Analysis of the quality of anticoagulation with vitamin K antagonists in three clinical scenarios in Mexico

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Abstract

Introduction: Vitamin K antagonists (VKA) are a therapeutic alternative in patients with venous thromboembolic disease; however, numerous factors affect their pharmacology. **Objective:** To evaluate the quality of VKA anticoagulation at three different time periods in Mexico. **Methods:** Prospective study, nested in patient cohorts at three different clinical scenarios between 2013 and 2019. Outpatients with indication for treatment with VKAs for at least 12 months were included. Patients were managed according to the criteria of the treating physician. **Results:** Patient general characteristics were similar between groups, except for the VKA indication. The results of 4,148 patients and 38,548 INR assessments were analyzed. The times in therapeutic range during the three phases of the study and pooled data were significantly higher for the anticoagulation clinic. Only the number of patient visits was significantly associated with the results, unlike age, gender, and type of VKA. **Conclusions:** VKAs are widely used, but it is difficult for therapeutic goals to be achieved, especially in non-specialized clinical services. Creation of anticoagulation clinics is an urgent need for the Mexican health system.

KEY WORDS: Vitamin K antagonists. Thrombosis. Thromboembolism. Anticoagulation clinics. International Normalized Ratio. Time in therapeutic range.

Análisis de la calidad de la anticoagulación con antagonistas de la vitamina K en tres escenarios clínicos en México

Resumen

Introducción: Los antagonista de la vitamina K (AVK) son una alternativa terapéutica en los pacientes con enfermedad tromboembólica venosa; sin embargo, numerosos factores afectan su farmacología. **Objetivo:** Evaluar la calidad de la anticoagulación AVK durante tres diferentes periodos en México. **Métodos:** Estudio prospectivo, anidado en cohortes de pacientes en tres escenarios clínicos entre los años 2013-2019. Se incluyeron pacientes no hospitalizados con indicación para recibir AVK por al menos 12 meses, quienes fueron manejados de acuerdo con el criterio del médico tratante. **Resultados:** Las características generales de los pacientes fueron similares entre los grupos, excepto por la indicación para usar los AVK. Se analizaron los

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Date of reception: 20-01-2021

Date of acceptance: 10-02-2021

DOI: 10.24875/GMM.M21000559

Gac Med Mex. 2021;157:284-292

Contents available at PubMed

www.gacetamedicademexico.com

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resultados de 4148 pacientes y 38 548 evaluaciones de INR. Los tiempos en rango terapéutico durante las tres fases del estudio y los datos acumulados fueron significativamente mayores en la clínica de anticoagulación. Solo el número de visitas de control de los pacientes se asoció significativamente con los resultados, a diferencia de la edad, el sexo y el tipo de AVK. **Conclusiones:** Los AVK se utilizan ampliamente, pero es difícil alcanzar la meta terapéutica, sobre todo en servicios clínicos no especializados. La creación de clínicas de anticoagulación es una necesidad urgente en el sistema mexicano de salud.

PALABRAS CLAVE: Antagonistas de la vitamina K. Trombosis. Tromboembolismo. Clínicas de anticoagulación. Cociente estandarizado internacional. Tiempo en rango terapéutico.

Introduction

Vitamin K antagonists (VKA) are an effective alternative for the prevention and treatment of patients with venous thromboembolic disease (VTE), non-valvular atrial fibrillation (AF) and in mechanical heart valve (MHV) carriers. VKAs still constitute a type of treatment commonly used in clinical practice, since they are backed by a large amount of evidence generated in clinical trials, which support their efficacy; their use is endorsed by countless national and international guidelines.¹⁻³

Maintaining VKA therapy control quality is necessary for reducing thrombotic and hemorrhagic complications associated with VKA use, which is why frequent monitoring of their effect is required. However, these anticoagulants are not easy to manage due to their multiple interactions with food and drugs, and because they are often indicated in elderly patients with multiple comorbidities. Due to all these difficulties and their consequent impact against constantly maintaining the desired therapeutic anticoagulation range, they are often underused.⁴

VKAs require individual dosing due to the high number of factors that affect their pharmacology, a fact that turns them into a challenge for achieving stable anticoagulation. Therefore, monitoring VKA therapy is an absolutely necessary strategy in order to minimize fluctuations of its pharmacological effect. Recent studies indicate that, in many national health systems, less than half the patients eligible for using VKAs take this medication, and even fewer are adequately maintained within the desired therapeutic range.⁵ Therefore, the possible consequences derived from a level of infra- or supra-therapeutic anticoagulation make for achieving the best control to be imperative.^{6,7}

The international normalized ratio (INR) is used to determine VKAs anticoagulant effect. INR time in therapeutic range (TTR) is the best tool to assess VKA treatment long-term effectiveness.⁸ TTR is the time during which INR remains within the desired

therapeutic range and is expressed as a percentage. The number of INR evaluations that are within the desired therapeutic range with regard to total number of INR evaluations performed in a specific period allows TTR to be obtained.⁶

VKAs are still considered oral anticoagulation gold standard; however, multiple studies show that VKA therapy control with INR is suboptimal in routine clinical practice. In fact, patients are kept up to almost 40 % of the time outside target INR. These figures depend on the type and place of medical care, on whether VKAs are indicated in an anticoagulation clinic or by general practitioners. It is a fact that the quality of VKA treatment is higher if the patient is treated in anticoagulation clinics.^{4,7}

VKAs remain the most widely used anticoagulant option in Mexico; however, no clinical study has been carried out to analyze the real quality of the effect of these medications. Therefore, the purpose of this study was to evaluate the quality of oral anticoagulation with VKA in three different clinical scenarios, at three different periods in Mexico.

Methods

In this prospective, descriptive, controlled, cohort-nested study, we included patients treated in three different clinical scenarios at the Mexican Institute of Social Security in Mexico City:

- Cardiology Hospital at National Medical Center Siglo XXI (HC-CMNSXXI – Hospital de Cardiología del Centro Médico Nacional Siglo XXI).
- Cardiology Department, “Carlos MacGregor Sánchez Navarro” Regional General Hospital (SC-HGRCSMN – Servicio de Cardiología, Hospital General Regional “Carlos MacGregor Sánchez Navarro”).
- Hematology Department Anticoagulation Clinic, “Carlos MacGregor Sánchez Navarro” Regional General Hospital (CA-HGRCSMN – Clínica de Anticoagulación del Servicio de Hematología,

Hospital General Regional "Carlos MacGregor Sánchez Navarro").

The study comprised three phases: from January 2013 to December 2014, from November 2015 to December 2016 and from January 2018 to December 2019. The study was carried out in three phases, since at the end of phases 1 and 2, a partial analysis of the obtained results was carried out in order to make adjustments for anticoagulation control at HC-CMNSXXI and SC-HGRCMSN and to restart quality assessment.

We included all patients of either gender who were cared for in the outpatient clinic, with any indication for being treated with VKA and who received active treatment for at least 12 months. Initial in-hospital treatment in both hospitals was always decided by the treating physician and, therefore, this information was not analyzed in this study. Once the patient was discharged from the hospital, he/she was treated according to the criteria of the treating physician or of the anticoagulation clinic when the patient was referred to it.

General data of each patient and INR evaluations were obtained from medical records. To be included, patients had to have at least four INR determinations within the 12-month period in order to have a faithful TTR estimation. Given that the study was conducted by reviewing INR records at both hospitals, treating physicians were never aware about the characteristics and implications of the study. If a patient was identified as a candidate, his/her medical record was reviewed to collect the following data: age, gender, diagnosis, comorbidities, indication for receiving a VKA (in order to establish INR optimal range in that patient) and type of VKA used (acenocoumarin or warfarin). INR values, monitoring frequency, and follow-up period were obtained from the laboratory databases. Patients were excluded from the analysis when the information was incomplete, which included INR missing values.

Sample size was determined by convenience; the highest number of patients in the three described periods was considered. Originally, including 900 patients at each phase of analysis was attempted. All patients were assigned to one of two treatment groups, according to globally accepted recommendations for VKA use.^{7,8}

- With an INR between 2.0 and 3.0.
- With an INR between 3.5 and 4.5.

At the beginning of study phase 1, international recommendations for VKA anticoagulation for patients with mechanical heart valve prostheses were 3.5 to 4.5; however, during the study, these recommendations

changed to 2.5 to 3.5.^{9,10} This change did not affect the analysis of the results, since they were standardized according to the INR obtained at the time of the respective analysis and the specific recommendations in that period. According to the intensity of the recommended anticoagulation evaluated by INR, patients were classified as:

- With a lower-than-desired therapeutic range (INR < 2.0 or < 3.5).
- Within the desired therapeutic range (INR = 2.0-3.0 or 3.5-4.5).
- With a higher-than-desired therapeutic range (INR > 3.0 or > 4.5).

According to the specific period the patient was evaluated in, both TTR and the percentage of patients between the desired therapeutic ranges were obtained. TTR was calculated according to the globally most widely accepted tool, for which a linear interpolation method was applied, which assumes a linear relationship between two INR values and assigns a specific value of it to each day between each patient's tests.^{11,12}

All INR evaluations were carried out using a point-of-care strategy (thrombotest), by means of which the value is directly evaluated using a CoaguChek® XS equipment, which uses test strips containing human recombinant thromboplastin, according to the manufacturer's instructions (Roche Diagnostics, Germany).¹³ This technique is widely validated and accepted in the literature for the control of anticoagulation with VKA in multiple clinical settings.^{14,15} The equipment requires a very small amount of blood collected by finger prick.

In some randomly selected patients, peripheral blood was obtained by antecubital vein puncture every three months in order to assess for concordance of the results of usual prothrombin time (PT) tactic with the thrombotest. This blood was collected in plastic tubes containing 0.109 M sodium citrate (vol: vol 1:9, Na Citrate, BD Vacutainer, Franklin Lakes, NJ, USA). The samples were centrifuged for 15 minutes at 2000 g to obtain platelet-poor plasma, which is necessary for measuring PT and calculating the INR in an automated ACL 1000 equipment (IL Werfen, Hartwell Road Bedford, MA, USA), with the HemosIL PT-Fibrinogen HS PLUS reagent and an ISI value of 1.0 (IL Werfen).

The study protocol was approved by the local research committees of both hospitals. This study entailed minimal risk for patients, since only their INR results were reviewed, which is a necessary and

Table 1. Patient general characteristics

Characteristic	HC-CMNSXXI		SC-HGRCMSN		CA-HGRCMSN		p
Median age, years (range)	63.6 (16-89)		65.1 (16-88)		65.9 (16-92)		NS
Phase 1	62.4		62.9		63.8		NS
Phase 2	63.8		65.7		64.6		NS
Phase 3	64.6		66.8		65.3		NS
	n	%	n	%	n	%	
Patient number	1,755	100	900	100	1,763	100	NS
Phase 1	500	28.5	300	33.3	500	28.4	NS
Phase 2	613	34.8	300	33.3	600	34.0	NS
Phase 3	642	36.8	300	33.3	663	37.6	
Gender (females/males)	868/887	50.3/49.7	450/450	50/50	877/886	49.8/50.2	NS
Phase 1	250/250	50/50	150/150	50/50	250/250	50/50	NS
Phase 2	308/305	50.2/49.8	150/150	50/50	302/298	50.3/49.7	NS
Phase 3	310/332	48.3/51.7	150/150	50/50	325/338	49.0/51.0	NS
Vitamin K antagonist indicated							
Acenocumarin	986	56.1	479	53.3	1,019	57.8	NS
Warfarin	769	43.9	421	46.7	744	42.4	NS
Indication for the use of vitamin K antagonists							
Venous thromboembolic disease	124	7.1	92	10.2	1,615	91.6	0.001
Atrial fibrillation	1,188	67.7	586	65.1	92	5.2	0.001
Mechanical heart valve	422	24.0	206	22.9	14	0.8	0.001
Other indications	21	1.2	16	1.8	42	2.4	0.030
Desired INRs							
Low therapeutic range (2.0-3.0)	1,312	74.8	678	75.3	1,707	96.8	0.045
High therapeutic range (3.5-4.5/2.5-3.5)	422	23.9	206	22.9	14	0.8	0.0007

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routine requirement for patients who are treated with VKAs. Therefore, no written consent was obtained from the patients prior to entering the study. Collected data were always anonymous.

For descriptive analysis, continuous data were expressed as means and ranges. Categorical data were indicated with percentages. Categorical data comparison between study groups was carried out using the chi-square test, while a one-way Anova test was used to compare quantitative data. Statistical analyses were carried out using the Statistical Package for the Social Sciences, version 26 (SPSS Inc., Chicago, IL, USA). A p-value > 0.05 was considered to be significant.

Results

Patient general characteristics, the VKA type and the indication for the use of these anticoagulants are shown in table 1. There were no significant differences between the groups during the three phases of the study, except in the indications for using a VKA, since

most CA-HGRCMSN patients were treated for suffering from VTD, unlike the cardiology indications at HC-CMNSXXI and SC-HGRCMSN.

We analyzed the results of INR evaluations performed in 5,576 patients; however, the results of 1,428 individuals (25.6 %) were not considered in the analysis, given that they failed to meet the inclusion criteria. The most common causes of patient exclusion were the lack of at least four INR evaluations in the 12-month period (n = 1,282, 89.8 % of all excluded patients). At the end, 4,148 patients were included in the analysis throughout the study. The entire study evaluation included 40,833 INR tests; however, 2,285 were excluded; 2,039 (89.2 %) were calculated with the traditional method based on PT. Finally, 38,548 INR evaluations were analyzed (Table 2). Specifically, INR assessments higher than 5.0 were analyzed to determine the percentage of patients with the highest level of bleeding risk (Table 3).

During the study period, the number of INR evaluations was significantly different between study groups (Table 4). In phase 1, evaluation averages for the

Table 2. Analysis of INR evaluations across the three phases of the study

Evaluations	INR						p
	Low		Desired		High		
	n	%	n	%	n	%	
Phase 1 (n = 11,613)							
HC-CMNSXXI (n = 4,452)	2,204	49.5	859	19.3	1,389	31.2	< 0.001*
SC-HGRCMSN (n = 2,420)	1,308	54.1	445	18.3	667	27.6	
CA-HGRCMSN (n = 4,741)	498	10.5	3,371	71.1	872	18.4	
Phase 2 (n = 12,740)							
HC-CMNSXXI (n = 4,854)	2,291	47.2	1,082	22.3	1,481	30.5	< 0.001*
SC-HGRCMSN (n = 2,502)	1,186	47.4	578	23.1	738	29.5	
CA-HGRCMSN (n = 5,384)	614	11.4	3,747	69.6	1,023	19.0	
Phase 3 (n = 14,195)							
HC-CMNSXXI (n = 5,086)	2,512	48.7	901	17.7	1,673	32.9	< 0.001*
SC-HGRCMSN (n = 2,651)	1,251	47.2	486	18.3	914	34.5	
CA-HGRCMSN (n = 6,458)	536	8.3	4,527	70.1	1,395	21.6	
Total (n = 38,548)							
HC-CMNSXXI (n = 14,392)	7,007	48.7	2,842	19.8	4,543	31.5	< 0.001*
SC-HGRCMSN (n = 7,573)	3,745	49.6	1,509	19.9	2,319	30.5	
CA-HGRCMSN (n = 16,583)	1,648	10.0	11,645	70.3	3,290	19.7	

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Table 3. High INRs across the three phases of the study

High INR	High INR								p
	5-6		6-7		7-8		> 8		
	n	%	n	%	n	%	n	%	
Phase 1 (n = 2,928)									
HC-CMNSXXI (n = 1,389)	671	48.3	486	35.0	144	10.4	88	6.3	< 0.001*
SC-HGRCMSN (n = 667)	295	44.2	208	31.2	101	15.1	63	9.4	
CA-HGRCMSN (n = 872)	496	56.9	274	31.4	61	7.0	41	4.7	
Phase 2 (n = 3,242)									
HC-CMNSXXI (n = 1,481)	786	53.1	471	31.8	152	10.3	72	4.8	< 0.001*
SC-HGRCMSN (n = 738)	297	40.2	225	30.5	167	22.6	49	6.7	
CA-HGRCMSN (n = 1,023)	469	45.8	392	38.4	122	11.9	40	3.9	
Phase 3 (n = 3982)									
HC-CMNSXXI (n = 1,673)	955	57.1	528	31.6	111	10.8	79	4.7	< 0.001*
SC-HGRCMSN (n = 914)	381	41.7	299	32.7	158	17.3	76	8.3	
CA-HGRCMSN (n = 1395)	998	71.5	269	19.3	96	6.9	32	2.3	
Total (n = 10,152)									
HC-CMNSXXI (n = 4,543)	2412	53.1	1485	32.7	407	8.9	239	5.3	< 0.001*
SC-HGRCMSN (n = 2,319)	973	41.9	732	31.6	426	18.4	188	8.1	
CA-HGRCMSN (n = 3,290)	1963	59.7	935	28.4	279	8.5	113	3.4	

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12-month period at HC-CMNSXXI, SC-HGRCMSN and CA-HGRCMSN were 5.7 (range: 4-9), 5.6 (range: 4-9) and 9.0 (range: 6- 11), respectively (p < 0.001 for

CA-HGRCMSN vs. the other two groups). The same data for phase 2 were: 6.1 (range: 4-10), 5.8 (range: 4-9) and 9.2 (range: 6-17), respectively (p < 0.001 for

Table 4. Number of INR evaluations throughout the study

Number of INR evaluations/ patient/year	Number of evaluations											p
	4	5	6	7	8	9	10	11	12	> 12	X	
Phase 1												
HC-CMNSXXI (n = 500)	71	121	204	85	11	8	0	0	0	0	5.7	< 0.001*
SC-HGRCMSN (n = 300)	64	75	98	49	11	3	0	0	0	0	5.6	
CA-HGRCMSN (n = 500)	0	0	24	45	78	192	125	20	10	6	9.0	
Phase 2												
HC-CMNSXXI (n = 613)	74	142	199	117	35	29	17	0	0	0	6.1	< 0.001*
SC-HGRCMSN (n = 300)	52	71	102	55	13	7	0	0	0	0	5.8	
CA-HGRCMSN (n = 600)	0	0	26	51	101	227	130	61	9	5	9.2	
Phase 3												
HC-CMNSXXI (n = 642)	63	185	201	94	64	35	0	0	0	0	6.0	< 0.001*
SC-HGRCMSN (n = 300)	47	75	92	67	10	9	0	0	0	0	5.8	
CA-HGRCMSN (n = 663)	0	0	12	27	89	114	304	94	12	11	9.6	
Total												
HC-CMNSXXI (n = 1755)	208	448	604	296	110	174	17	0	0	0	5.9	< 0.001*
SC-HGRCMSN (n = 900)	163	221	292	171	34	19	0	0	0	0	5.7	
CA-HGRCMSN (n = 1763)	0	0	62	123	268	533	559	175	31	22	9.3	

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CA-HGRCMSN vs. the other two groups). Finally, for phase 3, averages were 6.0 (range: 4-9), 5.8 (range: 4-9) and 9.6 (range: 6-15), respectively ($p < 0.001$ for CA-HGRCMSN vs. the other two groups).

The TTRs obtained at the three clinical sites during the three phases of the study, as well as the resulting cumulative data are illustrated in figure 1, panels A-D. Each panel shows the data obtained for the desired INR: 2.0-3.0, 3.5-4.5 or 2.5-3.5.

After evaluating the results of the groups in terms of TTR, neither age nor sex or the type of VKA used were significantly associated with the obtained results. In contrast, TTR results were significantly associated with the number of visits per patient during the 12-month follow-up ($p = 0.001$).

Discussion

Thrombosis, either arterial or venous, is the main cause of mortality in the world; in Mexico, the panorama is similar, although it is poorly recognized so far by the health system. When statistics are reviewed, final cause of death in a high proportion of patients with chronic non-communicable and communicable diseases is thrombosis; furthermore, it is also recorded as a cause of morbidity associated with high rates of temporary or permanent, partial or complete disability. Growing evidence shows that it also negatively

affects clinical outcomes in other scenarios such as cancer, the postpartum period, or the pediatric population, although this is unknown or frequently omitted.¹⁶ To prevent or treat patients at risk of thrombosis, more internal medicine physicians and surgeons should be trained, although also gynecology, obstetrics and pediatrics specialists. In the near future, a high percentage of the population will require temporary or permanent antithrombotic treatment, which is a reality that should be considered in the design of public and private strategies that promote and establish the basis for addressing the problem. The question is, are we prepared in Mexico to face this problem?

Antithrombotic treatment includes antiplatelet agents, anticoagulants, and thrombolytic drugs; the latter are used in acute settings, while the former two are also used in thrombosis prevention and chronic treatment. The basis of chronic treatment and prevention has been the VKAs acenocoumarin and warfarin, which are inhibitors of the production of vitamin K-dependent hemostatic factors, especially factor VII, which prolongs PT;¹⁷ therefore, permanent monitoring of its effect with INR is required.¹⁷

VKAs main advantages are their efficacy, apparent low cost, and rapid reversal of their effect. However, their use is complicated by various factors, some of which, inherent to the patient or external, are not

Figure 1. TTRs obtained at different clinical services during the three phases of the study and cumulative data. 1. Cardiology Hospital, National Medical Center Siglo XXI; 2. Cardiology Department, "Carlos MacGrégor Sánchez Navarro" Regional General Hospital; 3. Anticoagulation Clinic, Hematology Department, "Carlos MacGrégor Sánchez Navarro" Regional General Hospital. A) Desired INR = 2.0-3.0, B) Desired INR = 3.5-4.5/2.5-3.5. b) Lower-than-desired INR, d) Desired INR, a) Higher-than-desired INR.

easily controllable. The former include VKAs metabolism, which exhibits inter-individual variations, in addition to patient metabolic changes during treatment: in hepatic absorption, elimination, and metabolism.¹⁸ On the other hand, external factors are common and difficult to control: diet and its vitamin K content modify the effect of VKAs, almost all drugs affect their effect, therapeutic range is narrow and permanent control of the effect is required. External factors induce poor treatment adherence, which makes control difficult. Patient's own and external factors make it impossible for a therapeutic plan or a general dose for all patients to be proposed. Thus, establishing the exact dose requires time and a close relationship with the patient, who must be convinced of the reason and benefit of the treatment.

Anticoagulants are among the drugs that are associated with a high degree of adverse events, which generates high rates of hospitalization and death, especially in older patients.^{19,20} If cases of overdose are considered, VKAs are associated with 70 % of unintentional overdoses and induce 33 % of adverse drug events in patients aged > 50 years.²¹ The frequency of VKA-related bleeding ranges from 1.7 to 17 %.^{22,23} When the most common causes of hospitalization are analyzed, VKAs and antiplatelet agents are consistently found to

be the drugs that are most commonly associated with hemorrhage.^{24,25} Despite the usefulness of VKAs, bleeding is the main reason that explains their clinical underuse.²⁶

VKAs effectiveness and safety are strongly related to the quality of control, although both parameters do not depend only on anticoagulation being within therapeutic range, but on maintaining it as long as possible. We know that the patient is not within optimal anticoagulation levels up to 80 % of the time.²⁷ In a meta-analysis, only 56 % of patients had INRs within the desired range, with a TTR of barely 61 %; recurrent thrombosis occurred in > 50 % of the patients when INR was < 2, and > 40 % of hemorrhages appeared with an INR above the desired range.³ Another study analyzed routine clinical practice with TTR;²⁸ with the desired INR range between 2.0 and 3.0, 58.9 % of the patients had a TTR < 65%.²⁸ Patients with poor INR control were shown to have a higher risk of stroke, major bleeding, and all-cause mortality. Adverse events were more common at the beginning of treatment: the risk of ischemic stroke within the first four months was associated with a TTR < 65 %, while the hemorrhagic variety did not change with TTR < 65 %, but it did with TTR > 65 %.²⁸

TTR is the percentage of time INR remains within therapeutic range, an efficient parameter of the quality of management with VKAs.^{11,12,29-31} It does not evaluate individual patients (this is done by INR), but it critically analyzes the quality of anticoagulation of a clinical service, hospital or health system.^{11,12,29-31} We used TTR to evaluate, for the first time in Mexico, the quality of anticoagulation with VKAs.

Previously, VKA studies focused on practical goals such as clinical or laboratory monitoring or strategies to reverse their effect.¹⁵ Today, we know that the monitoring system efficacy is quite poor worldwide due to factors that include a lack of interest of most doctors who prescribe these drugs. The best way to properly control VKA was long shown to be the creation of anticoagulation clinics, a strategy that is almost absent in Mexico.

To reduce the complications associated with VKAs, it is suggested that monitoring should be carried out in these clinics since, for example, the frequency of hemorrhage decreases by almost 40 %.³² The data from our study show that TTR obtained in an anticoagulation clinic is superior to that of a regular clinical service. Although TTR decreases over time,^{33,34} in this study we did not find this trend among the analyzed groups, a key fact in the Anticoagulation Clinic, since quality was constantly maintained (Fig. 1). Anticoagulation clinics current focus is not only the control of VKAs but also of the other anticoagulants and antiplatelet agents; moreover, these clinics should promote, discuss, and advise on the best use of antithrombotic agents, including thrombolytic drugs. For this reason, the name now proposed for these services is antithrombotic clinics, a concept that expands their action spectrum.

The results of our research were independent of the analyzed population general characteristics (mainly age and gender) and were not associated with a specific VKA, unlike previously reported.³⁵ This finding is important because in Mexico there is a generalized belief that warfarin is superior in clinical practice. Long ago, one of the critical factors for successful anticoagulation with VKAs was shown to be the frequency of monitoring, with the ideal period for it being every four to six weeks, which is a strategy that allows close monitoring and prevents new thromboses or hemorrhages. Our results show that a key determinant for Anticoagulation Clinic success is the frequency of appointments, never beyond six weeks. We consider it necessary for anticoagulation clinics to be

implemented in secondary and tertiary care hospitals of the health system, a step that could increase the quality of patient care and decrease institutional costs associated with new thrombotic or hemorrhagic episodes due to poor anticoagulation.

Our study has limitations. Due to each group's patient characteristics, the TTRs that were obtained could be explained by significant differences associated with the anticoagulation indication. The elevated difference in TTRs between services could be due, in part, to the difference in target INRs (high and low ranges); however, perhaps such differences are due to the more standardized criteria for the therapeutic decision in an anticoagulation clinic. This is no surprise, since most high-level hospitals in developed countries have anticoagulation clinics that achieve high TTRs. Unfortunately, except for some hospitals, such clinics do not exist in Mexico.

Conclusion

Given that the incidence of thrombosis increases in almost all areas of medicine in an aging population, it appears to be mandatory to start conceiving an efficient and cost-saving strategy that allows offering better antithrombotic treatment to millions of Mexicans who already are or will be exposed to thromboembolic risk factors in the near future. Undoubtedly, the creation of antithrombotic clinics is a real alternative for solving this important pending issue of the Mexican health system.

Conflict of interests

None to declare.

Funding

This work received unrestricted funding from Bayer Healthcare AG.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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