Original Article

Effect of E-Learning on Appropriate Antibiotic Prescribing by Medical Students: A Quasi-Experimental Study during **COVID-19 Pandemic**

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Abstract

Aims: This study aimed to determine the effect of E-learning on the understanding of appropriate antibiotic prescribing (AAP) by medical students and to assess their satisfaction with this method. Materials and Methods: This quasi-experimental study was conducted among the physiopathology students of Kashan University of Medical Sciences in the first and second semesters of 2020-2021. Students were divided into E-learning education as an intervention group (IG) and face-to-face education as a control group (CG). After the final examination, the mean scores of students in both groups were compared. In addition, the level of students' satisfaction in the IG with E-learning method was assessed using a standard questionnaire. Data were analyzed using SPSS 22. Results: We included 85 and 47 students in the CG and IG. The mean and standard deviation (SD) of the understanding score about antibiotics in the E-learning group and the face-to-face education group were 18.8 ± 1.26 and 17.16 ± 1.93 out of 19, respectively, which were statistically significantly different (P = 0.004). The mean and SD of the overall score of satisfaction of the students in the IG was 85.48 ± 23.08 out of 130 points (medium level). Furthermore, the level of satisfaction of male students was significantly higher than female students (P = 0.009). Conclusion: E-learning was effective in improving the process of educating students to the AAP. This education method can be used as an alternative or complementary of face-to-face education, especially in critical conditions such as the pandemic of diseases including COVID-19.

Keywords: Antibiotic, antibiotic prescribing, COVID-19, E-learning, medical students

INTRODUCTION

Antibiotics are among the most frequently used medication groups. They must be used appropriately to provide optimal benefits. To have maximum benefits of antibiotics, the prescribing and using these medications must be appropriate, while a significant proportion of antibiotics are prescribed inappropriately. [1,2] Approximately, 31%-50% of antibiotic prescribing is inappropriate, which reaches 75% in surgical wards.[3-6]

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The inappropriate use of antibiotics has negative health consequences and can lead to various side effects including antimicrobial resistance (AMR).^[7,8] Therefore, the World Health Organization (WHO) and other health organizations in some developed countries have prioritized the appropriate antibiotic prescribing (AAP).[9] There is some evidence about lack of

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Sayyadi-Rahaghi, et al.: E-Learning and appropriate antibiotic prescribing

knowledge in physicians and medical students about antibiotics prescribing.^[10,11] Due to the low confidence in the prescribing the antibiotics and insufficient knowledge of medical students, there is a need for more training in this area.^[12]

Education is widely recognized as one of the basics of successful management programs in antibiotic prescribing. The WHO stated an effective training in antibiotic prescribing during the undergraduate medical curriculum is an important strategy to promote the appropriate use of antibiotics.^[13] Educational interventions improve physicians' antibiotic prescribing, but traditional tools and methods may be insufficient to meet the complex demands of healthcare professionals.^[14] It is recommended to use educational solutions that are timely, efficient, pragmatic, high quality, aligned to the needs of the professional in a specific context, sustainable, and cost-effective.^[13]

The sudden outbreak of COVID-19 at the end of 2019, in addition to health care, affected other areas including student education. [15] After the spread of this disease throughout the world, various organizations and health policymakers have always emphasized maintaining health protocols, observing social distance, reducing travel, and doing work remotely. [16] As well, there is possible to occur other critical conditions like COVID-19 or the closing the educational institutions.

In this regard, many countries have stopped face-to-face education in schools and universities to control and reduce the prevalence of this disease and also to maintain social distance. To avoid further disruption in the education of students and the continuation of their curricula, various solutions were suggested. One of the most important strategies was to use E-learning methods. These methods were used during the lockdown of universities and schools with the aim of helping educators and professors to teach students. [18]

E-learning involves the effective use of information technology (IT) to support teaching and includes the use of digital tools and media. This technology supports face-to-face processes, online learning, as well as combining traditional classroom methods with online approaches.^[19] E-learning, Online learning, or web-based learning is a current educational pattern that has created an environment which provides easier access to course-related study materials, instructions, and applications for medical students all the time.^[20,21]

The E-learning has played an effective role in educating AAP by physicians. [22,23] This technology could also be used as an alternative to face-to-face training to improve patient-related outcomes such as AMR and mortality. The results of a study [22] showed that E-learning in a limited period can significantly improve the performance of medical students in antibiotic consultation therapy. The results of another study [24] showed that the use of internet-based education could lead to a significant reduction in the antibiotic prescribing for patients with acute respiratory infections in Europe.

Although it has been emphasized on the use of educational methods to AAP,^[25] the results of a meta-analysis^[14] showed

that the traditional educational interventions have not had a significant effect on improving AAP in Iran. In this study, the use of IT-based interventions and evaluating their effects on antibiotic prescribing was recommended.

Based on our literature review, there was no study that investigated the effect of E-learning on understanding medical students toward antibiotic prescribing in Iran. Therefore, due to the stopping face-to-face training in the COVID-19 pandemic or future critical conditions, and using IT-based interventions; this study aimed to determine the effect of E-learning on the understanding of AAP and comparison with the face-to-face education among medical students. At the final, the level of students' satisfaction with the E-learning method was only evaluated.

MATERIALS AND METHODS

This quasi-experimental study was conducted with a control group (CG) in 2019 at KaUMS (Iran). The CG included all profit physiopathology medical students (PMSs) in the first semester of the academic year 2019–2020. This group participated in the face-to-face classroom of the relevant professor (Ph.D. in pharmacology). The intervention group (IG) also included all profit PMS in the second semester of the academic year 2019–2020. Both groups received the same educational content from the same professor based on their approved course content (code: 1111754). [26] The educational content was based on Katzung's book on clinical pharmacology. [27] The sections related to the AAP are provided to students. The electronic content (EC) was a video that created by Camtasia Studio 2019 software and presented to students by the professor, weekly. The period of both courses was 4 months.

An academic learning management system (LMS) (called: NAVID) is used in the KaUMS. Registering and using this LMS was explained to the IG before the beginning E-learning course. The EC was submitted by professor in the NAVID. To ensure the students received and read the EC, a reminder short message was sent weekly.

After the end of E-learning and face-to-face courses, a similar examination with 19 questions was used including four dimensions of selecting the appropriate antibiotics, understanding the side effects of in AAP, familiarity with the types of antibiotics and their mechanism of action, and understanding the spectrum of effect and clinical application of antibiotics from both groups. All questions in both groups were same and had four options and were designed by the professor. The professor also evaluated the questions and assigned a score to the students.

The examination for control and IGs were conducted in person and virtually, respectively. Two examination supervisors were in the meeting place to reduce the students' cheating in the CG. For this purpose, there were multiple ways for the IG including displaying one question on each page, limitations in going back to previous pages, and the order of questions being different for all students.

At the end of the E-learning course, the students' satisfaction with this method was evaluated using a standard questionnaire applied in the YS Wang study. This questionnaire has five dimensions of satisfaction with the educational content, system user interface, personalization, learning community, and global satisfaction. The questionnaire also had a 5-point Likert scale (from strongly agreeing to strongly disagreeing) with an option (this question is not related to topic with a score of zero).

Translation of the questionnaire was conducted by the researchers, initially. To ensure cross-cultural adaptation, the questionnaire was translated back to English by an English translator expert. The demographic questions of age, gender, marital status, place of residence, and previous experience of using E-learning were added in the demographic questions' section. The face validity of the questionnaire was examined and modified by three specialists in pharmacy, medical informatics, and health information management. The reliability of the questionnaire was also calculated using Cronbach's alpha ($\alpha = 0.94$). This questionnaire was presented to IG after completing the virtual training course through the NAVID.

Data were analyzed using SPSS.22 (IBM, Chicago, IL, United states). The descriptive statistics was used to calculate frequency, percentage, mean and standard deviation (SD). After checking the data normality, *t*-test, analysis of variance, and analysis of covariance analytical tests were used. Giving consideration to the maximum and minimum scores related to each of the satisfaction dimensions, the level of students' satisfaction in the IG with the E-learning method was divided into high, medium, and low categories.

RESULTS

A total of 132 students participated in face-to-face education (n = 85) and E-learning groups (n = 47). The mean and SD of age in the face-to-face and E-learning groups were 22.96 \pm 0.81 and 23.81 \pm 2.76 years, respectively. Approximately 46% and 57% of the students who participated

in the face-to-face and E-learning courses were male, respectively [Table 1].

The results showed that the mean scores of E-learning group in terms of understanding the consequence of in AAP (mean = 5.62), classification of antibiotics based on the mechanism of the action (4.87), and the antimicrobial spectrum of clinical application of antibiotics (3.8) were significantly higher than the face-to-face group (P < 0.044) [Table 2].

The findings of the study showed that 87% (n = 41) of the students in the IG were satisfied with the E-learning method and 81% of them (n = 38) believed that using this method was successful. Approximately 63% of the students (n = 30) considered the content used in the E-learning method useful and 53% of the total students (n = 25) were agree that the content of this course was sufficient and appropriate for their needs. Furthermore, more than 63% of students (n = 30) believed that the educational content used was new and up to date. Almost 85% of students (n = 40) agreed that the E-learning was easy to use and more than 32 students (61%) found the E-learning system user-friendly and easy to find and understand. The satisfaction levels with the different dimensions of E-learning. Accordingly, the mean and SD of the overall score of students' satisfaction was 85.48 ± 23.08 out of 130. The dimensions of the global and the learning community had the highest and lowest levels of satisfaction among students, respectively.

In addition, the overall satisfaction score of E-learning group with this method was 85.48 ± 23.08 out of 130, which was medium, and this score except for the students' gender (P = 0.009), had no significant relationship with their age, marital status, and place of residence during educating (P > 0.05) [Table 3].

DISCUSSION

The study revealed that the use of E-learning method could have a positive effect on medical students' understanding

Demographic information	Frequency (%)		P
	Face-to-face group	E-learning group	
Age (years), mean	22.96±0.81	23.81±2.76	0.04*
Gender			
Male	39 (46)	27 (57)	0.20^{\dagger}
Female	46 (54)	20 (43)	
Marital status			
Single	76 (89)	40 (85)	0.46^{\dagger}
Married	9 (11)	7 (15)	
Address			
Kashan	29 (34)	14 (30)	0.90^{\dagger}
Other cities in Isfahan province	25 (29)	16 (34)	
Neighboring province of Isfahan province	7 (8)	3 (6)	
Other provinces	24 (28)	14 (30)	

^{*}Independent t-test, †Covariance test

Sayyadi-Rahaghi, et al.: E-Learning and appropriate antibiotic prescribing

Table 2: Mean and standard deviation of the score between face-to-face education and E-learning groups								
Dimension	IG (E-learning group)	CG (face-to-face group)	t	P				
Selecting the right antibiotic (out of 4)	3.79±0.51	3.69±0.69	1.44	0.151				
Understanding the consequence of inappropriate antibiotic prescribing (out of 6)	5.62 ± 0.709	5.25 ± 0.858	2.52	0.013				
Classification of antibiotics based on mechanism of the action (out of 5)	4.87 ± 0.39	4.70 ± 0.53	2.04	0.044				
The antimicrobial spectrum of clinical application of antibiotics (out of 4)	3.80 ± 0.379	3.57 ± 0.624	2.60	0.01				
Total (out of 19)	18.08 ± 1.26	17.16 ± 1.93	2.93	0.004				

IG: Intervention group, CG: Control group

Dimensions under consideration	Frequency (%)	Mean±SD	Level
Content			
Low	9 (19)	14±4.28 (out of 20)	Medium
Medium	15 (32)		
High	23 (49)		
Learner interface			
Low	7 (15)	35.93±10.35 (out of 55)	Medium
Medium	26 (55)		
High	14 (30)		
Personalization			
Low	9 (19)	15.93±4.84 (out of 25)	Medium
Medium	24 (51)		
Much	14 (30)		
Learning community			
Low	15 (32)	11.57±4.42 (out of 20)	Medium
Medium	20 (43)		
High	12 (25)		
Global satisfaction (the E-learning system is successful)			
Low	4 (8)	8.04±1.94 (out of 10)	High
Medium	6 (13)		
High	37 (79)		
Total (as a whole)			
Low	8 (17)	85.48±23.08 (out of 130)	Medium
Medium	22 (47)		
High	17 (36)		

SD: Standard deviation

about antibiotics in the most of the studied dimensions. However, the effect of using this method in choosing an appropriate antibiotic dimension had no significant difference with the face-to-face educational method. In addition, the results of the study showed that the overall satisfaction of students using the E-learning with all aspects related to this method is medium.

The study showed that training the students by E-learning compared to the face-to-face method has a significant effect on understanding the side effects of in AAP, familiarity with different types of antibiotics and their mechanism of action, and the spectrum of effect and clinical application of antibiotics. Based on our knowledge, no study has not considered the effect of E-learning on the above dimensions, yet. It is suggested that these dimensions be considered in the future studies.

The results of a meta-analysis showed that most traditional educational interventions on physicians had not a significant effect on improving the AAP in Iran while the use of IT-based interventions may be more effective in this practice. [12] The results of some studies [24,29] are in line with our results. The results of another study showed that the combined education method (traditional and E-learning) has been more successful in increasing the score of pharmacology students. [30] It is suggested to use E-learning method as a complementary method along with face-to-face.

The study showed that there was no significant difference between both groups using face-to-face training and E-learning in terms of the mean scores related to antibiotic selection. The results of Sikkens *et al.*'s^[22] study showed that the use of E-learning method can significantly improve students' knowledge about the antibiotic prescribing, which did not align with our findings. It seems that one of the possible reasons for the difference in these results is the duration of the intervention, interval between conducting the intervention, and type of the evaluation.

The results of this study showed that students' satisfaction with E-learning was medium. However, the most students were satisfied with the variety of provided education in the E-learning method and stated the use of this method was successful. In compliance with these findings, the results of a study by Moreira et al.[31] showed that the most of the learners were satisfied with the E-learning course on breast imaging. Furthermore, they stated that participating in this course was a success for them. A study by Sikkens et al.[22] shows a positive evaluation on the use of E-learning method by students and believed that this learning method increased students' self-confidence about the antibiotic prescribing process. In addition, the results of a study,[32] showed that distance learning during the COVID-19 pandemic was a successful implementation. Students were generally satisfied with that and online assessment, but the clinical skills learning is critical care for the students. Another study^[33] also showed that students and staff were satisfied with the E-learning environment. They believed that E-learning method had improved their technological skills.

The use of E-learning techniques and E-learning systems are a new method that used in Iran's universities in recent years. The lack of widespread use of this method in Iranian universities of medical sciences like KaUMS and also the students' unfamiliarity with E-learning may be affected students' satisfaction.

The COVID-19 has caused disruptions in the students' education process. Then, E-learning can reduce the problems associated with the disruption of the students' face-to-face education, greatly. Doing some studies on the educating the principles of AAP is suggested. Furthermore, the use of E-learning method might save the cost and time for individuals and educational institutions and reduces travels. Due to the effectiveness of E-learning method on students' knowledge about antibiotic prescribing, various educational institutions and universities can invest and develop this educational method to continue their educational activities effectively, especially in critical conditions. Continuing education centers can also provide regular courses for physicians and medical students to help increase their knowledge about antibiotics.

This study was performed in one of the high-prevalence COVID-19 cities on two semesters of students of KaUMS. Continuity of the studies on a larger population can increase the generalizability of the results. The assessment of the students' understanding is a subjective process. The subjective assessments are not always strong. However, in this study, an attempt was made to strengthen the structured and systematic assessment approach. In addition, to the evaluation of students' satisfaction, qualitative methods such as interviews are recommended. In addition, we were not sure about the content sharing or discussion between students which may be affected our results.

CONCLUSION

The E-learning method is successful in increasing students' understanding toward AAP. This educational method caused a relatively satisfaction among the students. Therefore, the E-learning can be used as a complementary or alternative method to face-to-face education in the AAP. It seems the E-learning method can be used in the educating students in other fields. It is recommended to use this method in critical conditions such as COVID-19 or the closing the educational institutions.

Ethical considerations

This study is approved by the Research Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS. NUHEPM.REC.1399.031).

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Andrajati R, Tilaqza A, Supardi S. Factors related to rational antibiotic prescriptions in community health centers in Depok City, Indonesia. J Infect Public Health 2017;10:41-8.
- Ganguly NK, Arora NK, Chandy SJ, Fairoze MN, Gill JP, Gupta U, et al. Rationalizing antibiotic use to limit antibiotic resistance in India. Indian J Med Res 2011;134:281-94.
- Hecker MT, Aron DC, Patel NP, Lehmann MK, Donskey CJ. Unnecessary use of antimicrobials in hospitalized patients: Current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. Arch Intern Med 2003;163:972-8.
- Yadegarinia D, Zamiri S. Pattern of empiric antibiotic prescription in patients referred to an emergency department of a Medical University affiliated hospital in Tehran. Pajoohandeh J 2009;14:31-6.
- Gebeyehu E, Bantie L, Azage M. Inappropriate use of antibiotics and its associated factors among Urban and rural communities of Bahir Dar City administration, Northwest Ethiopia. PLoS One 2015;10:e0138179.
- Dache A, Dona A, Ejeso A. Inappropriate use of antibiotics, its reasons and contributing factors among communities of Yirgalem town, Sidama regional state, Ethiopia: A cross-sectional study. SAGE Open Med 2021;9:1-9. [doi: 10.1177/20503121211042461].
- Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2017;2:CD003543.
- Baktygul K, Marat B, Ashirali Z, Harun-Or-rashid M, Sakamoto J. An assessment of antibiotics prescribed at the secondary health-care level in the Kyrgyz Republic. Nagoya J Med Sci 2011;73:157-68.
- Ayuthya SK, Matangkasombut OP, Sirinavin S, Malathum K, Sathapatayavongs B. Utilization of restricted antibiotics in a university hospital in Thailand. Southeast Asian J Trop Med Public Health 2003;34:179-86.
- Lee CR, Lee JH, Kang LW, Jeong BC, Lee SH. Educational effectiveness, target, and content for prudent antibiotic use. Biomed Res

Sayyadi-Rahaghi, et al.: E-Learning and appropriate antibiotic prescribing

- Int 2015:2015:214021.
- 11. Pulcini C, Gyssens IC. How to educate prescribers in antimicrobial stewardship practices. Virulence 2013;4:192-202.
- 12. Organization WH. The Evolving Threat of Antimicrobial Resistance: Options for Action. Geneva: World Health Organization; 2012.
- Rocha-Pereira N, Lafferty N, Nathwani D. Educating healthcare professionals in antimicrobial stewardship: Can online-learning solutions help? J Antimicrob Chemother 2015;70:3175-7.
- Nabovati E, TaherZadeh Z, Eslami S, Abu-Hanna A, Abbasi R. Antibiotic prescribing in inpatient and outpatient settings in Iran: A systematic review and meta-analysis study. Antimicrob Resist Infect Control 2021:10:15
- Mian A, Khan S. Medical education during pandemics: A UK perspective. BMC Med 2020;18:100.
- Sajed AN, Amgain K. Corona virus disease (COVID-19) outbreak and the strategy for prevention. Europasian J Med Sci 2020;2:1-3.
- Viner RM, Russell SJ, Croker H, Packer J, Ward J, Stansfield C, et al. School closure and management practices during coronavirus outbreaks including COVID-19: A rapid systematic review. Lancet Child Adolesc Health 2020;4:397-404.
- Almaiah MA, Al-Khasawneh A, Althunibat A. Exploring the critical challenges and factors influencing the E-learning system usage during COVID-19 pandemic. Educ Inf Technol (Dordr) 2020;25:5261-80.
- Cook DA. Web-based learning: Pros, cons and controversies. Clin Med (Lond) 2007;7:37-42.
- Mukhtar K, Javed K, Arooj M, Sethi A. Advantages, limitations and recommendations for online learning during COVID-19 pandemic era. Pak J Med Sci 2020;36:S27-31.
- Jayara S. The advantages and disadvantages of online teaching in medical education. J Med Evid 2020;1:144.
- Sikkens JJ, Caris MG, Schutte T, Kramer MH, Tichelaar J, van Agtmael MA. Improving antibiotic prescribing skills in medical students: The effect of e-learning after 6 months. J Antimicrob Chemother 2018;73:2243-6.
- 23. Ellaway R, Masters K. AMEE guide 32: E-Learning in medical education

- Part 1: Learning, teaching and assessment. Med Teach 2008;30:455-73.
- Little P, Stuart B, Francis N, Douglas E, Tonkin-Crine S, Anthierens S, et al. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: A multinational, cluster, randomised, factorial, controlled trial. Lancet 2013;382:1175-82.
- Yimenu DK, Emam A, Elemineh E, Atalay W. Assessment of antibiotic prescribing patterns at outpatient pharmacy using world health organization prescribing indicators. J Prim Care Community Health 2019;10:1-14.
- Available from: http://medicine.kaums.ac.ir//UploadedFiles/400/Group/ pharma/tarh%20dars% 20pharma2%201400-2.pdf. [Last accessed on 2020 Sep 22].
- Katzung BG. Basic and Clinical Pharmacology. 14th ed. University of California, San Francisco: McGraw Hill Professional; 2017.
- Wang YS. Assessment of learner satisfaction with asynchronous electronic learning systems. Inf Manage 2003;41:75-86.
- Nourian A, Nourian A, Ebnahmadi A, Akbarzadeh Baghban A, Khoshnevisan MH. Comparison of e-learning and traditional classroom instruction of dental public health for dental students of Shahid Beheshti Dental School during 2010-2011. J Dent Sch 2012;30:174-83.
- Kayzouri A, Sadeghpour M. A comparison on the effects of traditional, e-learning and traditional-e learning on the pharmacology course of nursing students. Journal of Sabzevar University of Medical Sciences 2017;24:123-7.
- Moreira IC, Ventura SR, Ramos I, Rodrigues PP, editors. Learner's Satisfaction Within a Breast Imaging eLearning Course for Radiographers. Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems; IEEE; 2013.
- Tayem YI, Almarabheh AJ, Abo Hamza E, Deifalla A. Perceptions of medical students on distance learning during the COVID-19 pandemic: A cross-sectional study from Bahrain. Adv Med Educ Pract 2022;13:345-54.
- Elzainy A, El Sadik A, Al Abdulmonem W. Experience of e-learning and online assessment during the COVID-19 pandemic at the college of medicine, Qassim University. J Taibah Univ Med Sci 2020;15:456-62.