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Learning of Pharmacogenetics in human medicine students through PBL and ICTs

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Abstract

Objective: To describe the learning achievement after training in pharmacogenetics based on PBL and ICT and its persistence four years later in human medicine students of a public university in Peru. Materials and Methods: 160 students who received training on the pharmacogenetics of warfarin applying PBL and ICT were evaluated. The instrument was based on a clinical problem applied immediately after training and 4 years later. Results: Results of the first evaluation indicated a good analytical resolution of the problem with argumentation in the genetic conditions of the patient. The evaluation after four years showed that 89% of the students continued at higher levels of learning. Conclusion: It was shown that the use of a meaningful learning methodology with PBL and ICT can make knowledge last and serve in the future for decision-making in the selection of medication.

Keywords:*Pharmacogenetics, Warfarin, Problem-Based Learning, Students, Medical.*

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1. Introduction

Pharmacogenetics is a discipline that allows determining an optimal drug for a patient according to their genetic characteristics (Valdes & Yin, 2016). The genetic variability of each individual has relevance for dosage and treatment (Bishop, 2018). Currently, more than 30 drugs used for the central nervous system contain pharmacogenetic information on the product label, which refers to genetic variation in drug metabolism (Bishop, 2018).

Warfarin is an oral anticoagulant, the most prescribed for the diagnosis of thromboembolism (Shendre, Dillon, Limdi, 2018). However, its great variability between patients complicates its treatment with this drug (Alawan, Voils, Hartzema, 2017). Research has identified genetic factors that influence warfarin dosage, the most significant being single nucleotide polymorphisms in CYP2C9 (major drug-metabolizing enzyme) and VKORC1 (warfarin-inhibited target protein) (Shendre et al., 2018)

Medical education in Pharmacogenetics is still incipient. A cross-sectional study surveyed 900 medical students, finding that the average score of knowledge about the topic is low, even though there was a positive attitude towards pharmacogenetics (Zawiah, et al., 2021). In another investigation, the main barriers that the students identified in the implementation of genomic medicine and pharmacogenomics were the lack of training (59.7%) and lack of clinical practice guidelines (58.7%) (Rahma, et al., 2020)

The present study was carried out with the objective of determining the persistence of learning of the pharmacogenetics of the warfarin polymorphism in a population of human medicine students, through the use of Information and Communication Technologies (ICT) and Problem-Based Learning (PBL).

2. Materials and methods

Longitudinal study that evaluates the knowledge achieved after a training in pharmacogenetics based on PBL and ICT and its persistence four years later. The study population consisted of 160 third-year students from the Human Medicine School of the Universidad Nacional Mayor de San Marcos enrolled in 2014.

The training consisted of 10 hours (synchronous and asynchronous) of collaborative work. Different didactic materials were designed such as 1) Online guides for students and teachers, 2) Collaborative work strategies, 3) Creation of a virtual classroom where the material to be used and discussion forums were available, 4) Elaboration of a problem case related to polymorphism of metabolization of Warfarin and 5) Preparation of digital evaluation forms. In addition, other ICTs used were: search for information in databases and video viewing to review extraction techniques of DNA, PCR amplification and use of electrophoresis.

The students were divided into 16 teams, each led by a student and a teacher to discuss the genetic polymorphisms that altered the dosage of Warfarin, then present the findings and suggest an appropriate treatment. Participation in the study was voluntary, confidential, and had no influence on the grades of the subjects that the students were taking. The work was approved by the Ethics Committee of the Faculty of Human Medicine, UNMSM.

The instrument for measuring knowledge was based on solving the clinical problem: "Evaluation of CYP 2C9 and VKORC1 Polymorphism for Warfarin Administration"[1]. The instrument consisted of 4 open questions in google form and lasted 30 minutes. The evaluation of the answers was carried out by the teachers using a competency evaluation matrix with a score from 1 to 20, which was then categorized into 4 levels: Excellent, Very good, good and disapproved. (see table 1)

Table 1: Competency evaluation matrix.

Area	Competence	Score
Cognitive and procedural	Identify the problem of polymorphisms	1-5
	Explain the biotransformation of Warfarin	1-5
	It explains the results of the polymorphisms found and their relationship with therapeutic efficacy.	1-5
	Establishes therapeutic strategies, analyzes the main pharmacological groups for their safety and efficacy, showing polymorphisms and selects doses.	1-5
Attitudinal	Teamwork,	1-5
	Clear, precise exposure.	1-5
	Resolution of doubts with critical analysis	1-5

Source: Elaboration of the authors

The first measurement was carried out immediately after the end of the training, where in addition to the measurement of knowledge, other indicators of the learning process were measured, such as the creation of mental maps, co-evaluation among students of the same group (score from 1 to 20) and a self-evaluation. following the Bloom scale (score from 1 to 20)

[1] Available at https://drive.google.com/file/d/1oYqeOboS5ztvbqokFq74iRmGrWgkUT0O/view

Table 2: Co-evaluation matrix.

Values	Top Score.	Description
Commitment	4	Commitment to individual and collective self-learning with all team members through collaborative work.
Puntuality	2	Punctuality in the scheduled meetings and with the delivery of the work assumed.
Responsibility in the entrusted work	4	Responsibility for individual work and work with the team, towards the achievement of comprehensive learning.
Team Contributions	4	Contributions in synthesis of the reviews carried out based on indexed sources.
Ethical considerations of collaborative work	3	Ethical considerations in individual and team work, respect, assertive dialogue, avoid plagiarism, solidarity and altruism.
Reflections made	3	Reflections made for the construction of knowledge, self-assessment, co-assessment and the achievement of metacognition (how much did you learn about the subject, how does this knowledge demonstrate).
Total	20	

Source: Elaboration of the authors

The second measurement was made 4 years later. The same students were contacted and only the instrument was applied to measure knowledge based on the same clinical problem of the use of Warfarin. The qualification was carried out by the same teachers of the first measurement.

3. Results

All 160 enrolled students completed the Pharmacogenetics training and participated in the final evaluation. During the knowledge evaluation that was carried out immediately after the training, the elaboration of mental maps was also requested to reinforce the learning process. Each group developed a mental map evidencing the resolution of the problem with arguments based on the patient's genetic conditions, the drug analyzed, and the risks (safety) or benefit (efficacy).

The average of the qualification of knowledge on Pharmacogenetics obtained in the first measurement was 17.1 ± 1.2 points, where 67% of the students achieved the Excellent learning level, 22% achieved the "Very good" level, 8% achieved the "Good" level and 3% achieved a "Poor" level. Additionally, a co-evaluation between peers and a self-evaluation were carried out, obtaining average grades of 16.5 ± 1.7 and 6.6 ± 1.6, respectively. The scores of these two evaluations did not present a statistically significant difference with the knowledge score given by the teachers ($p<0.01$).

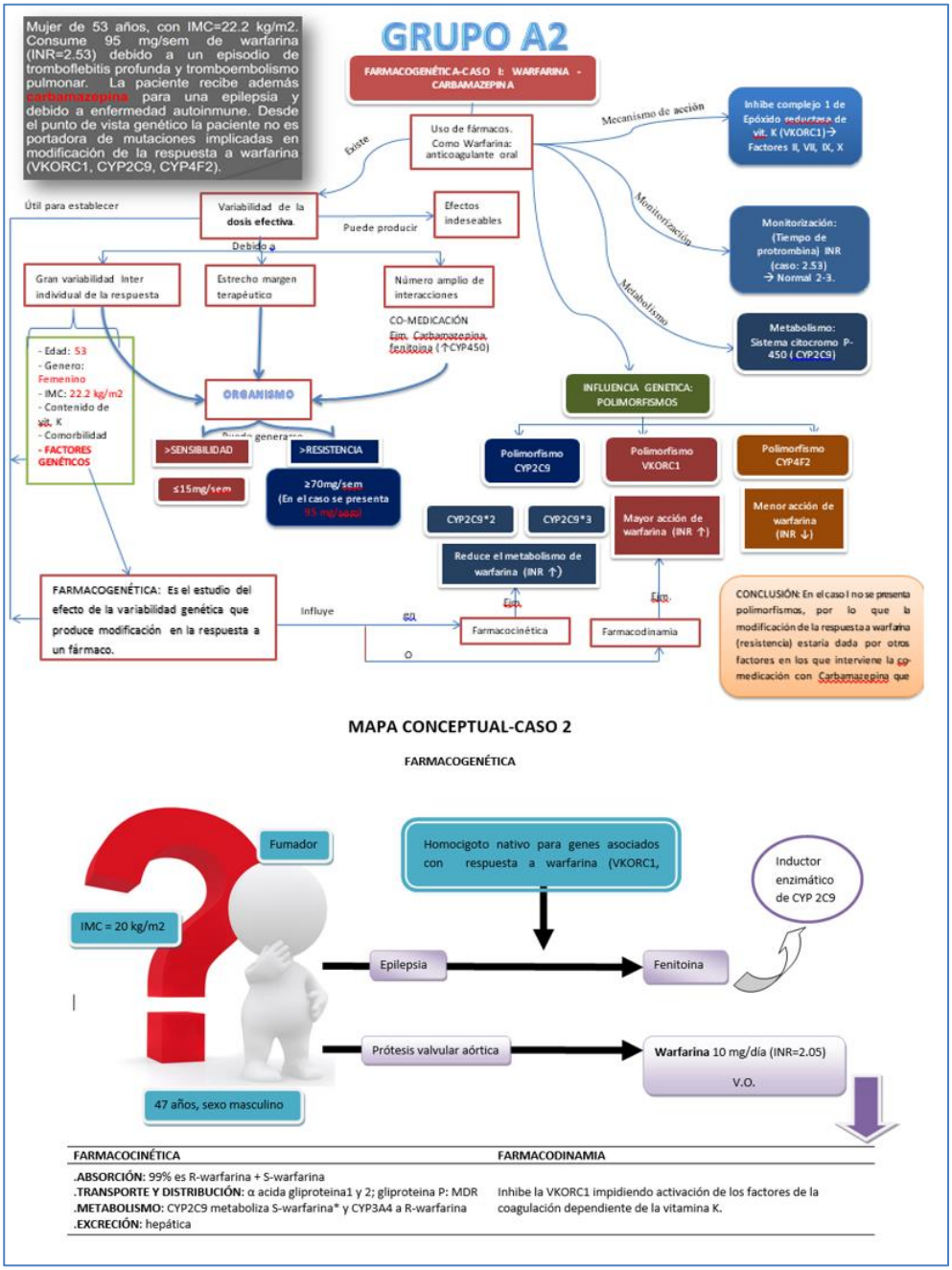

Figure 1. Example of the analysis performed by the students to solve the proposed case.

The second measurement was made 4 years later to 134 students who accepted or were available to take the evaluation. The average knowledge score on Pharmacogenetics was 17.2 ± 4.1 points, where 63% of the students achieved the Excellent learning level, 22% achieved the "Very good" level, and 12% achieved the "Good" level. and 3% achieved a “Poor” level.

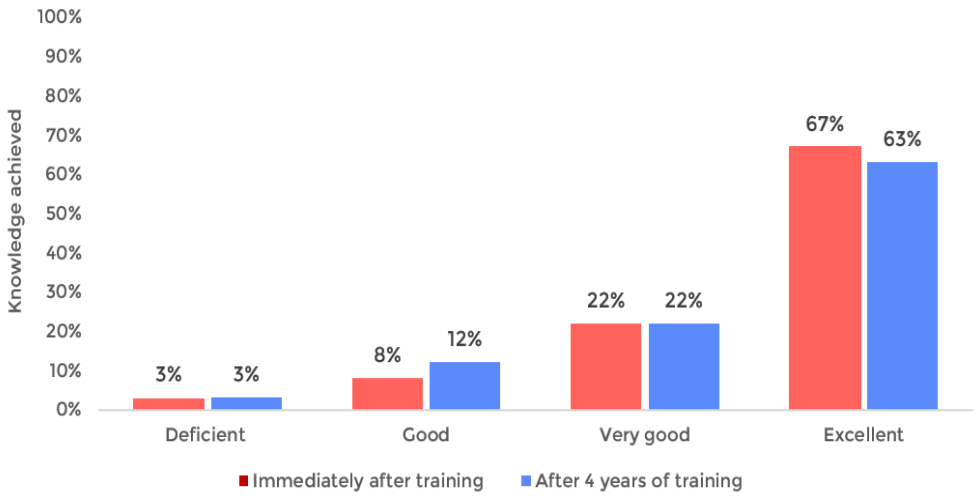

Figure 2. Knowledge achieved in pharmacogenetics, comparison of the year 2014 and 2018. Source: Elaboration of the authors

No significant difference was found between the first and second measurements. Of the 142 students who qualified with superior levels of learning in the first measurement (Excellent and Very Good), 80.3% continued with superior levels of learning four years later.

4. Discussion

According to Schunk (1997) defines learning as "a lasting change in behavior or the ability to behave in a given way as a result of practice or other forms of experience", when analyzing this concept three important elements are identified: 1. It is a change from the traditional lecture given by the teacher (2012), to a presentation built by the students themselves (2014) 2. Implies the development of a capacity to conduct oneself; it means that the person who learns acquires skills, and develops abilities. 3.It is a result of responsible self-learning practice. When analyzing the results over time, in 2014 the students raised what they know and do not know to solve the problem. The non-statistical difference between the results of the co-evaluation, hetero-evaluation and Bloom scale suggests an adequate reliability and validity of the assessments, for which it is justifiable to carry out a basically cognitive evaluation in the second moment of the investigation. In 2018, the students were already aware of the genetic polymorphism that patients present in their metabolism of warfarin, and the decisions to be made in the face of this problem.

In this constructivist scenario of individual and collective learning, among the factors to be highlighted are discipline, responsibility and the repetition of processes to acquire knowledge. This learning is complemented by collaboration and interaction between peers.

During the first stage, the investment of time is equivalent to 100 hours of collective work; which resembles the process of scientific research. These hours of work invested are evidenced by the results of the second stage, where all students received passing grades (considering that four years had passed since the intervention).

The learning model for warfarin metabolism indicates that we are working with the drug with the greatest impact in the treatment of thrombosis, as stated by Zambon, C.F., Pengo, V., Moz, S. et al. (2018),, this author has shown that therapeutic failures obey the patient even more than the drug and can be predicted knowing the INR results in the first 19 days of treatment and adjusting the dose.

Our teaching proposal has been developing since 2014, which includes methodologies such as PBL, which includes the resolution of public health problems Galindo Cárdenas, L. A., & Col. (2011); Aguilar, M.E., & Col. (2011)., Lermanda, C. (2016).In pharmacology, the problems elaborated deal with drugs recognized as essential by the WHO, in this way the students are prepared for the reasoned prescription of drugs with ethical responsibility.

Currently we continue to develop virtual and face-to-face teaching models. We are sure that in 2022 we will use the B-learning modality and also e-learning in all subjects, which have contributed to the development of meta-cognitive skills in students.

5. Conclusion

Cognitive ability is persistent over time using the methodology described in the Pharmacogenetics learning process. It was shown that the use of a meaningful learning methodology with PBL and ICT can make knowledge last and serve in the future for decision-making in the selection of medication.

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