

Physicians' Knowledge of Theophylline Use: A Cross-Sectional Study from Jordan

*Tasneem Basheer Ali*¹, *Huda Yousef Almomani*², *Fatima Mahmoud Al-Tarawneh*^{* 1},
*Maysa Waddah Alwadi*³, *Ahmad Shaher Suliman*⁴

¹ Department of Bioallied Science, Al-Balqa' Applied University, Al-Karak, Jordan.

² Department of Applied Pharmaceutical Sciences and Clinical Pharmacy, Isra University, Jordan.

³ Department of Bioallied Science, Al-Balqa' Applied University, Maan, Jordan.

⁴ Jordan Royal Medical Services (RMS), Department of Anesthesia and Intensive Care, Prince Rashed Ben Al-Hasan Military Hospital, Irbid, Jordan.

ABSTRACT

Objective: This cross-sectional study aims to assess physicians' knowledge regarding theophylline drug and other related characteristics in Jordan.

Materials and Method: The study was conducted prospectively among physicians in Jordan. Physicians were interviewed using an online questionnaire consisting of two sections. The first section included demographics and other relevant characteristics, while the second section comprised questions about theophylline drug.

Results: A total of 385 participants completed the questionnaire. The majority of participants knew that theophylline is used in clinical practice as a bronchodilator (75.6%). Nearly 39% of participants knew that theophylline can be administered orally and intravenously. The largest share of participants (76.1%) did not know that theophylline dosage is calculated based on ideal body weight. Sixty percent of participants knew that theophylline use was not contraindicated during pregnancy. On the other hand, only 27.3% knew that theophylline use was not contraindicated during breastfeeding. The majority of participants (76.1%) had an overall intermediate knowledge of theophylline.

Conclusions: It was noted that physicians had an overall intermediate knowledge of theophylline. Physicians demonstrated unsatisfactory knowledge about theophylline's indications, clinical use, administration, adverse effects, and other related aspects. These findings highlight the need for educational interventions and training programs to improve physicians' knowledge of theophylline and enhance its effective and safe use in clinical practice.

Keywords: Physicians; Knowledge; Theophylline; Jordan.

INTRODUCTION

Theophylline has been used in the treatment of airway diseases for over 80 years and remains one of the most widely prescribed drugs due to its cost-effectiveness and widespread availability (1, 2). Theophylline is a bronchodilator indicated for managing bronchospasm in

respiratory diseases like asthma and chronic obstructive pulmonary disease (COPD) (1, 3). It effectively treats and prevents bronchospasm-induced symptoms such as shortness of breath, wheezing, and chest tightness (1). Theophylline exerts its bronchodilatory effect by competitively inhibiting type III and type IV phosphodiesterase (PDE) enzymes (1, 4). It also has anti-inflammatory action by inhibiting PDE4 and activating histone deacetylase-2 (1, 4).

In clinical practice, theophylline can be used as an

**Corresponding author: Fatima Mahmoud Al-Tarawneh*
fatima.altarawneh@bau.edu.jo

Received: 26/9/2023 Accepted: 6/10/2023.

DOI: <https://doi.org/10.35516/jjps.v16i4.1789>

alternative therapy in the treatment of persistent asthma in combination with other asthma medications, such as inhaled corticosteroids and bronchodilators (5, 6). For COPD treatment, theophylline may be considered in patients who are intolerant of or unable to use inhaled bronchodilators (1). It can also be used as add-on therapy to the regimen of patients whose COPD is not controlled despite the use of inhaled bronchodilators (1).

Theophylline can be administered orally as extended-release tablets; capsules; and elixirs and as an intravenous solution (7). Aminophylline is an ethylenediamine salt of theophylline that has the same indications as theophylline (6). However, it is less potent and has a shorter duration of action than theophylline (1). In addition to its efficacy, theophylline is inexpensive and widely available (3). However, its use is limited by its narrow therapeutic index and multiple drug-drug interactions (1, 8, 9). Further, the serum theophylline concentrations require close monitoring (1, 10). Therapeutic concentrations for theophylline in adults should be maintained between 10-20 mcg/ml. Theophylline toxicity occurs when theophylline's serum concentration is above 20 mcg/mL and is manifested by gastrointestinal distress, insomnia, and tremor (1, 11). Moreover, theophylline may cause serious side effects including arrhythmias, convulsions, and seizures, and may lead to death (1, 12). According to the Association of Poison Control Centres (AAPCC), there were 2 deaths out of 81 patients due to theophylline toxicity (13).

Although theophylline use is limited nowadays, the most recent guidelines about the management of asthma and COPD, still list theophylline as a third or fourth-line therapy (2, 6, 14, 15). Additionally, interest in its use for the treatment of poorly controlled patients is resurging (8, 16-18). Due to several restrictions on theophylline use, physicians prescribing this drug should have an appropriate level of knowledge regarding theophylline's efficacy and safety to optimize treatment while avoiding adverse effects and toxicity (19, 20).

To the best of the researchers' knowledge, there are no related studies that have assessed the level of knowledge among physicians regarding theophylline use in Jordan. Furthermore, studies on the prescribing patterns of theophylline by physicians in Jordan are also lacking. However, strong evidence from several studies reveals a high prevalence of prescribing errors among physicians in Jordan, with most of these errors being clinically significant. These errors frequently include drug-drug interactions, inappropriate doses, wrong dosage forms, unnecessary drug therapy, and monitoring parameters, and theophylline was one of the treatments mentioned in these studies (21, 22).

Despite the absence of published data about theophylline prescribing patterns and use in Jordan, conducting this study addresses an essential gap in the literature and provides insights into theophylline management in the Jordanian healthcare system. The findings of this study can establish the basis for educational initiatives, empowering physicians with the necessary knowledge to make well-informed clinical decisions that ultimately enhance patient care and prevent potential toxicity. Additionally, enhancing physicians' knowledge of theophylline can help mitigate prescribing and medication errors, contributing to optimizing health outcomes for patients with respiratory disorders. Hence, we conducted this study to assess physicians' knowledge about theophylline and its use in Jordan and to identify the variables associated with a higher level of knowledge about theophylline.

MATERIALS AND METHODS

Study design and setting

A survey-based, cross-sectional study of Jordanian physicians was conducted using an online questionnaire between January and April 2023. Licensed physicians practicing medicine in Jordan, from all healthcare sectors and regardless of their specialties, were eligible to participate in the study. No restrictions were applied to the demographic characteristics of the invited physicians, resulting in an overall response rate of approximately 90%.

Eligible physicians were provided with a brief description of the study, and they were informed that their participation was voluntary, with assurances that their responses would be anonymized and kept confidential. Consent to participate was obtained from physicians before they answered the survey questions. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for reporting cross-sectional studies were used to develop and report this study (23).

Survey development

The survey questions were prepared by the research team based on a review of pertinent literature and international guidelines regarding theophylline use, and they were validated (26-24, 1). The survey questions were distributed to five clinical pharmacists and five physicians. They were asked to judge the scale items' validity and appropriateness. Their suggestions were taken into consideration. The criterion for accepting an item was the specialist's agreement with an average of 80%. A thorough examination of the literature was conducted to make sure that all relevant criteria were taken into account while establishing the content validity. The paper and questionnaire were located using the source databases Science Direct, PubMed/Medline, and Google Scholar. Next, 40 physicians were assessed using the scale. Since their data was gathered for the pilot, it was not included in the final analysis. The survey questions were prepared and distributed in English language since English is the official language of education for physicians in Jordan. The survey was created and distributed using Google Forms. The validation options "Required" and "Limit to one response" were applied to minimize any cases of missing data and to prevent the duplication of responses.

Flow of the survey questions

The survey consisted of two sections, featuring both open-ended and close-ended questions. The first section comprised demographic questions and other relevant characteristics, including years of experience, place of work, institution, and professional degree. The second

section included 16 items designed to assess physicians' knowledge of key information about theophylline, such as indications, mechanism of action, contraindications, and side effects. The final version of the survey, answered by 385 physicians, contained 22 questions. The internal consistency of the study elements was calculated, yielding a Cronbach's alpha of 0.764.

A score of one was assigned for a correct answer on each knowledge item, while a score of zero was given for an incorrect answer. For questions with more than one correct answer, half of one mark was assigned for each correct response. The total score for correctly answered survey items amounted to 30 marks. Subsequently, the knowledge level was categorized into three groups based on the total score: 0-10.5 was classified as Poor knowledge, 11-20.5 as Intermediate knowledge, and 21-30 as Excellent knowledge.

Sample size calculation

In this study, the online Raosoft sample size calculator was utilized to determine the sample size, with a confidence interval of 95% and a 5% margin of error (27). According to the Jordan Medical Association, the number of registered physicians in Jordan was 40,211 in 2022. Therefore, a minimum sample size of 381 was considered representative of physicians in Jordan.

Data analysis

The Statistical Package for Social Sciences (SPSS, version 25.0) software was employed for data analysis. Descriptive statistics, including frequencies and percentages, were performed for all sociodemographic information and knowledge items. Multiple linear regression analysis was conducted to assess the association between sociodemographic characteristics and knowledge scores, with a 95% confidence interval. The total score for each knowledge item was considered the outcome variable. A P-value < 0.05 was considered statistically significant.

Ethical Approval

This study received approval from the Institutional Review Board (IRB) committee of Al-Balqa Applied University in Jordan.

RESULTS

Demographic characteristics of the participants

The demographic characteristics of the 385 physicians who participated in this study are presented in Table 1. The largest share of the participants (46.8%) were less than 30 years old. Males were the predominant participants

compared to females (59.2%). Regarding the job title, 160 (41.6%) were residents. Nearly half of the participants, 186 (48.3%), were working in the Ministry of Health. Most participants obtained their medical academic degrees from Jordan (71.9%). About one-third of participants (63%) had experience in the medical field ranging from 2 to 5 years.

Table 1: Demographics characteristics of the participants (n= 385)

Characteristics	n (%)
Age	
Less than 30 years	180 (46.8)
30-39 years	136 (35.3)
40-49 years	43 (11.2)
More than 50 years	26 (6.8)
Gender	
Male	228 (59.2)
Female	157 (40.8)
Region	
North of Jordan	167 (43.4)
Middle of Jordan	84 (21.8)
South of Jordan	134 (34.8)
Place of work	
Ministry of Health	186 (48.3)
Royal Medical Services	115 (29.9)
University Hospitals	38 (9.9)
Private sector	46 (11.9)
Job title	
General Practitioner	96 (24.9)
Resident	160 (41.6)
Specialist	66 (17.1)
Consultant	63 (16.4)
Years of experience	
Less than 2 years	55 (14.3)
2-5 years	137 (35.6)
6-10 years	102 (26.5)
11-15 years	63 (16.4)
More than 15 years	28 (7.3)
Medical academic degrees source	
In Jordan	277 (71.9)
Outside of Jordan	71 (18.4)
Both	37 (9.6)

Physicians' knowledge of theophylline

Table 2 lists participants' knowledge of indications, mechanisms of action, and other related issues of theophylline. Regarding knowledge about theophylline drug, the majority of participants knew that theophylline is used in clinical practice as a bronchodilator (75.6%) and is a non-selective phosphodiesterase inhibitor (75.3%).

When participants were asked about the indications of theophylline, including asthma, chronic obstructive pulmonary disease (COPD), and infant apnea, about half of them knew at least one indication (50.1%). However, 141 participants (36.6%) chose at least one incorrect

indication of theophylline. More than half of participating physicians (67.3%) knew that aminophylline is the ethylenediamine salt of theophylline, while 16% of them did not know the relationship between aminophylline and theophylline.

When participants were asked when theophylline should be used in therapy, less than half of the participants (46.7%) chose one correct answer, while one-third of them (36.6%) answered with incorrect answers. Only 5.7% of participants knew all the listed clinical uses of theophylline. Nearly 39% of participants knew that theophylline can be administered orally and intravenously.

Table 2: Physicians' general knowledge of theophylline (n= 385)

Questions	n (%)
Role in clinical practice	
Bronchodilator (Correct answer).	291 (75.6)
Antibiotics or Mucolytics (Incorrect answer).	45 (11.7)
At least one incorrect answer with a correct answer.	45 (11.7)
Don't know.	4 (1)
The primary mechanism of action	
Nonselective phosphodiesterase inhibitors (Correct answer)	290 (75.3)
Cell wall inhibitors or Blocks potassium currents (Incorrect answer).	38 (9.9)
At least one incorrect answer with a correct answer.	19 (4.9)
Don't know.	38 (9.9)
Indication	
One correct answer.	193 (50.1)
Two correct answers.	109 (28.3)
Three correct answers.	13 (3.4)
Incorrect answer.	9 (2.3)
At least one incorrect answer with a correct answer.	55 (14.3)
Don't know.	6 (1.6)
When theophylline should be used in therapy?	
One correct answer.	180 (46.7)
Two correct answers.	22 (5.7)
Incorrect answer.	141 (36.6)
At least one incorrect answer with a correct answer.	26 (6.8)
Don't know.	16 (4.2)
The relationship between aminophylline and theophylline	
Aminophylline is an ethylenediamine salt of theophylline (correct answer).	259 (67.3)
Incorrect answer.	64 (16.6)
Don't know.	62 (16.1)
Route of administration	
One correct answer.	153 (39.7)
Two correct answers.	149 (38.7)
Incorrect answer.	20 (5.2)
At least one incorrect answer with a correct answer.	55 (14.3)
Don't know.	8 (2.1)

Table 3 shows participants' knowledge of multiple aspects of theophylline safety. The majority of participants (71.2%) knew that close monitoring of theophylline should be done regularly. The largest share of participants (76.1%) did not know that theophylline dose is calculated based on the ideal body weight rather than actual body weight, patient's age, or as a fixed dose. Only 25

participants (6.5%) knew that theophylline dose should be adjusted based on serum concentration. On the other hand, more than two-thirds (74.0%) of participants incorrectly thought that the dose is adjusted based on the presence of health conditions, including renal impairment, hepatic impairment, congestive heart failure, hyperthyroidism, or that the dose does not need any adjustments.

Table 3: Physicians' knowledge of theophylline safety (n=385)

Theophylline dose is calculated based on	
Ideal body weight	67 (17.4)
Incorrect answers	293 (76.1)
Don't know.	25 (6.5)
Need for dose adjustment.	
Based on serum theophylline concentration	25 (6.5)
Incorrect answers	285 (74.0)
At least one incorrect answer with a correct answer.	43 (11.2)
Don't know.	32 (8.3)
Common adverse effects at a therapeutic level	
One correct answer.	238 (61.8)
Two correct answers.	80 (20.7)
Incorrect answer.	13 (3.4)
At least one incorrect answer with a correct answer.	18 (4.7)
Don't know.	36 (9.4)
Theophylline toxicity	
One correct answer.	197 (51.1)
Two correct answers.	78 (20.3)
Three correct answers.	40 (10.4)
Incorrect answer.	10 (2.6)
At least one incorrect answer with a correct answer.	31 (8.1)
Don't know.	29 (7.5)
Which of the following drugs interact with theophylline?	
One correct answer.	196 (50.9)
Two correct answers.	67 (17.4)
Three correct answers.	32 (8.3)
Four correct answers.	8(2.1)
Five correct answers.	5 (1.3)
Not having a drug interaction	26 (6.8)
Don't know.	52 (13.5)
Which of the following types of food interact with theophylline?	
Foods high in caffeine, like coffee, tea, cocoa, and chocolate (correct)	253 (65.7)
Vitamin K-rich food (Incorrect answer).	70 (18.2)
Don't know.	62 (16.1)

Close monitoring should be done.	
Regularly	274 (71.2)
Incorrect answers	93 (24.2)
Don't know.	18 (4.7)
Monitoring Parameters	
One correct answer.	160 (41.6)
Two correct answers.	72 (18.7)
Three correct answers.	87 (22.6)
Four correct answers.	8 (2.1)
Incorrect answer.	5 (1.3)
At least one incorrect answer with a correct answer.	25 (6.5)
Doesn't need any monitoring.	4 (1.0)
Don't know.	24 (6.2)
Theophylline use is not contraindicated during pregnancy.	
Yes	231 (60)
No	108 (28.1)
Don't know.	46 (11.9)
Theophylline use is not contraindicated during breastfeeding.	
Yes	105 (27.3)
No	211 (54.8)
Don't know.	69 (17.9)

Participants were asked to indicate common adverse effects and symptoms of theophylline toxicity. More than 60% of participants were able to identify one of the listed adverse effects of theophylline use, including central nervous system and gastrointestinal effects. However, only about 20% knew both adverse effects. About half of the participants (51.1%) knew only one of theophylline toxicity symptoms, including tachycardia, seizures, and cardiac arrhythmia, while only around 10% of them were able to identify all three toxicity symptoms.

Concerning participants' knowledge about drugs that interact with theophylline, around half of the participants (50.9%) knew one correct interacting drug. However, twenty-five of the participants (6.8%) stated that theophylline does not have drug-drug interactions. Drugs that interact with theophylline include antibiotics, phenytoin, allopurinol, benzodiazepines, and oral contraceptives. Nearly two-thirds of participants (65.7%)

knew that foods high in caffeine, like coffee, tea, cocoa, and chocolate, have interactions with theophylline. On the other hand, seventy participants (18.2%) stated that vitamin K-rich food has interactions with theophylline, which is an incorrect answer. Participants were asked about the monitoring parameters of theophylline, which include serum theophylline level, heart rate and ECG, respiratory rate, and electrolyte concentrations. Less than half of the participants were able to identify only one correct monitoring parameter, while only 2.1% knew all four monitoring parameters.

Participants were asked whether theophylline can be administered during pregnancy and breastfeeding. A large proportion of participants (60%) knew that theophylline use is not contraindicated during pregnancy. Nevertheless, a notable proportion (28.1%) incorrectly thought that theophylline cannot be given during pregnancy. Regarding theophylline use in breastfeeding mothers, only 27.3% knew

that theophylline use is not contraindicated during lactation, while more than half of physicians (54.8%) incorrectly believed that lactating mothers should not use theophylline.

Physicians' knowledge description

The participants' knowledge score is presented in Figure 1. The mean knowledge score for the physicians who took part in this study was 13.06 ± 3.78 out of 30 points. The majority of participants (76.1%) had an overall intermediate knowledge of theophylline.

Association between the knowledge score and the different variables

Multivariable logistic regression analyses were performed to identify variables associated with the knowledge score (Table 4). The multiple linear regression model showed that no statistically significant association was found between the sociodemographic characteristics of the participants and the score of knowledge about theophylline.

Table 4: Association between participants' sociodemographic characteristics and knowledge score

Predictors	Knowledge related to Theophylline ¹	
	Beta	P value
Age	0.060	0.585
Less than 30 years		
30-39 years		
40-49 years		
More than 50 years		
Gender	-0.068	0.207
Male		
Female		
Place of work	-0.081	0.150
Ministry of Health		
Royal Medical Services		
University Hospitals		
Private sector		
Region	0.021	0.692
North of Jordan		
Middle of Jordan		
South of Jordan		
General Practitioner	0.199	0.101
Resident		
Specialist		
Consultant		
Years of experience	-0.146	0.149
Less than 2 years		
2-5 years		
6-10 years		
11-15 years		
More than 15 years		
Academic degree source	0.035	0.539
In Jordan		
Outside of Jordan		
Both		

¹Multiple linear regression.

DISCUSSION

In this study, the level of knowledge among Jordanian physicians regarding theophylline was assessed. Physicians demonstrated an overall intermediate level of knowledge concerning theophylline's role in therapy, administration, and safety issues. This study is the first of its kind in Jordan and the region, addressing multiple aspects of physicians' knowledge about theophylline and highlighting their role in managing patients using theophylline. The survey encompassed physicians' characteristics that could potentially affect their knowledge level, including the place of work, job title, and years of experience. Additionally, the study covered various general aspects of theophylline, such as its role in clinical practice, mechanism of action, indications, and route of administration. It also explored physicians' knowledge regarding theophylline safety aspects, including monitoring, dose calculation, adjustment, adverse effects, toxicity effects, drug-drug, and drug-food interactions, as well as its use during pregnancy and breastfeeding. Overall, studies on the level of knowledge about theophylline are scarce, and most of them involve pharmacists or a combination of pharmacists and physicians, focusing on specific aspects such as drug-drug interactions or indications (28, 29). In contrast, this study exclusively involved physicians and assessed their knowledge across various areas of theophylline use.

The study revealed that a significant proportion of physicians demonstrated adequate knowledge about theophylline's role in clinical practice and its mechanism of action. Satisfactory knowledge in these aspects is reassuring, as it lays the groundwork for effective and safe prescribing practices. However, physicians exhibited limited knowledge of theophylline indications, its clinical uses in therapy, methods of administration, and dose considerations. These knowledge gaps are concerning, as they could lead to suboptimal medication management, compromised therapeutic outcomes, and potential adverse events.

Other noteworthy findings include poor knowledge about theophylline's adverse effects, toxicity, and the required monitoring parameters. Physicians' lack of knowledge and awareness of the medication's possible side effects, toxicity symptoms, and reactions could lead to medication errors, including prescribing errors, inappropriate dosing, and inadequate monitoring. Insufficient knowledge in this area may result in severe consequences such as seizures, tachycardia, arrhythmias, and even death (10, 30). Although a considerable proportion of physicians (71.2%) recognized the need for close monitoring of theophylline, less than half of them (41.6%) could identify only one monitoring parameter, and a mere 2.1% knew all four monitoring parameters. In contrast, a cross-sectional study conducted in Saudi Arabia on the knowledge of healthcare professionals towards therapeutic drug monitoring showed that most of the involved physicians and pharmacists (95%) knew the indications of therapeutic drug monitoring of theophylline (30).

Our findings regarding physicians' knowledge about drugs interacting with theophylline are concerning. While about half of the physicians (50.9%) demonstrated awareness of one correct interacting drug, noticeable proportions (6.8%) incorrectly believed that theophylline does not have interactions with other drugs, and an additional 13.5% did not know whether theophylline interacts with other drugs. These findings are worrisome since theophylline is known to have many significant interactions with commonly prescribed medications such as antibiotics, allopurinol, and oral contraceptives (18, 31).

Similarly, knowledge about food interactions with theophylline revealed mixed results. A majority of physicians (65.7%) correctly identified that foods high in caffeine, such as coffee, tea, cocoa, and chocolate, can interact with theophylline. Conversely, notable proportions incorrectly thought that theophylline interacts with vitamin K-rich foods (18.2%) or did not know of any interacting foods (16.1%). In contrast to our results,

findings from a previous study conducted in South Africa revealed that only a few healthcare professionals working in hospitals knew specific food interactions with theophylline (29). Particularly, only 19.4% of healthcare professionals were aware that patients on theophylline should avoid consuming large quantities of tea, and 21.6% correctly answered about the need to avoid large amounts of chocolates. The disparity in results between the two studies may be attributed to variations in the healthcare professionals included in each study. In our study, the participants consisted solely of physicians, while the other study encompassed a broader range of healthcare professionals, including physicians, pharmacists, dietitians, and nurses. The diverse composition of participants in the other study could have influenced the level of knowledge observed, as different healthcare professionals may have varying degrees of exposure and experience with theophylline interactions.

While a considerable proportion (60%) knew that theophylline could be used during pregnancy, only a few physicians (27.3%) correctly recognized that lactating mothers could use theophylline. This misconception could lead to discontinuing or avoiding a medication that can be useful in the management of respiratory conditions in breastfeeding women.

The identified gaps in physicians' knowledge about the optimal management of theophylline could be due to several factors. First, theophylline possesses a complex pharmacokinetic profile and a narrow therapeutic window, making its appropriate use more challenging (1, 2). Second, physicians might not encounter theophylline as frequently as other medications, therefore, they might have limited exposure and fewer opportunities to practice and update their knowledge about theophylline (32, 33). Moreover, physicians might prioritize retaining knowledge about new medications and widely used therapies while neglecting established medications like theophylline.

This study did not find any significant association between physicians' characteristics and their knowledge

score regarding theophylline. The lack of association could be explained by including a limited range of physicians' characteristics, which might limit the ability to detect significant associations. Hence, a broader range of variables could be needed to identify potential associations with knowledge scores.

The main strength of this study is addressing the gap in the literature on the knowledge of physicians regarding theophylline use and safety in the Jordanian context. The study revealed aspects where physicians have insufficient knowledge of theophylline drug. Such findings may have practical implications for optimizing theophylline use and improving patient care and safety. Another strength is the large and diverse sample size of participants. Recruitment of physicians from different areas in Jordan, and from different specialties and healthcare institutions makes the sample more representative of the population of physicians in Jordan and enhances the generalizability of the study findings.

This study has some limitations that should be considered. Our study utilized an online-based questionnaire, introducing a potential source of selection bias. Participants who have a particular interest or concern about theophylline may be more inclined to take part in the survey, leading to self-selection bias. Hence, results should be interpreted while recognizing the potential impact of self-selection on the study's external validity. Further, information about the specialty of the participating physicians was not collected. Accordingly, we are unable to evaluate whether the level of theophylline knowledge varies among different medical specialties. This could affect the interpretation of the study findings since theophylline prescribing practices and familiarity could differ among physicians from various specialties.

CONCLUSION

In conclusion, intermediate knowledge of theophylline was reported among physicians in this study. Physicians demonstrated unsatisfactory knowledge about theophylline's indications, clinical use, administration,

adverse effects, toxicity, interactions with drugs and foods, monitoring parameters, and use in lactation. These findings highlight the need for educational interventions and training programs to improve physicians' knowledge of theophylline and enhance its effective and safe use in clinical practice.

ACKNOWLEDGMENT

The authors acknowledge physicians who took part in this study.

Author Contributions

Conceptualization: Tasneem Basheer Ali, Huda Yousef Almomani.

Data curation: Tasneem Basheer Ali.

Formal analysis: Tasneem Basheer Ali, Huda Yousef Almomani, Fatima Mahmoud Al-Tarawneh, Maysa Waddah Alwadi, Ahmad Shafer Suliman.

Investigation: Tasneem Basheer Ali, Huda Yousef Almomani.

Methodology: Tasneem Basheer Ali, Huda Yousef Almomani.

Project administration: Tasneem Basheer Ali.

Resources: Tasneem Basheer Ali.

Software: Tasneem Basheer Ali.

Supervision: Tasneem Basheer Ali, Huda Yousef

Almomani, Fatima Mahmoud Al-Tarawneh, Maysa Waddah Alwadi, Ahmad Shafer Suliman.

Validation: Tasneem Basheer Ali, Huda Yousef Almomani.

Visualization: Tasneem Basheer Ali.

Writing – original draft: Tasneem Basheer Ali.

Writing – review & editing: Tasneem Basheer Ali, Huda Yousef Almomani, Fatima Mahmoud Al-Tarawneh, Maysa Waddah Alwadi, Ahmad Shafer Suliman.

Informed consent

Informed consent was obtained electronically before answering the questionnaire from all individual participants included in the study.

Conflict of Interest

The authors declare no conflicts of interest. The authors are solely responsible for the content and writing of this paper.

Financial Disclosure

The authors declared that this study received no financial support.

Abbreviations

AAPCC	Association of Poison Control Centers
COPD	Chronic obstructive pulmonary disease
IRB	Institutional Review Board
PDE	Phosphodiesterase

REFERENCES

1. Barnes PJ. Theophylline. *American journal of respiratory and critical care medicine*. 2013; 188(8): 901-6.
2. Ma Y, Jiang D, Meng J, Li M, Zhao H, Wang Y, et al. Theophylline: a review of population pharmacokinetic analyses. *Journal of Clinical Pharmacy and Therapeutics*. 2016; 41(6): 594-601.
3. Kunisaki KM, Sin DD. Methylxanthines in COPD: yes to caffeine, no to theophylline. *Eur Respiratory Soc*; 2021.
4. Dar MH, Alam SM, Ismail K, Zaidi SAH. Low Dose Theophylline and Tiotropium Rotacap as Add on Therapy in COPD Patients-Clinical Trial. *Journal of Bahria University Medical and Dental College*. 2020; 10(2): 137-41.
5. Niimi A, Fukunaga K, Taniguchi M, Nakamura Y, Tagaya E, Horiguchi T, et al. Executive summary: Japanese guidelines for adult asthma (JGL) 2021. *Allergology International*. 2023; 72(2): 207-26.
6. Bereda G. Bronchial Asthma: Etiology, Pathophysiology, Diagnosis and Management. *Austin J Pulm Respir Med*. 2022; 9: 1085.

7. Barnes PJ. Theophylline. *Pharmaceuticals*. 2010; 3(3): 725-47.
8. Cazzola M, Matera MG. The effect of doxofylline in asthma and COPD. *Respiratory Medicine*. 2020; 164: 105904.
9. DV G, Khan MS, Aravindram A, Shivakumar H. Encapsulation of theophylline into binary blend of ethylcellulose and eudragit microparticles: development, characterization and kinetic release. *Jordan Journal of Pharmaceutical Sciences*. 2011; 4(3).
10. Hopkins ME, MacKenzie-Ross RV. Case Report: The risks associated with chronic theophylline therapy and measures designed to improve monitoring and management. *BMC Pharmacology and Toxicology*. 2016; 17(1): 1-4.
11. Jilani TN, Preuss CV, Sharma S. Theophylline. 2018.
12. Singh A, Prasad R, Gupta N. Theophylline and leukotriene modifiers: Is there any compelling role in COPD? *Indian Journal of Respiratory Care*. 2020; 9(2): 153.
13. Journey JD, Bentley TP. *Theophylline toxicity*. 2018.
14. Farooq MU, Saeed I, Hassan SU, Zaman S, Shah M, Hussain S. Role of Low-Dose Theophylline on Functional Improvement in Patients of Moderately Severe Chronic Obstructive Pulmonary Disease. *Pakistan Armed Forces Medical Journal*. 2023; 73(1): 306-09.
15. Boylan PM, Abdalla M, Bissell B, Malesker MA, Santibañez M, Smith Z. Theophylline for the management of respiratory disorders in adults in the 21st century: a scoping review from the American College of Clinical Pharmacy Pulmonary Practice and Research Network. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2023; 43(9): 963-90.
16. Haddad RM, AlSurehein SK, Alsamen GA, Khair YM, Al-Najada MM, Al-Momani JA. Efficacy and safety of oral low dose Theophylline in Jordanian patients with stable Chronic Obstructive Pulmonary Disease treated at King Hussein Medical Center. *JRMS*. 2016; 23(1): 34-40.
17. Oxley-Oxland J, Freercks R, Baker D, Van der Merwe E. The characteristics and costs of severe theophylline toxicity in a tertiary critical care unit in Eastern Cape Province, South Africa. *South African Medical Journal*. 2022; 112(11): 866-70.
18. Montaña LM, Sommer B, Gomez-Verjan JC, Morales-Paoli GS, Ramírez-Salinas GL, Solís-Chagoyán H, et al. Theophylline: Old drug in a new light, application in COVID-19 through computational studies. *International Journal of Molecular Sciences*. 2022; 23(8): 4167.
19. Al-Rusasi A. Patient-Centeredness in Pharmaceutical Care. *Jordan Journal of Pharmaceutical Sciences*. 2023; 16(2): 451-.
20. Matalqah LM, Albals D, Radaideh KM, Al-Khateeb H, Thabet RH, Abu-Ismael L, et al. Knowledge, Attitudes and Practice toward Antibiotic Use among Under and Post-Graduate Students at Yarmouk University in Jordan: A Descriptive Study. *Jordan Journal of Pharmaceutical Sciences*. 2022; 15(3): 378-89.
21. Rababa'h AM, Mardini AN, Ababneh MA, Rababa M, Hayajneh M. Medication errors in Jordan: A systematic review. *International Journal of Critical Illness and Injury Science*. 2022; 12(2): 106.
22. Abdel-Qader DH, Al Meslamani AZ, El-Shara' AA, Ismael NS, Albassam A, Lewis PJ, et al. Investigating prescribing errors in the emergency department of a large governmental hospital in Jordan. *Journal of Pharmaceutical Health Services Research*. 2020; 11(4): 375-82.
23. Ghaferi AA, Schwartz TA, Pawlik TM. STROBE reporting guidelines for observational studies. *JAMA surgery*. 2021; 156(6): 577-8.
24. Nakamura Y, Tamaoki J, Nagase H, Yamaguchi M, Horiguchi T, Hozawa S, et al. Japanese guidelines for adult asthma 2020. *Allergology International*. 2020; 69(4): 519-48.

25. Shuai T, Zhang C, Zhang M, Wang Y, Xiong H, Huang Q, et al. Low-dose theophylline in addition to ICS therapy in COPD patients: A systematic review and meta-analysis. *PLoS One*. 2021; 16(5): e0251348.
26. Goh JW, Thaw MM, Ramim JU, Mukherjee R, Ramim MJU. Theophylline Toxicity: A Differential to Consider in Patients on Long-Term Theophylline Presenting With Nonspecific Symptoms. *Cureus*. 2023; 15(11).
27. Raosoft I. Sample size calculator by Raosoft, Inc. 2020. 2021.
28. Alorfi NM, Alqurashi RS, Algarni AS. Assessment of community pharmacists' knowledge about drug-drug interactions in Jeddah, Saudi Arabia. *Frontiers in Pharmacology*. 2023; 14: 1209318.
29. Osuala EC, Tlou B, Ojewole EB. Assessment of knowledge of drug-food interactions among healthcare professionals in public sector hospitals in eThekweni, KwaZulu-Natal. *PLoS One*. 2021; 16(11): e0259402.
30. Al Mutarid M, Alhossan A, Khan T, Alyami MG, Almutared KM, Alshiban M, et al. Knowledge and Attitude of Healthcare Practitioners Toward Therapeutic Drug Monitoring Practices in the Najran Region, Kingdom of Saudi Arabia. *Cureus*. 2022; 14(12).
31. Matera MG, Page C, Cazzola M. Doxofylline is not just another theophylline! *International Journal of Chronic Obstructive Pulmonary Disease*. 2017: 3487-93.
32. Calzetta L, Hanania NA, Dini FL, Goldstein MF, Fairweather WR, Howard WW, et al. Impact of doxofylline compared to theophylline in asthma: a pooled analysis of functional and clinical outcomes from two multicentre, double-blind, randomized studies (DOROTHEO 1 and DOROTHEO 2). *Pulmonary Pharmacology & Therapeutics*. 2018; 53: 20-6.
33. Margay SM, Farhat S, Kaur S, Teli HA. To study the efficacy and safety of doxophylline and theophylline in bronchial asthma. *Journal of clinical and diagnostic research: JCDR*. 2015; 9(4): FC05.

معرفة الأطباء باستخدام الثيوفيلين: دراسة مقطعية من الأردن

تسنيم بشير علي¹، هدى يوسف المومني²، فاطمة محمود الطراونة^{1*}، ميساء وضاح الوادي³، أحمد شاهر سليمان⁴

¹ قسم العلوم الحيوية، جامعة البلقاء التطبيقية، الكرك، الأردن.

² قسم العلوم الصيدلانية التطبيقية والصيدلة السريرية، جامعة الإسراء، الأردن.

³ قسم العلوم الحيوية، جامعة البلقاء التطبيقية، معان، الأردن.

⁴ قسم التخدير والعناية المركزة، مستشفى الأمير راشد بن الحسن العسكري، الخدمات الطبية الملكية الأردنية، إربد، الأردن.

ملخص

الهدف: تهدف هذه الدراسة المقطعية إلى تقييم مستوى معرفة الأطباء فيما يتعلق بدواء الثيوفيلين والخصائص الأخرى ذات الصلة في الأردن.

المواد والطريقة: أجريت هذه الدراسة بأثر رجعي بين الأطباء في الأردن. تمت مقابلة الأطباء باستخدام استبيان عبر الإنترنت يتكون من قسمين تضمن القسم الأول التركيبة السكانية والخصائص الأخرى ذات الصلة. أما القسم الثاني فيتضمن أسئلة حول دواء الثيوفيلين.

النتائج: أكمل ما مجموعه 385 مشاركا الاستبيان. عرف غالبية المشاركين أن الثيوفيلين يستخدم في الممارسة السريرية كموسع للقصبات الهوائية (75.6%). عرف ما يقرب من 39% من المشاركين أن الثيوفيلين يمكن إعطاؤه عن طريق الفم أو الوريد. النسبة الأكبر من المشاركين (76.1%) لم تعلم أن جرعة الثيوفيلين يتم حسابها على أساس وزن الجسم المثالي. عرف 60% من المشاركين أنه يمكن استخدام الثيوفيلين ليس من موانع اثناء الحمل. من ناحية أخرى، فقط 27.3% يعرفون أن استخدام الثيوفيلين ليس من موانع اثناء الرضاعة الطبيعية. غالبية المشاركين (76.1%) لديهم معرفة متوسطة شاملة بالثيوفيلين..

الاستنتاجات: لوحظ أن الأطباء لديهم معرفة متوسطة شاملة بالثيوفيلين. كان لدى الأطباء معرفة غير مرضية حول مؤشرات الثيوفيلين، والاستخدام السريري، وطريقة الاعطاء، والآثار الضارة، والجوانب الأخرى ذات الصلة. تسلط هذه النتائج الضوء على الحاجة إلى تدخلات تعليمية وبرامج تدريبية لتحسين معرفة الأطباء بالثيوفيلين وتعزيز استخدامه الفعال والأمن في الممارسة السريرية.

الكلمات الدالة: الأطباء، معرفة، الثيوفيلين، الأردن.

* المؤلف المراسل: فاطمة محمود الطراونة

fatima.altarawneh@bau.edu.jo

تاريخ استلام البحث: 2023/9/26 وتاريخ قبوله للنشر: 2023/10/6.