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Original Article

Accuracy Assessment of an Android-Based Pharmacokinetic Application for Amikacin Using Mean Absolute Percentage Error (MAPE)

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Abstract

Background: This study evaluates the accuracy of an Android-based pharmacokinetic application, the "Indonesia Pharmacokinetic Calculator" (Kalkulator Farmakokinetik Indonesia - KFI), developed to calculate individual pharmacokinetic parameters in patients receiving amikacin, a narrow therapeutic index drug. **Objective:** To assess the accuracy of the KFI application in calculating pharmacokinetic and pharmacokinetic/pharmacodynamic parameters and to compare its performance with MS Excel. **Methods:** The KFI application incorporates pharmacokinetic algorithms to calculate patient-specific parameters (e.g., k, t½, Vd, CL, AUC, Cpss, and time to reach Cpss) and pharmacokinetic/pharmacodynamic parameters (e.g., Cpmax/MIC Ratio, AUC0-24h/MIC Ratio). The application allows the input of patient data, including two post-dose drug concentration measurements. Accuracy was assessed by comparing the KFI outputs with those obtained from MS Excel using identical formulas. The Mean Absolute Percentage Error (MAPE) was used to quantify differences between the two methods. **Results:** The KFI application demonstrated high accuracy in calculating pharmacokinetic parameters, with an average MAPE of 0.04% and a standard deviation of 0.13%. Most parameters exhibited an APE of 0.00%, indicating near-perfect agreement with MS Excel calculations. Minor differences were observed for clearance (CL) and minimum steady-state concentration (Cpss min), with APE values of 0.05% and 0.50%, respectively. These differences were considered clinically acceptable. **Conclusion:** The Android-based pharmacokinetic application has been shown to provide a reliable and accurate tool for calculating pharmacokinetic and pharmacokinetic/pharmacodynamic parameters for amikacin, offering significant potential for clinical decision-making and optimising therapy.

Keywords: *Amikacin; Android Application; MAPE; Pharmacokinetics; Therapeutic Drug Monitoring*

Introduction

Since the onset of the COVID-19 pandemic and the implementation of Large-Scale Social Restrictions (Pembatasan Sosial Berskala Besar - PSBB) in Indonesia in March 2020, computers, laptops, and smartphones have become essential tools for work-from-home and study-from-home activities. This shift has led to the widespread adoption of digital technologies to enhance work, learning, and public health strategies, thanks to the accessibility and ease of use of information and communication technology (Komalasari, 2020). In this context, Android-based pharmacokinetic calculation applications offer an innovative solution to optimise drug therapy, particularly for drugs with a narrow therapeutic range, such as amikacin. Mobile devices, including smartphones and tablets, have become indispensable in the daily practice of healthcare professionals, providing easy access to information

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and decision support tools at the point of care. The development of user-friendly and widely accessible pharmacokinetic applications holds the potential to improve the efficiency and accuracy of dose adjustments and therapeutic drug monitoring (TDM), thereby enhancing the effectiveness and safety of drug therapy (Munar *et al*., 2006; Davit, Conner & Shargel, 2016).

Despite the availability of various pharmacokinetic software packages, many face limitations in terms of accessibility, cost, and ease of use for clinical practitioners in Indonesia. Commercial software is often expensive and requires specialised training, while web-based applications may not be suitable for use in hospital environments with limited connectivity. Thus, the development of an Android-based pharmacokinetic application tailored to the specific needs of pharmacists and physicians in Indonesia is highly relevant. In 2024, the "Indonesia Pharmacokinetic Calculator" (KFI) Android application was developed to address this gap (Sentat *et al*., 2024a). This study aims to assess the effectiveness of the KFI Android-based pharmacokinetic application for amikacin. The application includes features that calculate individual patient pharmacokinetic parameters based on therapeutic drug monitoring (TDM) data. The study will evaluate the accuracy of these calculations and the application's user-friendliness to ensure that it can be an effective tool for healthcare professionals in optimising amikacin therapy and enhancing patient safety.

Methodology

The MAPE test is one of the evaluation methods used to measure the accuracy of the calculation model, specifically the calculation, including in the context of calculations with existing algorithms, an application that will be made with the function of calculating pharmacokinetic parameters by entering 2 TDM data. MAPE gives an idea of how much the average error of the calculation is compared to the actual value of the calculation result with the same algorithm in MS Excel, expressed in percentages. How to calculate the modified Absolute Percentage Error (APE) can be seen in equation (1) below (Makridakis, 1993).

$$\text{APE} = \left|\frac{\text{Calculation Value in the KFI Application} - \text{Calculation Values in MS Excel}}{\text{Calculation Values in MS Excel}}\right| \times 100\% \quad (1)$$

Results

The application of KFI in the second calculation mode can be used to calculate individual pharmacokinetic parameters of patients by entering 2 TDM data, specifically in the data output of the calculation mode part 1. The MAPE test was used to assess how well the KFI application on Android can calculate the pharmacokinetic parameters of TDM performed on patients, when compared to calculations with the same algorithm in MS Excel on a computer. The MAPE results from this comparison can be seen in table 1 below.

Table 1: MAPE Results from Comparison of Pharmacokinetic Parameter Calculation Values in MS Excel and KFI Application

Pharmacokinetic Parameters*	Calculation Values in MS Excel	Calculation Value in the KFI Application**	APE (%)
k	0.236827469	0.23683	0.00
t½	2.926180835	2.92618	0.00
V_d (L)	12.08334318	12.08334	0.00
V_d (%)	0.201389053	0.2014	0.00
CL	2.861667578	2.86	0.05
$AUC_{0\text{-}24j}$	348.6651757	348.67	0.00
Cp_{ss} max	82.75855327	82.76	0.00
Cp_{ss} average	14.52771565	14.53	0.01
Cp_{ss} min	0.281413017	0.28	0.50
t 95% Cp_{ss}	12.64110121	12.64	0.00
t 96.87% Cp_{ss}	14.63090417	14.63	0.00
t 99% Cp_{ss}	19.45910255	19.46	0.00
Cpmax/MIC Ratio	10.34481916	10.34	0.04
$AUC_{0\text{-}24h}$/MIC Ratio	43.58314696	43.58	0.00
		MAPE Average	0.04
		MAPE SD	0.13

** Using the same TDM data: Patient weighing 60 Kg, Initial Dose 500 mg Amikacin IV Bolus followed by 1000 mg Amikacin IV Drip (over 1 hour) as maintenance dose every 24 hours. First TDM at 54 hours (65.53 µg/mL) and second TDM at 56.5 (36.25 µg/mL).*
*** Output of the data of the second calculation mode in the KFI application*

The average MAPE obtained was 0.04%, which shows that the difference between the calculation results in MS Excel and the KFI application is very small. The standard deviation of MAPE is 0.13%, which indicates that the variation in percentage absolute error between different parameters is also very small. Most of the parameters have an APE of 0.00%, indicating a perfect fit between the two calculation tools. Only a few parameters such as Clearance (CL) and Cp $_{ss}$ min showed slight differences, with APE of 0.05% and 0.50%, respectively. Nonetheless, these differences are still within acceptable limits for most pharmacokinetic applications.

Discussion

Discussion should emphasise the present findings and the variations or similarities with other work done in the field by other researchers. The detailed data should not be repeated discussion again. Emphasise the new and important aspects of the study. It must be mentioned whether the hypothesis mentioned in the article is true, false or no conclusions can be derived.

The MAPE test compares the results of the calculation of pharmacokinetic parameters with the KFI application on Android with MS Excel on a computer. In the context used to calculate, MAPE provides an indication of how accurate the KFI application is in calculating parameters compared to MS Excel which is trusted in performing calculations correctly. The average MAPE obtained was 0.04%, which shows that the difference between the calculation results in MS Excel and the KFI application is very small. The standard deviation of MAPE is 0.13%, which indicates that the variation in percentage absolute error between different parameters is also very small. This means that the consistency between the two calculation methods is quite good. This shows that both calculation tools give almost identical results.

Most of the parameters have an APE of 0.00%, indicating a perfect fit between the two calculators. Only a few parameters such as CL and $C_{p\ ss}$ min showed slight differences, with APE of 0.05% and 0.50%, respectively. This difference is due to the numerical value of the calculation result in small decimals of CL and Cp $_{ss}$ min while the calculation in MS Excel is carried out without interruption with digits larger than the application.

A MAPE value close to 0.00% indicates that KFI applications on smaller hardware can be used to replace MS Excel functions on larger devices. The MAPE value is an important aspect in the evaluation of application performance in calculating pharmacokinetic parameters with the input of 2 patient TDM data. The existence of the KFI application on Android phones for clinical practitioners in hospitals who need to adjust the dose of amikacin in critical patients is very useful, because the patient's individual parameters are immediately calculated quickly, as well as the assessment of the effectiveness and safety of ongoing therapy, so that clinical pharmacists can immediately provide appropriate advice to doctors.

Pharmacokinetic data of the critical patient population with a large standard deviation due to the metabolism of critical patients is very individual, the basic data entered has a wide discrepancy (Sentat *et al.*, 2024b). These differences can be due to factors such as individual differences in pharmacokinetics, or the quality of the underlying data used in the predictions. However, if the basic data entered into the system is a population with a stable metabolism, for example in healthy subjects in Indonesia, then this can make this calculation tool can replace TDM in clinical applications. But in obtaining data on healthy subjects for amikacin drugs that have a narrow therapeutic index, and side effects (ototoxic and nephrotoxic) that can be detrimental to normal subjects, of course the Research Ethics Committee will not issue ethical approvals (Logre *et al*., 2020; Mahmoudi *et al*., 2013; Taccone *et al*., 2010). To improve prediction accuracy, for the development of KFI applications, it is necessary to consider adjusting the prediction model or using basic data of pharmacokinetic parameters of patients with a larger population. While collecting more representative data from a wider patient population can

be helpful in improving the accuracy of the application, the time span of the study must be extended at a cost and time.

In clinical pharmacy practice, the performance of the application of KFI in calculating the pharmacokinetic parameters of amikacin in critical patients with the comparison of clinical conditions that can be seen in the improvement of patients' vital signs, these two things are major breakthroughs in the application of clinical pharmacokinetics that are rarely done in Indonesia. While there is room for improvement, these MAPE results suggest the accuracy of the application in calculations can support clinical practice to make decisions regarding drug doses. With further adjustments and improvements in data collection, the KFI app could become a more effective tool in drug therapy management.

Conclusion

This study's accuracy assessment, using MAPE, confirms the reliability of the developed Android-based pharmacokinetic application for amikacin. The application offers a user-friendly and portable means for clinical pharmacists to calculate individual pharmacokinetic parameters, ultimately facilitating timely and accurate dosing adjustments to improve therapeutic outcomes and minimise toxicity risks associated with narrow therapeutic index drug. Future developments could explore the integration of real-time patient data and artificial intelligence to further enhance the precision of dosing recommendations. Additionally, expanding the application's capabilities to other drugs with narrow therapeutic indices could broaden its clinical utility and improve patient safety across diverse therapeutic areas.

Conflict of Interest

The authors affirm that there are no conflicting objectives.

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