



# Survey on the Level of Knowledge of Pharmacists in the Follow-Up of Patients on Vitamin K Antagonists

Momar Dioum<sup>1\*</sup>, P. Badiane<sup>1</sup>, P.H. Diagne<sup>2</sup>, I.I.M. Hanifa<sup>1</sup>, Aw. Kane<sup>1</sup>, C. Gaye<sup>1</sup>, F. Aw<sup>3</sup>, M. Diao<sup>3</sup>

<sup>1</sup>Department of Cardiology, University Hospital of Fann, Dakar, Senegal, <sup>2</sup>Department of Cardiac Surgery, University Hospital of Fann, Dakar, Senegal, <sup>3</sup>Department of Cardiology, University Hospital Aristide Le Dantec, Dakar, Senegal

## ABSTRACT

**Introduction:** Vitamin K Antagonists (VKAs) are an anticoagulant treatment widely prescribed in cardiology. However, their therapeutic margin is narrow with hemorrhagic risk (overdose) or thrombotic risk (under dosage). The objective of this work was to assess the level of knowledge of pharmacists on the management of patients on VKAs.

**Methodology:** This was a cross-sectional and descriptive study conducted during the period from January 7<sup>th</sup> to November 25<sup>th</sup>, 2020 concerning pharmacists practicing in Dakar who agreed to participate in the study. Data on molecules, indications, contraindications, surveillance and iatrogenia were collected in an Excel<sup>®</sup> file.

**Results:** One hundred and three pharmacists were included, including 26 biologists and 77 pharmacy pharmacists. The sex ratio (M/F) was 2.02 and the average age was 36.5 years. The most cited VKAs was acenocoumarol (45.3%). Venous thromboembolic disease (34.7%) and emboligenous heart disease (25.3%) were the most listed indications. The major contraindication reported was hemorrhage (31.7%). The most recovered VKAs intake time (38%) was in the evening. More than half (66%) of pharmacists recommended taking International Normalized Ratio (INR) in the morning. Our investigation identified hemorrhages as a major sign of overdose to VKAs (86.9%). For signs of underdosing, we noted thrombotic complications (46.2%). Non-steroidal anti-inflammatory drugs (31.5%) and aspirin (26%) were the most cited contraindicated common molecules.

**Conclusion:** Our work reveals an average knowledge level of pharmacists on VKAs treatment. The integration of pharmacists in therapeutic education and monitoring has become necessary to ensure the safety of VKAs treatment.

**Keywords:** Vitamin K Antagonists; Knowledge; Pharmacists; Senegal

## INTRODUCTION

Vitamin K Antagonists (VKAs) are, for more than 60 years, one of the main anti thrombotic treatments available. Their prescriptions continue to increase due to an aging population with a proportional increase in the incidence of cardiovascular disease [1]. Their indications are many dominated by emboligenous heart diseases including atrial fibrillation; then we have mechanical cardiac prostheses and venous and arterial thromboembolic disease [2-4].

VKAs are administered orally. Their therapeutic margin is narrow with hemorrhagic risk in case of overdose and thrombotic risk if under-dosage [5]. Biological monitoring is done by the International Normalized Ratio (INR) with specific therapeutic objectives.

According to numerous French studies [2,6-8], VKAs are still credited with the highest incidence of hospitalization for adverse

effects. There is therefore a real public health problem related to the use of VKAs by their impact on morbidity and mortality, the cost of managing these complications and their prevention [2]. The National Agency for Health and Medicine specifies that the control of information by health professionals (pharmacists, doctors, biologists) as by patients is necessary for better control of VKAs [9,10].

In Senegal, there remains a significant delay in studies on the importance of VKAs iatrogenia despite an existing morbidity [11-13]. Noting the few studies carried out on the VKAs mainly concerning the education of patients and the census of accidents related to their use [13,14], we undertook to assess in our study the level of knowledge on the overall management by pharmacists of patients on VKAs. The specific objectives were to identify known drugs, to give indications and contraindications of treatment to VKAs and to evaluate clinical and biological monitoring of iatrogenicity.

**Correspondence to:** Momar Dioum, Department of Cardiology, University Hospital of Fann, Dakar, Senegal, E-mail: momar.dioum@yahoo.fr

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## MATERIALS AND METHODS

This was a cross-sectional, descriptive, analytical study carried out between January, 07<sup>th</sup> and November 25<sup>th</sup>, 2020 with pharmacists, pharmacy assistants and pharmacists-biologists from the Dakar region. Thesis year students, salespeople, pharmacy vendors and laboratory technicians were not included.

An anonymous questionnaire was given to all pharmacists in person and immediately retrieved.

Several parameters were studied:

- Data on the pharmacist's profile (age, gender, work experience)
- Name of known drugs
- Indications and contraindications of treatment at the VKAs
- Methods of taking VKAs and biological monitoring of treatment (INR)
- Complications of treatment (signs of overdose or under dosage)
- Drug interactions

The data was collected and compiled into an Excel® file and processed through the SPHINX® application. Confidentiality of responses was respected.

## RESULTS

One hundred and three pharmacists were included, including 26 biologists and 77 pharmacy pharmacists. The population consisted of 22 pharmacists (21.4%), 55 assistants in pharmacies (53.4%) and 26 pharmacists biologists (25.2%). The sex ratio (M/W) was 2.02 and the average age was 36.5 years (extreme 24-71 years). The average duration of practice was 9.6 years.

The majority of practitioners cited acenocoumarol (45.3%); followed by fluindione (31.4%) and warfarin (23.3%). The most cited indications were venous thromboembolic disease (34.7%), emboligenous heart disease (25.3%) and stroke (10%). The most reported contraindications were hemorrhagic diseases (coagulopathies, thrombocytopenia, hemophilia, recent hemorrhages) by (31.7%) practitioners followed by allergies or intolerance (16.9%). Then came pregnancy (13.1%) and liver failure (11.1%). Less than 1% did not know the contraindications.

To the question concerning the hour of taking, more than a third of pharmacists (38.8%) had chosen the evening, 22.3% practitioners in the morning and 1.9% at noon. However, 17.5% of pharmacists had offered a dose at a free but still fixed time. Finally, 19.4% of practitioners did not know the time of taking VKAs. More than half (66%) of pharmacists recommended a sample in the morning for the dosage of INR, compared to 34% who did not know this time. Regarding the target INR value, 68% knew the value in the context of emboligenous heart diseases and 45.6% in the context of mechanical cardiac prostheses.

Our investigation identified hemorrhages as a major sign of overdose to VKAs (86.9%), followed by extensive hematomas (7.6%). For the signs of underdosing, we noted thrombotic complications (46.2%). Nine pharmacists (5.2%) cited stroke. "Don't know" was 48.6% of responses.

Non-steroidal anti-inflammatory drugs (31.5%), aspirin (26%) and nitrogen antifungals (13.7%) were the most cited contraindicated common molecules. All these results are compiled in Table 1.

**Table 1:** Associations contraindicated with the AVK.

Common drugs contraindicated	Percentage (%)
NSAIDs	31.5
High dose aspirin	26
Nitrogen antifungals	13.7
Sulfonamide antibiotics	6.8
Long-term LMWH	4.1
Corticosteroids	3.8
Anti-platelet gloves	3.1
Phenobarbital	1.7
Oral contraceptives	1.7
MAO inhibitors	1
Etamsylate	1
3 <sup>rd</sup> generation cephalosporins	1
Chloramphenicol	1
Cimetidine	0.7
Allopurinol	0.3
Fibrates	0.3
Don't know	1.4

**Note:** NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; LMWH: Low Molecular Weight Heparins; MAO Inhibitors: Monoamine Oxidase Inhibitors

## DISCUSSION

When asked about known VKAs, acenocoumarol was the most cited. This result is consistent with the study by Dia K et al., in Senegal [13]. These results contrast with those found in studies conducted in Burkina such as Millogo et al., [15], and Coulibaly in Mali [16], with fluindione corresponding to 96% and 67% of prescriptions respectively. On the other hand, there is a clear domination of Warfarin worldwide [17,18]. These results could be explained by the fact that acenocoumarol is almost the only VKAs marketed in our country for several years, with prescription habits, as well as the affordable cost of this molecule.

The indications were generally well known. However, the answers provided, even if accurate, lack precision and specificity. This lack of specificity is also observed at the level of contraindications with the majority response, hemorrhagic syndromes grouping many pathologies each having their specificity. The need for good control of indications and contraindications is therefore necessary to ensure the safety of treatment.

The responses regarding the time of taking the VKAs were varied. This shows the interest of a correct writing of prescriptions to facilitate the work of the pharmacist and compliance for the patient. Indeed, the study of Mbaye A et al., showed that only 46% of patients know the time of taking VKAs [14].

The time of blood test for INR is well known by most practitioners. This tendency to dose INR at fixed times (in the morning) should not prevent its dosage in certain urgent situations and does not prevent reliable INR values [19]. Two-thirds of practitioners know the average target INR value for emboligenous heart disease. However, this number dropped considerably for mechanical prostheses (45% of correct responses). Several studies show

that poor monitoring of INR is a factor increasing the risk of hemorrhage and or thrombosis, the intervention of our colleagues would greatly improve the management of patients on VKAs [20]. Overall, our investigation reveals a good knowledge of the signs of major and minor accidents. On the other hand, the signs of underdosing to VKAs were poorly known. This situation is problematic because rapid and accurate identification of these signs is necessary for early and appropriate management [13, 20]. Iatrogenia related to VKAs is the main problem related to their use [2,6]. VKAs have many interactions with common molecules. The latter were mastered by pharmacists.

## CONCLUSION

Our work reveals an average knowledge level of pharmacists on VKAs treatment. The integration of pharmacists in therapeutic education and monitoring has become necessary to ensure the safety of VKAs treatment. This requires ongoing medical training and knowledge updates. But also there needs to be good collaboration between health professionals.

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