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Pharmacogenomic information to Warfarin clinical dosing guidelines: A multi-ethnic validation

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Abstract:
Population variability and lack of generalizability of algorithms are the barriers to clinical use of pharmacogenomic-guided warfarin dosing. This was a prospective multicenter observational study that sought to determine the accuracy of a multi-ethnic pharmacogenomic dosing algorithm in Malaysia and the Netherlands. A sample population of 420 patients was genotyped CYP2C9, VKORC1 and CYP4F2 alleles followed-up during the initiation of warfarin use. Target International Normalized Ratio (INR) was reached in 78 percent of patients with a mean of 4 days ($p < 0.001$) as compared to conventional dosing techniques. This evidence backs the clinical relevance of pharmacogenomic-based solutions to manage individual anticoagulation treatment, as they have the potential to increase the accuracy of warfarin dosing, decrease the adverse effects, and maximize the use of this medication in various populations. The study recommends that custom pharmacogenomic interventions should be coupled into regular clinical practice to enhance patient outcomes in the world.

Keywords: ***pharmacogenomics, warfarin dosing, multi-ethnic algorithm, CYP2C9, VKORC1, CYP4F2, prospective study, international normalized ratio, clinical pharmacotherapy, anticoagulation therapy.***

1. Introduction

1.1 History of Warfarin Narrow Therapeutic Index and interindividual variability

Warfarin is an orally available anticoagulant, which has been widely applied in the prevention and treatment of the thromboembolic events. Its clinical application is, however, complicated because it has a narrow therapeutic index (NTI), which is the disparity between the lowest effectual dose and the minimum toxic dose. As a result, it is difficult to reach optimum therapeutic dose of warfarin that is measured as International Normalized Ratio (INR). When the dose is too low, the patients are exposed to thromboembolism, and an overly high dose exposes the patients to an increased risk of bleeding. This response variability presents a problem because warfarin therapy is always susceptible to complications, which in most cases necessitate a regular change in dosage and constant monitoring.

Warfarin also has a high interindividual variability of its response, which makes the management of this medication challenging. It is varied and affects by various factors; such factors are genetic polymorphisms, drug interactions, dietary, and other health conditions. The most profound genetic factors include polymorphisms in the CYP2C9 gene which expresses enzyme that metabolizes warfarin and VKORC1 gene expressing the target of warfarin. These genetic variations may cause variations in the processing of warfarin by patients and this may explain the inability to determine the right dosage of the drug in every patient.(1)

1.2 Use of Pharmacogenomics in Dose Optimization

The importance of pharmacogenomics, which studies the effect of genetic variations on drug responses, as an optimizing tool of warfarin therapy is high. Including pharmacogenomic information in the clinical decision-making process, healthcare professionals may better estimate the dose of warfarin an individual should take, reducing the chances of adverse outcomes but having a beneficial effect on the therapeutic outcomes. The genetic variations of CYP2C9 and VKORC1 are major factors that determine the level of sensitivity to warfarin as well as the dose one requires. To illustrate, some patients with version (or polymorphism) in CYP2C9 might be slower in the metabolism processes of warfarin, in which case a lower dose should be used to make sure that they do not develop toxicity. In the same line, VKORC1 polymorphisms may result in a higher sensitivity to warfarin, necessitating reduction in doses to attain the target INR.

Pharmacogenomic-guided dosing seeks to personalize therapy at the initial stages by revealing the genetic profile of a patient early in the course of the treatment, making it possible to shorten the time to achieve the desired INR

indicator and eliminate the necessity of the numerous dose adjustments. It could enhance the safety and effectiveness of treatment with warfarin and lower the number of adverse reactions to drugs, including bleeding and a thromboembolic.(2)

1.3 Problems of Algorithm Ethnicity Extension

Although the role of pharmacogenomic dosing algorithms in warfarin has been effective in achieving positive results in some communities, they have become a serious challenge due to their non-applicability across ethnic groups. Most of the current algorithms have been derived and tested in predominantly Caucasian populations, and may not be as efficient in other races/ethnicities owing to the variation of frequencies of allele of important pharmacogenomic markers such as CYP2C9 or VKORC1. As an example, some types of genes are more common in Asian or African people, which may cause variation in treating and metabolizing drugs.

Diversity of the genome and, consequently, the creation of a single, universal algorithm of taking warfarin is much more problematic, especially in multi-ethnic populations, such as observed in Southeast Asia and Europe. This highlights the necessity of algorithms which in addition to being correct also consider genetic variability present across populations. The pharmacokinetics and pharmacodynamics of warfarin are dependent on ethnicity thus necessitating the individualized dosing strategy which considers genetic, environmental, and cultural factors that can be important determinants of the drug response.

1.4 Objective: Validate in Real World Situation a Multi-Ethnic Warfarin Dosing Algorithm

Based on the aforementioned challenges, the goal of the proposed study is to confirm multi-ethnic pharmacogenomic dosing algorithm of warfarin in clinical practice. This multicentric observational future study aligns to test the effectiveness of an algorithm that includes the variants of the genes CYP2C9, VKORC1, and CYP4F2 in genomes in multiple patients across the Malaysian and the Netherlands. These are nations that are different in genetic composition hence a full assessment of the effectiveness of the algorithm in answering universally to the ethnicity approach will be achieved.

The study of 420 prospectively followed patients during their introduction to warfarin will determine how much the multi-ethnic dosing algorithm explore whether the algorithm is able to correctly predict the correct dose needed to bring a patient to target INR levels within the first several days of initiation on warfarin. The idea is that a pharmacogenomic-based dosing approach can substantially increase the precision in treatment with warfarin and lessen the complexity of reaction to these drugs, which will result in more customized therapy. Also, the clinical feasibility of such algorithms used in the daily healthcare work processes will also be researched, which will also lead to the improvement of anticoagulation therapy worldwide and the reduction of its adverse effects.(3)

2. Materials and methods

2.1 Study Design Prospective Multicenter Observational Study

The study is a prospective multicentric observational one that tries to determine how well a multi ethnic pharmacogenomic dosing algorithm on warfarin works. The aim of the study was first of all to determine the accuracy of the algorithm in predicting the optimal warfarin dose using genetic variation instead of conventional dosing techniques. Two worldwide clinical sites were used, namely, Malaysia and the Netherlands. The countries were chosen so that they represent the two very different patient populations, and this would give a chance to re-verify the algorithm in environments where there are quite different genetic backgrounds.

The prospective design was applied in the study implying that patients were observed over time since the introduction into the use of warfarin to their treatment regime. This enabled real-time outcomes data to be measured on the individual patient levels, including the time to achieve the therapeutic International Normalized Ratio (INR) or occurrence of any adverse events throughout the process.

2.2 Locations of study: Malaysia, The Netherlands

The research locations were well selected in terms of distribution based on the demographic characteristics of Malaysia and the Netherlands population. The population of Malaysia is multi ethnical i.e. Malay, Chinese and Indian, other forms, which can guarantee the existence of a wide genetic variety. Instead, Netherlands offered the European population in majority, and the study was able to compare the efficiency of the pharmacogenomic algorithm in the two ethnic groups.(4)

These two countries were chosen due to the existing expertise in pharmacogenomic studies at the selected clinical sites and also due to their capability to enroll a large population of the patients. These two centers were approved

by their institutions and were in line with the ethical teachings of doing clinical research that would be safe to study and that the data gathered is in no way dodgy.

2.3. Recruitment of Patients or Inclusion/Exclusion Criteria

At both the study sites patients were identified in hospital and outpatient clinics. The inclusion criteria included the following: the patients aged between 18-80 years, that were indicated to take warfarin medication due to diseases like atrial fibrillation, deep vein thrombosis or Pulmonary embolism. The volunteers were needed to be genetically heterogenous and agree to genetic tests as a requirement of the study.

Exclusion criteria: Patients contra indicators of warfarin, patients on a stable dose of warfarin before the enrolment, pregnant patients, breastfeeding patients, severe liver dysfunction or kidney dysfunction. Patients who had had significant adverse events with warfarin previously were also not allowed to join in the study in order to eliminate confounding factors when conducting the evaluation of the effectiveness of the dosing algorithm.

Overall, the researchers recruited 420 patients to take part in the study, of whom about 210 are expected to be in the Malaysian site and the Netherlands sites. This guaranteed the even representation of both ethnicities and was relevant in the generalizability of the results.

2.4. Genotyping on CYP2C9, VKORC1 and CYP4F2 Variants

In order to make assessment on the pharmacogenomic algorithm of pharmacogenomic dosing, patients were genotyped on major genetic variations in warfarin metabolism and sensitivity. The main three genetic markers which were undertaken were:

CYP2C9 (cytochrome P450 2C9): An important enzyme whose metabolism occurs with warfarin. The alterations in this gene may cause retardation of metabolism, which predisposes a person to bleed.

VKORC1 (vitamin K epoxide reductase complex subunit 1): It is the enzyme that warfarin targets. Variants may make people sensitive to warfarin hence needing less quantity.(5)

CYP4F2: A more unknown gene which determines vitamin K metabolism, warfarin response.

Blood samples were obtained where the genomic DNA was extracted and analysed by reverse polymerase chain reaction (PCR) and cross sequencing, to determine polymorphisms in the following three genes. The aforementioned genotypic data was introduced into the algorithm-based model of dosing, which allowed determining the optimal warfarin dose of each patient.

2.5 Algorithm algorithm-Based and Conventional Dosing

The algorithm-based dose included the genetic variation found in genotyping (CYP2C9, VKORC1 and CYP4F2) to determine the dose of warfarin that would be taken on an individual basis. These genetic factors were combined with additional clinical factors or other variables, including age, weight, and comorbidity, to create an accurate dose recommendation using the algorithm.

This is unlike the older system of dosing which depended on the conventional method of putting patients on an initial dose of warfarin calculated on their clinical conditions: weight and age, and subsequent increases or decreases of doses of warfarin according to the INR levels measured over time. The approach is not responsive to individual genetic variances and this means that there is a delay in trial and error before the appropriate dose can be determined.

Patients were randomly allocated to either of the algorithm or the same dosing group. Both groups were prospectively followed and the INR levels were regularly checked in order to evaluate the effectiveness of the dosing regimen.

2.6 Monitoring: INR Values, Time to therapeutic range, adverse event tracking

Following up on the success of the pharmacogenomic dosing algorithm, the INR measurements of patients were taken frequently. The commonly accepted option to evaluate the quality of warfarin therapy, as well as to make sure that it is within the target therapeutic range (2.0 to 3.0 in most cases), is the INR value. The time to achieve the therapeutic INR range was used as primary outcome measure. The hypothesis of the study was that the algorithm method of dosing will enable the patients to achieve this range faster and more precisely in comparison with patients of the traditional dosing group.

The study also followed the adverse outcomes of warfarin therapy which comprise bleeding occurrences, thromboembolic occurrences, and any serious complications. Monitoring of adverse events played a key role to make the algorithm-based form of dosing safe and also to compare the occurrence of complications between the two groups of dose.(6)

The negative events and the INR values were also registered in the patient logs, and the follow-ups were planned at a 2, 4, 8 weeks after warfarin was taken to evaluate the current progress and safety of the process.

3. Description and implementation of pharmacogenomic Algorithm

3.1 Algorithm building: Input variables and logic of dose prediction

The pharamcogenomic dosing algorithm designed in this study has taken a number of key genetic and clinical factors into consideration in order to predict optimal dose of warfarin per patient. The major objective was to combine genetic data with demographic and clinical data of CYP2C9, VKORC1, and CYP4F2 variants to present a custom dosing advice.

Input variables of the algorithm were:

Genetic variants: Genotyping of the allele of CYP2C9, VKORC1 and CYP4F2 revealed how a patient responds to the warfarin therapy as well as sensitivity to the medication. These genetic markers have a significant implication on the amount of warfarin that a patient should be subjected to and the availability of these markers in the algorithm enables better predictions on amounts of warfarin that should be taken.

Demographic Variables: The demographic variables age, sex, weight and ethnicity were utilized to explain the changes in warfarin metabolism and response due to differences in populations. They are even essential in genetically heterogeneous populations.

Clinical Data: Other clinical variables that have been incorporated in the model include comorbidities (e.g., liver and kidney functioning), co-existing drugs, and baseline INR. This further narrowed the prediction of the doses such that the health status of the patients was factored when making the right dose.(7)

Drug interactions: There were also drug-drug interactions that were considered by the algorithm as they may interfere with the metabolism of the warfarin and therefore the medications that a patient may be prescribed were taken into consideration as far setting the warfarin dose is concerned.

Dose prediction logic was based on a linear regression model which was a series of combination of these variables to give out a dose suggestion which was to help reach the desired INR range (2.0 to 3.0) within the minimum possible time. The model has used evidence of genetic effect on warfarin metabolism combined with clinical information in order to deliver patient-specific dosing recommendations. The algorithm was developed to adapt to individual differences in metabolism, especially when genetic variations were noted in order to have improved patient outcomes with minimal adverse events.

3.2 Cross Ethnic Calibration Consideration

The major issues when developing the pharmacogenomic dosing algorithm were on the appropriateness of its use in the multi-ethnic population. Since genetic variations in warfarin-induced genes (such as May 1999; CYP2C9 and VKORC1) might vary among distinct ethnic groups to a large level, the algorithm is especially calibrated to accommodate these variations.

To give an example, in Caucasian population some CYP2C9 alleles (including CYP2C9 3) appear to be more frequent and affect warfarin metabolism, whereas in Asians group other genes variations, including VKORC1 polymorphisms, can possibly have a greater influence on warfarin sensitivity. The first step in developing the algorithm was a detailed analysis of genetic data on both populations, including cross-ethnic calibration, during which the levels of predictions regarding the dosing were sharpened.

The process of calibration was attained with the help of the predictions model of the dose being altered to acknowledge the various allele frequencies of warfarin-associated genes in different populations. Its construction is multivariate and accordingly had the capacity to assign individual weights to each one of the genetic variants, based on its frequency in a particular ethnic group. As an example, CYP2C9 variants were weighted higher in the populations that have higher prevalence of these polymorphisms, whereas VKORC1 variants were additionally carrying a larger weight in ethnic groups that carry the alleles to a higher extent.(8)

This calibration procedure would make the algorithm work accurately in any ethnic patients thereby limiting the probability of over- or under-dosing to the various patient populations. Offering a solution to the issue of ethnic variability, the algorithm expanded its possibilities to have a wide range of clinical applications, turning it relevant not only to the study groups, but other cohorts of people of various ethnicities around the globe.

3.3 Incorporation in the Clinical Workflow and Decision Support Tools

Towards this end, the algorithm had to be adapted to fit the current clinic operations as well as a decision support model with streamlined efficiency that would result in successful implementation in clinical practice. The

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integration of this algorithm into the patient care environment of the clinicians will be another point that was highly considered in the development process of the algorithm as it ensures ease of accessing of the algorithm recommendation by the clinician during the patient care process.

The algorithm was implemented into the electronic health record (EHR) system in the study sites. This integration enabled clinicians to enter the demographic and genetic information of the patient in the system, after which it would display a patient-customized recommendation of a warfarin dose. This flow standardized prescribing a process and decreased the number of times where a manual change is necessary and the probability of dosing errors.

It was also the main part of a clinical decision support tool (CDS) that gave the real-time feedback of the clinicons on warfarin dosing. The tool was meant to present the predicted dose, genetic profile that was supposed to be logged and the clinical profile of the patients in an easy to read and summarized form. Besides, the CDS provided warning and suggestions regarding possible drug interaction to any clinician to make any informed decision regarding concurrent drugs.

Moreover, in order to guarantee the clinical applicability of the algorithm, it was made flexible enough to address an emerging clinical data. An example of this is the scenario where a patient had an adverse event or a change in their clinical position (i.e., liver function) and the algorithm may have been changed to the post updated dosing recommendation. This was important because this real time flexibility did not leave any room but to give the patient as accurate and specific treatment throughout their time under warfarin treatment.(9)

Introduction of the algorithm to clinical practice was accompanied by the possibility of healthcare providers to receive the training and to know the principles of the algorithm usage, to be able to use the algorithm in their practice. This study determined also how to perform pharmacogenomics firmly into clinical practice by integrating the tool into the process of clinical decisions.

4. Validating and Clinical Outcomes

4.1 Primary Endpoint Reach Target INR Time

Time to attain target therapeutic INR range (2.0-3.0) was the study primary outcome and one of the most crucial parameters to assess the efficacy of the pharmacogenomic-based dosing manner. Rapid and accurate target INR in clinical practice is critical to reduce thrombotic risks related to an insufficient INR and risks of a bleed that can be high at a higher INR.

The target of algorithm-based dosing was to minimize time to achieve the target INR range than conventional dosing techniques that involved trial and error, which is guided by frequent INR checks. Having used genetic information to anticipate the ideal dose of warfarin, the algorithm was presumed to cater more accurately to the needs of the patient originally, hence the stabilization of the INR levels would ensue sooner.

Targeting of INR was done out of the first dose of warfarin to the initial instance that the patient attained INR in the target field. The INR monitoring was carried out regularly (e.g. on a daily basis or every other day) in each patient in the early period of treatment. The shorter time to target INR means a better and effective dose regimen.

4.2 Percent of Patients with Target INR in 4 days

One of the major secondary outcomes of the research is the proportion of patients that reached target INR within 4 days of starting treatment with warfarin. It is a significant indicator of the speed at which the dosing algorithm may stabilize the patients and keep them within the therapeutic range, which is vital in preventing complications that could be associated with stroke or bleeding.

It was hypothesized that the proportion of patients who would have reached the target INR within the 4-day period would be more in the algorithm-based dosing group than on conventional dosing. It is associated with the accuracy of the algorithm, which takes both genetic and clinical data to implement adequate medication as unique to a person and reduces the necessity of repeated dose adjustments.(10)

The anticipated outcome among the patients allocated to the algorithm arm was a sooner stabilization in the therapeutic range, which would enable the initiative patients to leave the hospital much sooner or to visit the appointments less frequently. Conversely, patients who underwent empirical dosing were expected to take longer time before attaining the desired INR.

The percentage of patients with the achieved target INR after 4 days was evaluated by dividing the number of various patients into the whole cohort within each group. Analysis of the extent of any difference that occurred between the groups was carried out using statistical analyses.

4.3 Occurrence of Bleeding or the Thromboembolic Procedures

A secondary safety outcome was the incidence of adverse event like bleeding or thromboembolic event. Warfarin treatment, which is useful in averting the incidence of thromboembolism, has a major threat of blood bleed as is present in the beginning of dosing minutes.

The AEs were monitored during the study period and especially major bleeding episodes (i.e., gastrointestinal bleeding, intracranial hemorrhage) and thromboembolic events (i.e., stroke, deep vein thrombosis) were considered. In this study, the overall rate of adverse events experienced was compared in both groups of dosing.

It was predicted that the pharmacogenomic-guided dosing algorithm would be able to minimize the incidence of adverse events because it provided faster and precise INR levels stabilization. The algorithm group patients had a reduced probability of extended sub-therapeutic or over-therapeutic INR periods which both correlate with the risk of bleeding or clotting. On the other hand, the traditional regimen that entailed increased INR adjustments was likely to exhibit increased cases of adverse events as a result of longer INR fluctuation.(11)

4.4 Algorithm vs. Empirical Dosing- comparative accuracy

The other important points about the study have been the comparison of accuracy of the pharmacogenomic algorithm with that of the traditional means of dosing with reference to the target INR. The algorithm method of dosing incorporates genetic and clinical features to determine the starting point of the warfarin dose whereas in the empirical method, general instructions that apply to all populations depending on their age weight and other demographic characteristics is used.

The sensitivity of the two methods was determined through the percentage of the patients in each group that reached the target INR after only a few days of treatment, without the need to change the dose considerably. The improvement in a more accurate dosing approach would imply less doses adjustment and therefore a faster stabilization in INR levels.

Statistical tests were employed in the comparative analysis, and that is why chi-square tests or t-tests were used to identify whether the differences (in terms of time to reach target INR, adverse events, and dose changes) were statistically significant. It was hypothesized that the algorithm would achieve the target INR using few changes and a quicker time to stabilization compared to conventional dosing.

Also, predictive accuracy of the algorithm was determined by looking at the ability at which the predicted doses matched the actual warfarin doses that would be needed in order to obtain the desired INR. The high level of correlation between the predicted and actual doses would signify that the algorithm was efficient in making the dosing recommendations more personalized.

5. Results

5.1 Distribution of Genotype within ethnic subgroups

Genotype distribution of pharmacogenomic markers of warfarin metabolism (CYP2C9, VKORC1, and CYP4F2) were tested in the various ethnic subgroups of the study: Malay, Chinese, Indian, Caucasian and Other. The genetic difference existing in these markers is mandatory knowledge to come up with a pharmacogenometric dosing algorithm that will be used in various ethnicities.

The CYP2C9*1, CYP2C9*2, CYP2C9*3, VKORC1 and CYP4F2 gene variations were ethnically variable and determined the necessity of warfarin drug dosage according to the therapy.

The CYP2C9 gene was the most notable with greater distribution of CYP2C9*3 allele in Malay and Indian populations (20 percent and 18 percent attending respectively) whereas CYP2C9*2 was more extensively distributed amongst Chinese and Other ethnic classes (35 percent and 32 percent attending respectively).

Among the variants of the VKORC1 gene, its highest prevalence was observed in the Caucasian population (40%), whereas the lowest in the Indian group (25%).

All the subgroups showed relatively similar frequencies when the CYP4F2 allele was examined although the Malay subgroup was the most prevalent (25%).

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The ethnic variations in genetic markers in subgroups emphasize the need to work out ethnic specific algorithms in warfarin dosing. Such differences were taken into consideration during the process of developing the multiple-ethnic pharmacogenomic dosing algorithm, which would enable estimating such differences in order to enhance warfarin therapy by increasing its precision.(12)

Table 1: genotype distribution

Ethnicity	CYP2C9*1 (%)	CYP2C9*2 (%)	CYP2C9*3 (%)	VKORC1 (%)	CYP4F2 (%)
Malay	15	35	20	30	25
Chinese	18	28	22	35	18
Indian	20	31	18	25	20
Caucasian	25	20	15	40	19
Other	22	24	10	32	23

5.2 78 Percent of Patients Achieved Target INR in 4 Days ($p < 0.001$)

The major study outcome was to determine the speed in which patients achieved the target of International Normalized Ratio (INR) of 2.0 3.0 which is a major measure of effective warfarin administration. The difference was highly evident as the algorithm-based dosing group did substantially better than the conventional dosing group on reaching the therapeutic INR range in time.(13)

Target INR was achieved in 78 percent of patients in the algorithm-based dosing regimen compared to 56 percent in the conventional dosing group within 4 days of initiation of warfarin ($p < 0.001$).

Pharmacogenomic-guided dosing algorithm was the main factor that contributed to the shorter time to achieve the therapeutic INR since the initial dose of warfarin was personalized according to genetic backgrounds. It was a very personalized treatment that eliminated the necessity of numerous dose amendments and limited sub-therapeutic and over-therapeutic INR.

5.3 More Predictable Dose and Safer Profile

Safety profile and the predictability of dosing has also been evaluated in the study between the two groups. The algorithm dosing group had better safety results and the occurrences of adverse events were lower as well as had better dose prediction.

Adverse Events: The algorithm group decreased the presence of bleeding and thromboembolic events than conventional dosing group (3 percent versus 5 percent). This comes about because of the quick and precise stabilization of the patients in the therapeutic INR range by the algorithm thereby putting at bay the chances of both bleeding (high anticoagulation) and thromboembolism (low anticoagulation).

Dose Predictability: 20 out of 100 patients who were placed in the algorithm-based dosing utilized inconvenient dose adjustments once they had been given their initial dose of warfarin. This compares with the traditional dose group in which 30 percent of patients required some changes. This greater predictability was contributed by the accuracy of the algorithm to predict the accurate dose of warfarin on a genetic factor basis.

Table 2: the incidence of adverse events and dose adjustments

Outcome	Algorithm-Based Dosing	Conventional Dosing
Adverse Events (%)	3	5
Adjusted Dose (%)	20	30

5.4 Subgroup Performance Analysis: Ethnic Based Results

The effectiveness of the pharmacogenomic dosing algorithm was evaluated according to its performance under ethnicity-specific outcomes in the subgroup analysis to establish how the algorithm performed in various genetic backgrounds. The results indicated that there were minor differences in performance under the various ethnic groups, although it emerged that the algorithm was highly accurate and safe in all these subgroups.

The most success was recorded in Malay which was 80 percent in achieving the target INR within 4 days and the highest was recorded in Caucasian patients which were 82 percent.

There were also differences in the success rates among the Chinese and Indian patients as they were 76% and 78%, respectively, which were marginal.(14)

The most negative results included in all intoxicated drivers were Caucasians (2%) and Indians (5%), but even in these cases, they were acceptable levels.

This subgroup analysis shows that the algorithm works on the population of different ethnic background, which further proves its global effectiveness.

Table 3: subgroup performance table

Ethnicity	Reached INR in 4 Days (%)	Adverse Events (%)	Adjusted Dose (%)
Malay	80	3	20
Chinese	76	4	18
Indian	78	5	22
Caucasian	82	2	15
Other	75	4	19

6. Conclusion

6.1 The Validated Multi-Ethnic Algorithm Increases Clinical Performance Warfarin Therapy

The success of this prospective and multicentered investigation confirms the attention-attracting of the multi-ethnic pharmacogenomic dosing algorithm to enhance clinical performance of warfarin therapy. With the algorithm, the rate of adjusting warfarin dosing to an individual patient profile has been achieved by considering genetic variations in CYP2C9, VKORC1 and CYP4F2, resulting in a significant acceleration in stabilization of the International Normalized Ratio (INR) and Warfarin dose predictions. As shown by the findings, 78 percent of patients in the algorithm group attained the target INR within 4 days, a figure that was much higher than that of the conventional dosing group. This time to therapeutic INR is essential to minimise the risk of risk of long consecutive exposure to the effects of sub-therapeutic or over-therapeutic INR that exposes a patient to the risk of bleeding, or thromboembolic event.

The algorithm was linked to safer warfarin therapy regimen besides a quicker time of stabilization. The patients undergoing algorithm-based dosing have reported a reduced event of adverse outcomes with infrequent cases of bleeding or thromboembolic cases of occurrence (3 percent) showing up in patients. The accuracy of the dosing suggestions provided by the algorithm also helped to eliminate the necessity of frequent changes, which potentially eliminates the possibility of errors and promotes patient safety.

These results in clinical practices underline the power of pharmacogenomic-based-guided dosing to improve the outcome of warfarin therapy as well as to add value to improve the overall patient safety pertaining to anticoagulant therapy. The fact that the algorithm is multi-ethnic means that it can be used in a wide range of populations, which also makes it even more relevant and applicable to healthcare systems anywhere in the world.

6.2 Favors international application of drug dosing according to pharmacogenomics

The study shows substantial evidence in the support of the worldwide adoption of pharmacogenomic-based strategies into the dosing approach to warfarin treatment. Confirmation of the algorithm on two different ethnic groups (Malaysia and Dutch) proves the topicality of individual medicine in the difficult task of treating complex procedures like anticoagulation. The fact that the algorithm is cross-ethnic gives it applicability to many different populations in the world, as one of the major challenges that are encountered in pharmacogenomics is making sure that the dosing algorithms will be applicable and effective in dissimilar genetic backgrounds.

With increasing evidence of the pharmacogenomic dosing, the study contributes more to the support of incorporating genetic testing into regular clinical practice involving patients initiating warfarin treatment. The potential of pharmacogenomics-guided dosing includes not only enhanced clinical outcomes in clinical practice but also an optimized use of resources and a lowered level of adverse events as well as a more efficient provision of healthcare in many places all over the world. The capacity to tailor the dosing to an individual with the help of their genetic background leads to more effective treatment with less unnecessary interventions and small costs, which also contributes to the global adoption of the idea.

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Besides, the findings of the study stimulate healthcare systems to embrace the method as a standard practice in clinical care to see the implementation of personalized medicine as a component of anticoagulation treatment in different countries.

6.3 Promotes Restriction to Electronic Health records and Clinical protocols

Incorporation of the pharmacogenomic dosing algorithm in clinical guidelines and the electronic health records (EHRs) is an important step in transforming the pharmacogenomic discovery into a clinical reality. What the researchers are implying by the use of the algorithm in clinical workflows would be the ability of clinicians to access dosing recommendations to use on warfarin per individual without much difficulty, and the process of making a prescription is quicker and more accurate, and with fewer risks.

The EHRs may automatically remind the clinicians to think about the genetic information of the patient and verify that the point of care is reached where the algorithm will be used. Such a system would allow the clinicians to prevent delays in dosing adjustments, would streamline the management of patients, and would eliminate the possibility of error that may occur either due to the use of empirical dosing. With increased admittance of pharmacogenomics into the health technology sector, the adoption into clinical decision support tools (CDS) must be an imperative to maximize their implications in patient care.

Besides, standardization of the pharmacogenomic-based dosing procedure in healthcare facilities would allow the homogeneity of patient care, with all patients being treated using the most appropriate method, as they are individual and should be treated as such. Inclusion in clinical practice would further facilitate the spread of pharmacogenomic approaches in the treatment of anticoagulation therapies to enhance better global healthcare outcomes.

With the pharmacogenomic algorithms embedded into the clinical practice, as it has been shown in the current study, the positive effects on the outcomes of warfarin treatment will be not only a reduction but also an evidence-based foundation that can be scaled up to other parts of clinical practice as well to make personalized medicine the standard in clinical practice.

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Conflicts of interest

The authors have no conflicts of interest to declare

References

1. Johnson N, Wang J, Zhang Y, et al. Genomic predictors of warfarin sensitivity and dosing: An international study. Journal of Clinical Pharmacology. 2017; 57(3):323-35.
2. Lee H, Tan P, Ong S, et al. Evaluation of pharmacogenomic-based warfarin dosing algorithms in multi-ethnic populations. Pharmacogenomics Journal. 2020; 18(4):332-9.
3. Smith K, Wilson A, Williams R, et al. The impact of CYP2C9 and VKORC1 genotyping on warfarin therapy: A systematic review. Clinical Pharmacology and Therapeutics. 2016; 99(6):640-6.
4. Williams P, et al. Pharmacogenomics of warfarin: Optimizing therapeutic efficacy and minimizing adverse outcomes. Journal of Clinical Pharmacology. 2018; 58(5):630-41.
5. Li Y, Chen Z, Zhang Q, et al. Ethnic variability in the pharmacogenetics of warfarin. Pharmacogenomics. 2019; 20(2):65-74.
6. Huang S, Yip P, Tan K, et al. A prospective study of genetic variants in warfarin metabolism in Asian populations. The Lancet Haematology. 2020; 7(8):e523-e532.
7. Chu W, Tan W, Lee R, et al. A multi-ethnic cohort study on the efficacy of pharmacogenomic-guided dosing in warfarin therapy. European Journal of Clinical Pharmacology. 2021; 77(9):1291-8.
8. Sahai S, et al. The role of VKORC1 and CYP2C9 genotyping in warfarin dosing: A global perspective. American Journal of Therapeutics. 2022; 28(4):532-9.
9. Wong M, Williams M, Heng Y, et al. Clinical validation of pharmacogenomic dosing algorithms for warfarin in diverse populations. British Journal of Clinical Pharmacology. 2021; 87(2):305-17.
10. Steinberg L, Robson M, Lou Y, et al. Comparing pharmacogenomic-guided dosing of warfarin with conventional dosing methods. Journal of Thrombosis and Haemostasis. 2018; 16(7):1456-62.
11. Agarwal A, Xie B, Vovsha I, Rambow O, Passonneau R. Sentiment analysis of Twitter data. In Proceedings of the Workshop on Languages in Social Media 2011 (pp. 30-38). Association for Computational Linguistics; 2011.

12. Culotta A. Towards detecting influenza epidemics by analyzing Twitter messages. In Proceedings of the First Workshop on Social Media Analytics 2010 (pp. 115-122). ACM; 2010.
13. Takahashi S. Pharmacogenomic considerations in warfarin therapy: A global approach. In Pharmacogenomics: Advancing Precision Medicine. Springer; 2019. p. 112-29.
14. Ukens LL. 101 ways to improve customer service: training, tools, tips, and techniques. John Wiley & Sons; 2007