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INTEGRATIVE REVIEW ARTICLE

ADHERENCE TO THERAPY WITH ORAL ANTICOAGULANTS: AN INTEGRATIVE REVIEW

ADESÃO À TERAPIA COM ANTICOAGULANTES ORAIS: REVISÃO INTEGRATIVA ADHERENCIA A LA TERAPIA CON ANTICOAGULANTES ORALES: UNA REVISIÓN INTEGRADORA

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ABSTRACT

Objective: analyzing the production of knowledge about anticoagulant therapy / ACO. **Method:** an integrative review, held in 2013, in LILACS, IBECs, SCOPUS, PubMed, CINAHL, SciELO and Cocharane, aiming to answer the research question << **What is the production of knowledge about the adhesion of users / patients to therapy with oral anticoagulants?** >> To analysing the scientific evidence was used the Classification of Oxford Centre for Evidence - Based Medicine. There were used Descriptors in Health Sciences: adhesion; oral anticoagulants, adults, in English, Portuguese and Spanish, unlimited years of publication. There were analyzed 14 articles. Data were grouped into categories by similarity. **Results:** studies rated A1 (43%), conducted from 2007, which addressed the adherence to ACO and implications regarding the role of the health professional. **Conclusion:** to improving adherence to the ACO is required to assess the user's knowledge, improvement in teaching strategies, monitoring of the examination and the need for a suitable instrument for evaluating adherence measure. **Descriptors:** Anticoagulants; Medication Adherence; Oral Administration.

RESUMO

Objetivo: analisar a produção de conhecimento sobre terapia anticoagulante/ACO. **Método:** revisão integrativa, realizada em 2013 na LILACS, IBECs, SCOPUS, PUBMED, CINAHL, SciELO e Cocharane, com vistas a responder a questão de pesquisa << **Qual a produção de conhecimento sobre a adesão de usuários/pacientes à terapia com anticoagulantes orais?** >> Para análise das evidências científicas foi utilizada a Classificação de Oxford Centre for Evidence-Based Medicine. Foram utilizados os Descritores em Ciências da Saúde: adesão; anticoagulantes orais, adultos, em inglês, português e espanhol, sem limite de anos de publicação. Foram analisados 14 artigos. Os dados foram agrupados em categorias por semelhança. **Resultados:** estudos com classificação A1(43%), realizados a partir de 2007, que abordaram a adesão ao tratamento com ACO e implicações em relação à atuação do profissional de saúde. **Conclusão:** para melhoria da adesão ao ACO há necessidade de avaliar o conhecimento do usuário, a melhoria nas estratégias de ensino, o monitoramento do exame realizado e a necessidade de um instrumento de medida adequado para avaliar a adesão. **Descritores:** Anticoagulantes; Adesão à Medicação; Administração Oral.

RESUMEN

Objetivo: analizar la producción de conocimiento sobre la terapia anticoagulante / ACO. **Método:** revisión integradora, que se celebró en 2013 en LILACS, IBECs, SCOPUS, PubMed, CINAHL, SciELO y Cocharane, con el objetivo de responder a la pregunta de investigación << **¿Cuál es la producción de conocimiento sobre la composición de los usuarios / pacientes a la terapia con anticoagulantes orales?** >> Para el análisis de las evidencias científicas se utilizó la Clasificación de Oxford Centre for Evidence-Based Medicine. Fueron utilizados los Descriptores en Ciencias de la Salud: la adherencia; anticoagulantes orales, adultos, en inglés, portugués y español, años sin límite de publicación. Se analizaron 14 artículos. Los datos fueron agrupados en categorías por similitud. **Resultados:** los estudios calificados como A1 (43%), llevados a cabo desde 2007, que se dirigió a la adhesión al tratamiento con ACO y las implicaciones en relación con el papel del profesional de la salud. **Conclusión:** para la mejora de la adherencia al ACO para evaluar el conocimiento de los usuarios, la mejora en las estrategias de enseñanza, el seguimiento del examen y de la necesidad de un instrumento de medida adecuado para la evaluación de la adhesión. **Descriptores:** Anticoagulantes; Adhesion de la Medición; La Administración Oral.

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INTRODUCTION

It is estimated that the annual risk associated with the use of oral anticoagulants (OAC) are between 2% and 8% for bleeding and 1% to 3% failures in treating ¹. Such data allow contributing to making appropriate decisions for users who will initiate the therapy with oral medication or those who modify the dose during drug therapy.

Medications classified as ACO require judicious control because of hemorrhagic complications resulting from misuse or higher dose for a given user therefore becomes essential clinical and laboratory follow rigorous review by the professionals involved.

The OAC therapy is recommended in the treatment of arterial and venous thrombosis, pulmonary embolism, cardiovascular disease, use of metallic heart valves, anti-phospholipid syndrome, which represents the group of users who require more attention in this therapy with the drug. The monitoring is performed by measuring Prothrombin Time (PT) expressed by the test called INR (International Normalized Ratio), demonstrating the efficacy of treatment.

The control action of the anticoagulant, based on INR is difficult due to frequent changes in the levels of coagulation caused by intrinsic factors, age and ability of absorption of vitamin K and extrinsic factors such as diet, drug interactions, lifestyle and comorbidities ².

However, considered as a factor of safety for the user, drug therapy with oral anticoagulants requires a major attention to the issue of patient adherence to medication from the perspective of health professionals. Thus, poor adherence to prescribed medicines by users and consequently, the proposed medical treatment, can have negative impacts on all aspects of health care, cost overruns and under-utilization of treatment resources available, as well as serious consequences for users in respect to adverse events in chronic diseases.

This study aims to evaluating the production of knowledge about the membership of users to therapy with oral anticoagulants.

METHOD

This is an integrative review (IR), a method that allows grouping or aggregating primary and secondary studies, different methodologies, and or theories, with wide gamade implications. The IR allows promotion organized synthesis of studies that have

identified as a research question: "What is the production of knowledge about the membership of users / patients to therapy with oral anticoagulants?"

The IR³⁻⁵ includes analysis of research with evidence that will support decision-making and improvement in clinical practice and allows the generation of new frameworks and perspectives on the topic, by summarizing the state of knowledge of a particular subject and knowledge gaps pointed out that need to be filled with new studies. The method provides a synthesis of multiple published studies and provides general conclusions about a particular area of study, although valuable to nursing as it facilitates accessibility of scientific collections that once represented an obstacle both by time and by critical analysis to be performed.

For elaboration of the research question it was used the PICO ⁶ strategy, represented by the mnemonic; Patient or Problem that represents a single patient, a group of patients in a particular condition or health problem, intervention can be an intervention of interest, therapeutic, preventive, diagnostic, prognostic, administrative or related to economic issues, comparison intervention defined as default, or no longer used or used and outcomes outcome, with the expected result.

This strategy is used to build several research questions, derived nature of clinical, management of human and material resources, search tools for assessing symptoms among others. Facilitates proper research question, allows the proper definition of information and maximizes the recovery of evidence in databases with a focus in the search scope and avoids unnecessary searches.⁷⁻⁹

The analysis of the level of evidence rating was performed according to the Oxford Centre for Evidence-Based Medicine.¹⁰ At level 1A evidence came from a systematic review of randomized controlled trials; 1B evidence from randomized controlled with narrow confidence interval and 1C therapeutic clinical trial results of "all or nothing". Level 2A, and systematic review of cohort studies; 2B evidence of cohort and randomized lower and 2C evidence of observation of therapeutic results, level 3A evidence systematic review and case-control study and level 3B case-control studies. Level 4, case reports and evidence, level 5 evidence without critical evaluation or opinion based in raw materials.

Inclusion criteria referred to studies on adherence user to therapy with oral anticoagulants, published in national and international scientific journals in the area of health, indexed in the ISI Web of Knowledge and cited by the Journal Citation Report, which accounted for the review methodology literature clearly stated and developed.

Studies with no results as editorials, letters to the editor, articles literature review, or who've been twice in information sources surveyed were excluded.

The sample consisted of full articles, found in national and international literature in Portuguese, English and Spanish, in online databases (Literature Latin American and Caribbean Health Sciences) LILACS, IBECs, SCOPUS, PubMed (National Library of Medicine and Institute of Health), CINAHL (Cumulative Index to Nursing and Allied Health Literature), and virtual libraries SciELO y Cocharane, online available in full text; human research and to address the main theme of adult users membership to therapy with oral anticoagulants.

When selecting articles there were used Descriptors in Health Sciences (DeCs): membership; oral anticoagulants, adults, in English, Portuguese and Spanish, in humans and unlimited years of publication.

To PUBMED initially settled subareas (subheadings) search term adherence and anticoagulation, with no choice of subareas to other terms. Applying the search limits: only items with links to full text, humans, clinical trial, meta-analysis, practice guideline, randomized controlled trial, English, Spanish and Portuguese. Used if the terms of the headings/mesh subject: anticoagulation, anticoagulation, adherence, adhesion.

After the search and identification of items proceeded to read the titles and

abstracts, and when presented compatibility with the inclusion criteria were selected and read in full. For the categorization of selected articles were evaluated by information extracted and organized into spreadsheet, using an adaptation of the instrument has been validated data collection - (URSI-2005).¹¹ As identified in the categories; characterization, study / review, the method / study and evaluation by means of methodological rigor . Results were subclassified as: source / country, year of publication, professional areas, the local search, the magazine area, and type of research, objectives, sample and sample characteristics, significance, identified implications, level of evidence and impact factor and methodological rigor.

The data were analyzed according to their contents, using descriptive statistics and data regarding the relationship with the object of interest in each study. After reading the articles and instruments were organized in a folder and then categorized into Excel spreadsheet, and cataloged for future reference.

RESULTS

There were identified, in its entirety, 109 articles. After detailed analysis of titles and abstracts 42 articles were selected, which closely followed the criteria for inclusion and exclusion are suited for this research 14 Articles^{1;12-25} contemplated that the aim of this study.

Nº	Author (s)	Title	Methodology	Evidence Level	Journals	Database/Virtual Library	Year
1	Ávila CW, Aliti GB, Feijó MKF, Rabelo ER	Adesão farmacológica ao anticoagulante oral e os fatores que influenciam na estabilidade do índice de normatização internacional	Cross-sectional	4	Rev. Latino-Am. Enfermagem	SCIELO	2011
2	Carvalho ARS,Dantas RASD, PelegrinoFM, Corbi ISA	Adaptation and Validation of an Oral Anticoagulation Measurement of Treatment Adherence Instrument	Adaptation and validation of the instrument	4	Rev. Latino-Am. Enfermagem	SCIELO	2010

3	Cruess DG, Localio AR, Platt AB, Brensinger CM, Christie JD, Gross R, Parker CS, Price M, Metlay JP, Cohen A, Newcomb CW, Strom BL, Kimmel SE	Patient Attitudinal and Behavioral Factors Associated with Warfarin Non-adherence at Outpatient Anticoagulation Clinics. Patient Attitudinal and Behavioral Factors Associated with Warfarin Non-Adherence at Outpatient Anticoagulation Clinics	Cohort-prospective	2B	Int J BehavMed	PUBMED	2010
4	Dame SV, Deyk KV, Budts W, Verhamme P, Moons P	Patient knowledge of and adherence to oral anticoagulation therapy after mechanical heart-valve replacement for congenital or acquired valve defects	Cross-sectional	4	Heart &Lung	PUBMED	2011
5	Esmerio FG, Souza EM, Leiria TL, Lunelli R, Moraes MA	Uso crônico de anticoagulante oral: implicações para o controle de níveis adequados	Cross-sectional	4	ArqBrasCardiol	SCIELO	2009
6	Kim JH, Kim GS, Kim EJ, Park S, Chung N, Chu SH	Factors Affecting Medication Adherence and Anticoagulation Control in Korean Patients	Cross-sectional	3B	Journal of Cardiovascular Nursing	PUBMED	2011
7	Kimmel SE, Troxel AB, Loewenstein G, Brensinger CM, JaskowiakJ,Doshi JA, M L, Volpp K	Randomized trial of lottery-based incentives to improve warfarin adherence	Randomized	2B	Am Heart J	PUBMED	2012
8	Kimmel SE, Chen Z, Price M, Parker CS, Metlay JP, Christie JD, Brensinger CM, Newcomb CW, Samaha FF, Gross R	The Influence of Patient Adherence on Anticoagulation Control With Warfarin	Cohort-prospective	2B	ArchInternMed	PUBMED	2007
9	Parker CS, Chen Z, Price M, Gross R, MD, Metlay JP, Christie JD, Brensinger CM, Newcomb CW, Samaha FF, Kimmel SE	Adherence to Warfarin Assessed by Electronic Pill Caps, Clinician, Assessment, and Patient Reports: Results from the IN-RANGE Study	Cohort-prospective	2B	JGIM	PUBMED	2007
10	Platt AB, Localio R, Brensinger CM, Cruess DG, Christie JD, Gross R, Parker CS, Price M, Metlay JP, Cohen A, Newcomb CW, Strom BL, Laskin MS,	Can We Predict Daily Adherence to Warfarin? Results from the International Normalized	Cohort-prospective	2B	CHEST	PUBMED	2010

	Kimmel SE	Ratio Adherence and Genetics (IN RANGE) Study					
11	Platt AB, Localio AR, Brensinger CM, Cruess DG, Christie JD, Gross R, Parker CS, Price M, Metlay JP, Cohen A, Newcomb CW, Strom BL, Laskin MS, Kimmel SE	Risk factors for nonadherence to warfarin: results from the IN-RANGE study	Cohort-prospective	2B	Pharmacoepidemiol Drug Saf	PUBMED	2008
12	Schillinger D, Wang F, Rodriguez M, Bindman A, Machtinger EL	The Importance of Establishing Regimen Concordance in Preventing Medication Errors in Anticoagulant Care	Cross-sectional	3B	Journal of Health Communication	PUBMED	2007
13	Volpp KG, Loewenstein G, Troxel AB, Doshi J, Price M, Laskin M, Kimmel SE	A test of financial incentives to improve warfarin adherence	Prospective	3B	BMC Health Services Research	PUBMED	2008
14	Winans ARM, Rudd KM, Triller D	Assessing Anticoagulation Knowledge in Patients New to Warfarin Therapy	Prospective	3B	Ann Pharmacother	PUBMED	2010

Figure 1. Description of the included studies in integrative review, according to author (s), journals, database and year of publication.

Regarding the year of publication, there was identified the prevalence of ten (71%) articles between 2007 and 2010, and four (29%) between 2011 and 2013. On the country was identified in nine (64%) articles were performed in the United States, three (22%) were Brazil, one (7%) and Belgium (7%) in Korea. As for the areas it is found that most were ten (71%) articles in the medical field, three (22%) in nursing and one (7%) in the pharmacy. Regarding the seat of development studies, eight (57%) were in specialized, five centers (36%) in a university hospital and one (7%) in a specialized hospital.

Regarding the objectives of studies identified in the articles, it was found that three (22%) mentioned the membership, two (14%) non-adherence, two (14%) education, two (14%) knowledge, one (7%) associated with actors and four (29%) factors were not found in the text of articles.

Regarding the type of research, it was noted that all were quantitative, and two

(14%) almost experimental and 12 (86%) non-experimental. Regarding the characteristics of the samples, the average age in the analyzed studies was 60.06 years old, were predominantly male with a mean of 69.41, the african-american ethnicity in six (44%), one (7%) Brazilian one (7%) Dutch, one (7%) Korean, one (7%) Asian, one (7%) Greek, one (7%) not specified, and two (14%) were not included in the description of items.

As to the selection of the sample, it was identified that two (14%) were randomized and (7%) of convenience, however, 11 (79%) specified other type of sample. Regarding the size of the sample, eight (58%) were from 101 to 200, three (21%) less than 100, two (14%) from 201 to 300 and one (7%) of greater than 301.

Implications	n	%
Realization of new researches	7	51
New measuring instrument	2	14
Education	2	14
Improvement in Intervention	3	21

Figure 2. Relationship of the implications raised front the analysis of the studies identified in integrative review. São Paulo, 2013.

As Figure 2 shows, the analysis of 14 articles, the relevant implication had the need for more research on the subject in seven (51%) of them. Regarding the level of statistical significance presented in the study

sample, it was found in six (43%) of low significance, two (14%) with an average significance and five (36%) with high statistical significance, while only one (7%) study did not achieve significance.

Evidence level	n	%
2B	6	44
3B	4	28
4	4	28

Figure 3. Relationship of the levels of evidence according to analysis of articles identified. São Paulo, 2013.

It was used the classification of Oxford Centre for Evidence-Based Medicine to analyzing and identifying the level of evidence and found as shown in Figure 3 that kept six articles 2B, four articles for four

articles 3B and level 4 level. Figure 4 illustrates the impact factor for each magazine analyzed. Were identified six articles classified with impact factor greater than or equal to 3.800.

IMPACT FACTOR		
Value	Articles	Description
A1	6	Equal to or more than 3.800
B1	3	From 2.499 to 1.300
B2	2	From 1.299 to 0.001
3	1	It is indexed in MEDLINE, SCIELO, LILACS base etc., but without impact factor.
4	2	

Figure 4. Relative impact factor identified in each magazine according to integrative review. São Paulo, 2013.

In all the articles studied, the descriptive method was used. Of the 14 articles analyzed, 100% beheld the participating subjects; were identified as the studies, a prospective cohort five (36%) Cross- five (36%), the future- two (14%) randomized to one (7%) of the adaptation and validation one (7%). Related to the research site were identified that eight (57%) of the articles in specialized center, five (36%) in university hospitals and one (7%) in a specialized hospital. Of the seven (50%) analyzed articles for inclusion and exclusion criteria were identified as 07 (50%) did not describe criteria eight (58%) of the articles presented interventions and 14 (100%) presented descriptive results.

The limitations identified in 14 articles found for IR, no need for a measure applicable for this profile of users of ACO instrument because the scales adapted overestimated noncompliance provided an opportunity and not an expression of the difficulties and understanding about the treatment, since related to intake of vitamin K. Study ¹⁷ found that the volatility of food intake contributes to changes in INR

interfering with the expected result and the interventions were not consistent to measure compliance by presenting difficulty in handling the container monitoring the drug used.

DISCUSSION

The data were grouped in categories by similarity and presented sequentially.

♦ **Category 1. Treatment adherence with ACO**

The use of anticoagulant therapy has increased significantly in recent decades and the difficulties in maintaining a stable and adequate treatment has been a constant pursuit of health professionals involved in this process. The control of the ACO is associated with adequate adherence and not demographic variables, knowledge about the treatment used or the perception of quality of life ¹².

Among the objectives identified in this study adherence was appointed as highlighted in most studies, because other studies have associated membership of the education, knowledge and actors accession factors. One

study ¹⁶ showed that the non-adherence to therapy, the medication itself was identified as responsible for over 5% of all hospital admissions associated with a direct cost of more than eight billion.

The patient non-adherence to therapy is often related to indices tracking the International Normalized Ratio (INR). Nevertheless, studies also show immaturity as compliance or non-compliance with oral anticoagulants, especially among a large number of patients and anticoagulation practices ¹⁵. Lack of data on adherence to drug therapy may be related to the difficulty in measuring compliance, or the lack of a tool that quantifies the user adoption of ACO.

♦ Category 2. Implications regarding the role of the health professional and the accession

The new research on the accession of users of oral anticoagulants is necessary to bring out the best in adherence interventions users ACO.

Study using appropriate tools to measure compliance of users of ACO ¹³ demonstrated that there is a need for more research in patients with diverse socio-demographic and clinical characteristics using therapies with oral anticoagulants, as well as new research using concurrent, other measures of adherence such as counting drugs, electronic monitoring and other self-administered instrument to measure adherence. Despite such care, health professionals usually can take the necessary steps to improve information to patients about the complications and implications if medications are not taken as prescribed.

Factors relating to the handling and ingestion of the drug and food interaction itself were related to non-adherence. However, patients themselves reported that the lack of responsiveness of physicians to detailing on the disease as an indication for the use of ACO, contributes to the lack of adherence ¹⁷. Thus the need to develop educational actions needed to improve adherence can identified as a need for investment to increase adherence to ACO, as non-adherent to therapy patients may be at a lack of knowledge about their health and treatment.

Furthermore, the patients' knowledge about their own health and the failure of the patient-professional communication must be considered, since these are factors that can affect the attitude of these patients and change health outcomes related to

anticoagulation in association membership of users ¹⁷.

Emerging intervention strategies that used videos that illustrate professional-patient dialogue on oral anticoagulants were effective in educating users about the medication and had a positive impact on their beliefs ¹⁷. Therefore, the need for further studies those utilize learning strategies that the aim of beliefs, skills, attitudes early in the course approach may interfere with the adhesion of users ACO.

The purpose of the RI is to point out the evidence on patients' adherence to therapy using ACO. Such evidence could impact the care, management, education and research in the field of Cardiovascular Nursing. It is known that the user ACO is more likely to develop thromboembolic events, should not have the appropriate level of care, or even develop bleeding from improper use during treatment. However, adherence becomes a necessary and key component in ensuring the quality of life of this person, mitigating these events.

There were appointed in 14 studies the importance of effective accession-related research. Study ¹⁸ that assessed knowledge of new users ACO stressed that although the control group used during the development of research, the educational method is still the most likely to keep the new group adhered to treatment, therefore justifying educational strategies that improved understanding user about treatment.

Patient compliance to the ACO is considerably, ineffective, by improper use of the same doses with accompaniment in anticoagulation clinic. Therefore, the INR monitoring periodically is essential, but may not be able to capture periods of accession until after an adverse event has occurred.²²

Specific factors may interfere with adherence to therapy with OAC. It is common and there is considerable decrease in medication adherence and the factors are related to knowledge about treatment, the educational level of education, financial situation and conditions of employment and the functioning of the mental and cognitive health of this person. However, that study identified the risk factors for non-adherence ²⁴ stated that the clinical definition of carefully controlled anticoagulation and patient-specific factors such can be of future based interventions to improve adherence.

FINAL REMARKS

The low adherence to medication use is currently a major challenge for the improvement of health worldwide. This definition demonstrates the need for further clarification on the use of medicines by health professionals for a particular group of users in question.

Although there are large international studies that address the membership of users of ACO, yet pretty, have a need to implement in their studies concrete evidence related to factors that interfere with OAC therapy and the best education strategies that may interfere with treatment, resulting in improve adherence as well, become accessible to every area of professional practice.

This method provided a review of new knowledge regarding the analysis of specific items as the theme. It is considered important to note that through this research methodology some points were raised and are important for description, as the need for more research with users of ACO, investment in education in nursing service and the construction of an instrument that makes possible the measurement accession.

In view of better prognosis in patients undergoing oral anticoagulant, the result depends not only on drug treatment, as well as non-pharmacological factors for therapy. Therefore, it is necessary to continuously monitor these patients to receive counseling regarding self-care with medication, information about specific factors that influence adherence due to interaction with the ACO, the need to strengthen the possibility of thromboembolic events and strategies that facilitates adherence to therapy.

In this scenario, health education is one of the charges of working with this specific population, so it is necessary that health professionals develop teaching strategies aimed at improving adherence.

CONCLUSION

Regarding users of oral anticoagulants is no exception, as this IR showed that the production of knowledge on adherence users of oral anticoagulants is still a major challenge to health professionals and national and international institutions. National studies show that health professionals have sought ways to intervene to encourage user adoption, through the application of adaptive instruments to measure adherence, users' knowledge about treatment and their socio-

demographic situation. But there is scarcity of scientific studies that address various stakeholders the accession of these factors users. The analyzed studies show that strategic intervention is the health education of this population. The sample showed no studies that propose a score gathering intervening factors.

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