and is carried out using the International Normalized Ratio (INR)[11,12]. The variation in INR values can be greater among older adults, reinforcing the need for even more careful follow-up[13]. In this context, warfarin monitoring services have been implemented in different contexts in Brazil and worldwide, and their effectiveness has already been demonstrated[14-20].

Telemedicine and telehealth have had a resolution approved by the World Health Organization since 2005; however, they began to form part of health services more robustly and gained notable visibility with the COVID-19 pandemic[21]. On the international scene, some studies used telemedicine services combined with the use of applications to monitor patients on anticoagulants[22-24]. From a national point of view, only one Brazilian study described the use of telemonitoring to manage older patients on oral anticoagulants[25].

Recently, the Federal Pharmacy Council approved a resolution that defines telepharmacy as the exercise of clinical pharmacy carried out using information and communication technology remotely, synchronously, or asynchronously, intending to promote, protect, monitor, and recover health, disease prevention, and other health difficulties, as well as for solving pharmacotherapy problems, for the rational use of medicines and other health technologies (CFF, 2022)[26].

In this sense, the present study aimed to investigate the profile of use, effectiveness, and safety of warfarin among frail older people followed up at a senior outpatient clinic in supplementary health in Belo Horizonte, state of Minas Gerais, as well as the impact of a pharmaceutical INR telemonitoring service.

METHODOLOGY

STUDY DESIGN

This was a *quasi*-experimental before-and-after study with a single group of individuals. This type of study is recommended by the World Health Organization for evaluating real-world services[27].

LOCATION OF THE STUDY

The study was carried out in a supplementary health senior outpatient clinic located in Belo Horizonte, state of Minas Gerais, which serves older patients (aged 60 years or over, according to legislation in Brazil)[28]. More than 4,000 older people who have health insurance plans are under the care of the health team at this location.

The multidisciplinary team is made up of geriatricians, cardiologists, nephrologists, endocrinologists, psychiatrists, family and community physicians, nurses, pharmacists, nutritionists, psychologists, physical therapists, and speech therapists. With a holistic, horizontal, and comprehensive approach, these people are monitored through consultations, telemonitoring, therapeutic groups, and matrix support.

THE OUTPATIENT INR MONITORING SERVICE

The outpatient INR monitoring service was developed to help patients taking warfarin who need to undergo regular tests to check whether the INR is within the established therapeutic range. The implementation of the service took place in four stages, and the last one represented the moment when the follow-up began. In this stage, which began in January 2020, the pharmacist communicated with all older people on warfarin to monitor its effectiveness and safety parameters. This service was provided exclusively by telephone, and everyone received at least one contact for monthly telemonitoring. In this study, questions were asked about IRN value and exam date, eating routines and habits, use of other medications (such as inclusion or deprescription), and intake of alcoholic beverages.

Patients/caregivers were also asked to send the results of INR exams, which were entered into the medical record. If the pharmacist identified altered values (outside the range of 2 to 3), dose adjustment was provided as necessary, in partnership between the pharmacist and the attending physician.

STUDY POPULATION

The study included 53 older patients (aged 60 years or over) on warfarin and treated at the senior outpatient clinic from January 2020 to April 2022 and who had at least two INR exams during the period.

DATA COLLECTION AND VARIABLES

All data were collected retrospectively through reports generated by the electronic system "LifeCode – Intelligence & Health," in which information regarding patients treated at the institution is recorded. The following data documented in the initial assessment of the older patients were collected: age, sex, and IVCF-20 (Clinical-Functional Vulnerability Index-20). Other data relating to any hospitalization due to thromboembolic or hemorrhagic events during the study period were also obtained.

Information on the use of warfarin, including dosage and therapeutic indication, was also collected for all patients, in addition to the first and last INR values documented during the study period.

DATA ANALYSIS

A descriptive analysis of the demographic and health data of all older people was carried out by determining the absolute and relative frequencies of qualitative variables and means and standard deviation for quantitative variables.

The frequency and cause of hospitalizations due to thromboembolic or hemorrhagic events were described for the period before and after inclusion in the outpatient INR monitoring service.

The use of warfarin was reported according to the concentration used and frequency of use. The initial (first documented value in the medical record for the study period) and final (last documented value) INR values were presented as mean and standard deviation.

Furthermore, the frequency of values below, within, or above the INR target range established for older adults was determined, which was sometimes defined as between 2 and 3 (lower target) and between 2.5 and 3.5 (upper target), according to the patient's clinical profile.

The proportions of older adults with an INR value within the target range before and after the telemonitoring service were compared using the chi-square or Fisher's tests. A statistical significance level of 5% was adopted. All statistical analyses were carried out using the Stata® program, version 12.0.

ETHICAL AND LEGAL ASPECTS

The present study is part of the project "Profile of medication use and deprescription in an outpatient clinic," approved by the Research Ethics Committee (CEP) of UFMG on November 30, 2021, under registration number CAAE 52595821.1.0000.5149.

RESULTS

Participants were 53 older adults, with a predominance of female patients (n = 35; 66.0%), mean age of 78.1 ± 8.8 years (minimum = 62 years; maximum = 99 years), and mean IVCF-20 value of 18.5 ± 5.6 (minimum = 12; maximum = 37). The main indication for the use of warfarin was atrial fibrillation (n = 26; 49.0%), followed by venous thromboembolism (n = 11; 20.7%) (Table 1).

Table 1. Frequency of indications for the use of warfarin in a senior outpatient clinic (n = 53). Belo Horizonte, state of Minas Gerais, 2020-2022

Indications	n	%
Atrial fibrillation	26	49
Venous thromboembolism	11	20.7
Atrial fibrillation + valvulopathy	4	7.5
Atrial fibrillation + prostheses	3	5.7
Atrial fibrillation + venous thromboembolism	2	3.8
Prosthetics/Pacemaker	2	3.8
Venous thromboembolism + thrombophilia	1	1.9
Valvulopathy	1	1.9
Thrombophilia	1	1.9
Thrombophilia + atrial fibrillation	1	1.9
Mitral stenosis	1	1.9
Total	**53**	**100**

*11 older adults had more than one diagnosis.

Source: prepared by the authors.

Regarding the profile of warfarin use, most older patients used the drug at a dose of 5 mg, once a day, every day of the week (n = 35; 66.0%). The second most used dose was 2.5 mg administered once a day on every day of the week (n = 12; 22.6%) (Table 2).

Table 2. Warfarin concentration and frequency of administration (n = 53). Senior outpatient clinic. Belo Horizonte, state of Minas Gerais, 2020-2022

Warfarin concentration	Frequency of administration n (%)		
	Once a day	Every other day	Three times a week
1 mg	1 (1.9)	0 (0)	0 (0)
2.5 mg	12 (22.6)	1 (1.9)	1(1.9)
5 mg	35 (66.0)	0 (0)	0 (0)
7.5 mg	1 (1.9)	0 (0)	0 (0)

* The dosage was not documented in the system for two older adults.

Source: prepared by the authors.

Telemonitoring of all older adults on warfarin occurred monthly; however, not every attempt was successful. Therefore, 1,392 effective telemonitoring services were carried out (monthly average of 49.7).

At the beginning of the study period, the average INR was 2.4 ± 0.8 (minimum = 1.0; maximum = 4.5); at the end, this average was 2.6 ± 0.8 (minimum = 1.4; maximum = 6.0). Before implementing the outpatient telemonitoring service, most participants had INR within the target range (n = 27; 50.9%), followed by those with values below the target range (n = 20; 37.7%) and those with values above the target range (n = 6; 11.3%). At the end of the follow-up, 11 individuals had INR values below the target range (20.8%) and eight above the range (15.1%). The proportion of people with an INR value within the desirable therapeutic range increased to 64.1% (n = 34), a statistically significant difference (p = 0.022) (Table 3).

Table 3. Comparison of the first and second INR values documented according to the target range (n = 53). Senior outpatient clinic. Belo Horizonte, state of Minas Gerais, 2020-2022

Variable	First documented INR value* n; (%)	Last documented INR value * n; (%)	*p-value*
Below therapeutic range	20; (37.7)	11; (20.8)	**
Within therapeutic range	27; (50.9)	34; (64.1)	p = 0.022
Above therapeutic range	6; (11.3)	8; (15.1)	**

*Within the target range: 2 to 3 or 2.5 to 3.5 according to the patient's clinical profile.

** p-value with no statistical significance

Source: prepared by the authors.

In the period before joining the service, there were two hospitalizations related to thromboembolic events (one case of deep vein thrombosis and another of deep vein thrombosis associated with pulmonary thromboembolism). After entering the service, there was one hospitalization due to an upper digestive hemorrhage, and another, due to a stroke.

DISCUSSION

The present study demonstrated an increase in the proportion of older people with INR values within the therapeutic range and a decrease in extreme values after the start of outpatient follow-up; such an increase was considered statistically significant. This

difference demonstrates that the outpatient INR telemonitoring service had a positive impact on the older adults, reducing the risk of a thromboembolic or hemorrhagic event. This is especially relevant when taking into account a group of older people with a high average age and IVCF-20, demonstrating a more complex frailty profile.

Therefore, closer follow-up of patients on warfarin has significant positive potential, mainly because it is a high-alert medication and requires even more caution in its use, especially among older adults. International literature states that the pharmacist included in the multidisciplinary team is responsible for promoting health, adding quality to the care provided, and essential for improving the parmacotherapy management and the control of anticoagulation[17,29-31].

The pharmaceutical telemonitoring service was carried out during the COVID-19 pandemic, when care for older patients was highly challenging, as this population was considered at risk for developing more severe cases of the disease. It has already proven effective in managing patients with chronic diseases, with significant results[32]. However, this is the first study evaluating the impact of a pharmaceutical INR telemonitoring service in a senior outpatient clinic. National and international studies have also identified positive advances with similar services in other settings.

Research carried out in an American hospital also highlighted the impact of pharmacist-led warfarin management protocol. The percentage of INR values within the therapeutic range increased from 27.8% to 38.5% with this protocol[33].

Another study developed at the Heart Institute (InCor) of the Medical School of the University of São Paulo (FMUSP) recorded an increased risk of some thromboembolic or hemorrhagic events before being monitored by a pharmacist[34]. A literature review on the pharmacotherapeutic follow-up of outpatients on warfarin revealed a variation of 60.0% to 88.0% in INR values within the therapeutic range of those treated in anticoagulation outpatient clinics and monitored by a multidisciplinary team, including the pharmacist. Furthermore, the frequency of INR values above the range is reduced for patients in these outpatient clinics with multidisciplinary teams[10].

Work developed in Colombia demonstrated benefits after implementing monitoring of patients on warfarin, including the reduction in INR rates outside the therapeutic range and bleeding complications (reduction in emergency care and fewer hospitalizations per year)[35].

Some challenges faced in the service may have minimized its impact. Firstly, it is worth highlighting the fact that, even with the communication effort on the part of the pharmacist, many patients (20.0% to 30.0%) did not send the test results within the proposed period, requiring more contacts by this professional.

The availability of patients and/or those in charge of their care to answer the phone is also a factor that may have interfered with the lack of more significant responses. When the telephone call could not be answered, a callback was requested, or a new contact attempt was made, this callback did not always happen. Therefore, new test results and/or complementary information, such as new medications included in pharmacotherapy (or even suspension of others) and changes in eating habits, which were relevant data for recording during follow-up, could not be collected and consequently not counted for assess whether any change in the INR value could be explained by these causes.

Nevertheless, even given the limitations characteristic of a real-world service, follow-up made it possible to obtain positive results, evidencing its potential to provide better effectiveness and safety in warfarin treatment in the senior outpatient clinic studied. Furthermore,

pharmacotherapeutic follow-up favors patients' quality of life and, in the present study, proved to be a great ally in achieving favorable results similar to those found by Cope et al. during the Covid-19 pandemic.[36]

When talking about health promotion for older adlts on warfarin, better INR control is considered a fundamental strategy in preventing thromboembolic events and bleeding, providing a lower risk of hospitalizations for these causes. In this sense, the present study also reinforces the role of the pharmacist, inserted in a multidisciplinary team, as a health promoter with regard mainly to the correct guidance for frail users of oral anticoagulants on an outpatient basis.

From a practical point of view, the telemonitoring service made it possible to improve INR values and expand pharmaceutical care. In addition, it proved capable of guaranteeing access to information, health education, and solving problems related to pharmacotherapy more quickly.

The limitations found during follow-up may explain the lack of more significant results and serve as a model so that, in other studies and/or telemonitoring services, strategies can be created to minimize the influence of these limitations.

CONCLUSION

The positive impact of the pharmaceutical telemonitoring service in a senior outpatient clinic is proven by the increase in the number of patients who presented, at the end of the analyzed period, INR values within the established therapeutic range. In this way, the importance and responsibility attributed to the pharmacist in health promotion are also observed, highlighting the need for pharmacotherapeutic follow-up to obtain more effective and safe pharmacotherapy, especially in cases of using more complex medications with a narrow therapeutic index.

Therefore, opportunities open up for this professional to be present throughout the treatment along with other members of the multidisciplinary team to achieve the outlined objectives and be responsible for contributing to the excellence of care provided to patients and improving their quality of life.

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