Impact of Infectious Diseases Training in the Perception of Antibiotic Resistance and Rational Use of Antibiotics Among Spanish Medical Students. A Case-Control Study

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Abstract

Antibiotic resistance is one of the main public health problems worldwide. A key tool to optimize antibiotic prescription is medical training. The aim of this study is to compare the impact of training in infectious diseases in the knowledge of the antibiotic resistance problem and the rationale use of antibiotics. We performed a case-control study in the medical school of the University of Navarra, one of the top private Universities in Spain. We conducted an anonymous presential survey of students in each year of formation. Data were analyzed grouping the students: GROUP 1: first three years of education. They have not trained in Clinical Microbiology (CM) neither in Infectious Diseases (ID); GROUP 2: fourth-year students; they have training in CM but not ID; GROUP 3: Fifth and sixth-year students; they have completed the training in CM and ID.

A total of 994 students answered the survey, 80.4% of the eligible students. Almost all students who have completed infectious diseases formation perceive antibiotic resistance as a relevant problem in comparison with students who did not complete the formation (99.5% in group 3 vs 94.5% in group 1, $p=0.02$). Knowledge of antibiotic stewardship statistically significant change with infectious diseases formation (from 9.2% in group 1 to 52.2% in group 3, $p<0.001$). In the training questions block we also found an increase in the average of the correct answers (21.4% in group 1 vs 44.7% in group 3, $p<0.001$). When comparing the results of subgroups 3A and 3B we found a significant loss of knowledge as we move away from training (49% vs 40.9%, $p<0.001$).

The training of medical students is key both to improve the perception and knowledge of infectious diseases. However, we have an opportunity to educational improvement in infectious diseases in both the acquisition of knowledge and its loss when we move away from training.

Introduction

According to the World Health Organization, antibiotic resistance crisis is one of the main public health problems worldwide [1, 2]. Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. The problem has been attributed to several aspects, misuse of antibiotics, use without prescription, veterinarians use, overuses of long therapies and lack of knowledge of resistance mechanisms. Infections by resistant bacteria cannot be treated with standard antibiotic treatment, the lack of activity increase number of morbidity and mortality cases and increase healthcare expense. But some authors showed that general practitioners consider antibiotic resistance as a rare issue and misinterpreted the evidence that links inappropriate antibiotic prescription with bacterial resistance [3]. The recognition of antibiotic resistance as public health problem is mandatory, and basic infectious diseases training in medical school is an excellent opportunity to achieve this need.

In several studies between thirty and fifty percent of cases in which antibiotics were prescribed, their use can be optimized. The most common misused were unnecessary prolonged therapy, antibiotic coverage

too broad in empirical therapy, delay in the change of administration route or de-escalation. Education of healthcare and medical students on rational antimicrobial prescribing or antimicrobial stewardship is a key tool to contain antimicrobial resistance [4, 5]. To date, investigation of students attitudes towards antibiotic prescription and perceptions of antibiotic resistance has focused on final-year medical students [6–8]. We thought that comparing students before and after receiving training in infectious diseases could give us fundamental information to understand the learning process and which concepts, we should need to emphasize.

The aim of this study is to evaluate the impact of the infectious diseases training in the perception of medical students about antibiotic resistance and the impact in the rational use of antibiotics.

Material And Methods

Participants

We conducted a case-control study including all medical students at the medical school of the University of Navarra. University of Navarra is one of the top private universities in Spain. It is located in Pamplona and was ranked 266th in QS Global World Rankings 2022.

In September 2018, at the beginning of the academic year, there were a total of 1,236 students: 214 in first year, 199 in second year, 193 in third year, 222 in fourth year, 204 in fifth year and 204 in sixth year. In the University of Navarra, the training in clinical microbiology is carried out during the third year and infectious diseases education in the fourth year. Students who complete the six-year program receive a medical degree and the authorization for prescription of any antibiotic.

To simplify the analyses, we divided subjects in 3 groups and 2 subgroups. GROUP 1 is made up untrained students of first, second and third year of education. Students who completed training in Clinical Microbiology but not Infectious Diseases formed GROUP 2 (Fourth year students). Fully trained students in Clinical Microbiology and Infectious diseases formed GROUP 3 (fifth and sixth year). We divided group 3 in two subgroups according to the time elapsed from completed training. In the SUBGROUP 3A they completed training in Infectious Diseases in the same year to the survey (fifth year students) and in the SUBGROUP 3B they completed training in Infectious Diseases one year before the survey (sixth year students). See figure 1 for a graphic division of groups.

Preparation of the survey

We developed a questionnaire of 19 questions (see Online Resource 1). Survey was divided into 2 blocks. A first block to understand the student's knowledge about diagnosis, bacterial resistance, and appropriate use of antibiotics, and a second block to evaluate the expertise in infectious diseases.

The first block included 12 questions with 4 possible answer options: always, frequently, rarely, and never. To facilitate the analysis, options always and frequently were grouped as "Positive" and rarely or never as

"Negative". The second block included 7 questions; six of them had 4 distractors with only one correct answer. Questionnaire was approved by the dean of the medical school.

Participation was voluntary, anonymous and without compensation. The surveys were conducted in classrooms in 15 minutes through the online educational platform Socrative (available at www.socrative.com).

Questions in the first block assessed the magnitude of the antimicrobial resistance, the importance of collection of sample for microbiological cultures; the indication for initiation of empirical antibiotic treatment; the value of microbiological information and clinical evolution for the de-escalation therapy; the usefulness of combination therapy; the duration of antibiotic therapy; the route of administration; the rationale use of restricted antibiotics; the antibiotic cost assessment and the knowledge about antibiotic stewardship programs. Questions in the second block were oriented to evaluate the knowledge in basic infectious diseases scenarios like microorganism associated with multidrug resistant, appropriate media cultures, best antibiotic empirical treatment, the use of antibiotic in no bacterial infection, treatment of asymptomatic bacteriuria, route of treatment and length of therapy.

To consider a survey as valid it had to have at least 5 questions answered. Surveys that did not meet this criterion were not analyzed in this study.

Statistical analysis

All analyses were performed on a per protocol basis using SPSS software (version 25.0). Chi-square test (or Fisher's exact test when appropriate) was performed to evaluate potential associations. Wilcoxon test was used to compare the median correct answers between groups. P-values < 0.05 were considered as statistically significant.

Results

Out of 1,236 eligible medical students, 994 (80.4%) responded to the survey with 944 (76.4%) valid surveys. Table 1 shows the students surveyed by year and group of training.

Table 1
Proportion of students surveyed by year and group of training

	<i>Total students n</i>	<i>Students surveyed n (%)</i>	<i>Not valid surveys n (%)</i>	<i>Valid surveys n (%)</i>
Year of training				
First	214	198 (92.5)	4 (1.9)	194 (90.6)
Second	199	178 (89.4)	12 (6.0)	166 (83.4)
Third	193	158 (81.9)	10 (5.2)	148 (76.7)
Fourth	222	150 (67.6)	8 (3.6)	142 (64.0)
Fifth	204	155 (76.0)	4 (2.0)	151 (74.0)
Sixth	204	155 (76.0)	12 (5.9)	143 (70.1)
Group of training				
Group 1	606	534 (88.1)	26 (4.3)	508 (83.8)
Group 2	222	150 (67.6)	8 (3.6)	142 (64.0)
Group 3	408	310 (76.0)	16 (3.9)	294 (72.1)
Subgroup 3A	204	155 (76.0)	4 (2.0)	151 (74.0)
Subgroup 3B	204	155 (76.0)	12(5.9)	143 (70.1)
Global				
	1236	994 (80.4)	50 (4.0)	944 (76.4)

Students' knowledge

Table 2 presents an overview of student's knowledge by training. Comparing responses of students of group 3 and group 1, 99.3% of students considered that antibiotic resistance always/frequently represents a Public Health problem and 94.7% in group 1 thought as a problem ($p=0.02$), and 98.4% in group 3 believed antibiotic resistance should be always or frequently consider before to start an empirical antibiotic treatment compared with 96.4% in group 1 ($p=0.17$).

Table 2

Comparison between answers of the students without training (Group 1) and the trained students in infectious diseases (Group 3)

	<i>Group 1</i>	<i>Group 3</i>	<i>p</i>
	%	%	
Relevance of the problem	94.7	99.3	$p=0.02$
<i>Question 1.</i> Do you think antibiotic resistance is a public health problem?	5.3	0.7	
Always-Frequently			
Rarely-Never			
Microbiological cultures	68.6	90.3	$p<0.001$
<i>Question 2.</i> Do you think collect specimen for microbiological cultures before start empiric antibiotic is mandatory?	31.4	9.7	
Always-Frequently			
Rarely-Never			
Empiric antibiotic treatment	78.3	75.7	$p=0.37$
<i>Question 3.</i> In a clinical stable patient with documented clinical infection, is it necessary to start empirical antibiotic treatment?	21.7	24.4	
Always-Frequently			
Rarely-Never			
<i>Question 4.</i> Before starting an empirical antibiotic treatment, we should consider the problem of antibiotic resistance?	96.4	98.4	$p=0.17$
	3.6	1.6	
Always-Frequently			
Rarely-Never			
De-escalation therapy	96.9	97.8	$p=0.63$
<i>Question 5.</i> Do you think empirical antibiotic treatment should be adjusted according to microbiological data and clinical evolution?	3.1	2.2	
Always-Frequently			
Rarely-Never			

	<i>Group 1</i>	<i>Group 3</i>	<i>p</i>
	%	%	
Combination therapy	93.5	85.3	p=0.61
<i>Question 6.</i> Do you think antibiotic combinations improve clinical results?	6.5	14.7	
Always-Frequently			
Rarely-Never			
Prolonged duration	23.2	9.5	<i>p<0.001</i>
<i>Question 7.</i> Do you think prolonged duration of antibiotic treatment more than recommended by clinical guidelines improves clinical outcomes?	76.8	90.5	
Always-Frequently			
Rarely-Never			
Appropriate route	48.3	84.2	<i>p<0.001</i>
<i>Question 8.</i> Conversion from parenteral to oral therapy of antibiotics with excellent bioavailability in clinically stable infected should be consider?	51.7	15.8	
Always-Frequently			
Rarely-Never			
Antibiotics for restricted use	65	45.9	<i>p<0.001</i>
<i>Question 9.</i> Do you think use of restricted drugs provide a clinical and microbiological benefit over first-line drugs?	35	54.1	
Always-Frequently			
Rarely-Never			
Antibiotic cost	67	85.4	<i>p<0.001</i>
<i>Question 10.</i> Do you think cost of antibiotic treatment should be considered before its prescription?	33	14.6	
Always-Frequently			
Rarely-Never			
Antibiotic stewardship program	9.3	52.2	<i>p<0.001</i>
<i>Question 11.</i> Do you know the Antibiotic Stewardship Program?	90.7	47.8	
Yes			
No			

	<i>Group 1</i>	<i>Group 3</i>	<i>p</i>
	%	%	
<i>Question 12.</i> Do you think antibiotic Stewardship Program can improve medical training and clinical outcomes in the hospitals in which they are established?	99	99.1	p=0.97
	1	0.9	
Always-Frequently			
Rarely-Never			

In empirical antibiotic treatment 78.3% of group 3 students assumed that antibiotic therapy always/frequently should be started in a clinical stable infected patient related with 75.7% in group 1 (p=0.37). Between fully trained students, 90.3% of them believed that prior microbiological samples collection always or frequently should be made compared with 68.6% of students in the group who did not receive microbiology or infectious disease formation yet (p<0.001).

In adjusted antibiotic treatment, de-escalation therapy was always/frequently considered by 98.4% of students in group 3 and 96.4% in group 1 (p=0.63). 84.2% of fully trained students always or frequently considered conversion from parenteral to oral treatment when available compared with just 48.3% of students in group 1 (p<0.001). Regarding combination therapy no statistically significant differences were detected, because 85.3% of students in group 3 always or frequently estimated combination therapy as useful and 93.5% of students in group 1 had the same perception (p=0.61). There was statistically significant difference between groups in the perception of the use of restricted drugs for improve clinical and microbiological results (45.9% in group 3 vs 65% in group 1; p<0.001). Just 9.5% of group 3 students always/frequently evaluated prolonged therapy improve clinical outcomes compared with 23.2% of students in group 1 (p<0.001).

In the group 3, 52.2% of students knew antibiotic stewardship programs compared with 9.3% students in group 1 with a statistically significant difference (p<0.001)

Impact of undergraduate training in infectious diseases.

The percentage of correct answers was 25.3% in group 1, 32.4% in group 2 (after training in clinical microbiology), and 52.7% in group 3 (after training in infectious diseases). The median number of correct answers of students in group 1 is 1.60 [95% CI 1.50-1.70], in group 2 is 1.93 [95% CI 1.74-2.12] and in students in group 3 is 3.14 [95% CI 2.98-3.30] (p <0.001).

The percentage of correct answers for the group that had just received infectious disease training (group 3A) was 49% while the group that received it a year earlier (group 3B) was 40.9%. The median number of correct answers by students in group 3A is 3.43 [95% CI 3.21-3.65] and in students in group 3B 2.86 [95% CI 2.63-3.08] (p <0.001). (See Figure 2)

Discussion

Training is an important key to improve the rationale use of antibiotics and help control antibiotic resistance. This study shows, in medical students, the high perception about the problem of antibiotic resistance and the rationale uses of antibiotics. We also demonstrated the impact of training in infectious diseases in the knowledge of antibiotic resistance and the need for continuous medical education to avoid the loss of the formative impact.

A global participation of 76.4% indicates a high participation rate and a great interest in antimicrobial resistance. The perception and assessment of the problem is high since the first grades, but after training in infectious diseases, 99.3% of medical students consider that antibiotic resistance currently represents a Public Health problem and 98.4% think the problem of antibiotic resistance should be considered before starting an antibiotic prescription.

Training and education of future prescribers is one of the main interventions to improve the rationale use of antibiotics. Training should begin in medical schools and continue throughout the professional life. Studies have shown that doctors with limited knowledge about antibiotics tend to unnecessarily prescribe more potent antibiotics and with a wider spectrum of action [9, 10].

In the study by Hecker et al, they observed that the most frequent reasons to inappropriate antibiotic therapy are the duration of therapy longer than necessary, treatment of noninfectious or nonbacterial syndromes, treatment of colonization or contamination and redundant antimicrobial coverage [9].

In the first situation, even 90.5% of students in group 3 consider that there is no need to carry out long-term antibiotic, but in the training questions section we found that only 14.3% of the students of this group hit the appropriate duration of antibiotic therapy. Comparison of the findings with those of other studies confirms a lack of confidence of medical students identifying the correct duration of treatment or oral treatment alternatives [7]. The second most frequent cause of inappropriate antibiotic use was the treatment of patients with noninfectious or a non-bacterial syndromes [11].

Regarding the duration of treatment, most of the students with complete training considered prolonged therapy unnecessary compared to 76.5% of the students without training ($p < 0.001$). This finding is relevant because it shows that future prescribers are more likely to modify their treatment approaches during their formative years. Modifying these attitudes in infectious diseases physicians is often harder, despite clinical trials showing that the result does not differ. Recognizing the undergraduate training as the imprinting phase to instill the concept of shorter-is-better, could avoid future adverse effects, resistance to antibiotics, and reduce cost.

In our study, we observed a significant improvement in the ability of medical students to make an accurate diagnosis of infection after infectious diseases training. Misdiagnosis has been found to be a leading cause of unnecessary treatments [12]. In the questions to evaluate the value of microbiological data, the impact of training is also relevant, although it has already begun after training in clinical

microbiology (group 2). Finally, related the impact of redundant antimicrobial coverage in inappropriate antibiotic use, we do not observe a significant improvement after training in infectious diseases. As in other points such as the choice of an empirical antibiotic treatment, it is related to the high perception of students of these problems from the first years.

After training in infectious diseases, knowledge of the stewardship antibiotic program increases from 9.3% in medical students in group 1 to 52.2% in group 3. This situation contributes to a better perception of the problem of antibiotic resistance and a better and rationale use of them. However, these results represent another important point of improvement in medical student to accept the benefit of these programs. It is likely that improving the training at these points from medical schools can improve future prescribing [13].

In the second block, we also observed an improvement in results after training in infectious diseases. The average of correct answers was 1.6 in group 1, 1.93 in group 2 and 3.14 in group 3, with statistically significant differences ($p < 0.001$). The average percentage of correct answers in students after training in infectious diseases was 52.7%. As in the work of Hecker et al, in the hospital setting up to 50% of the prescriptions are inappropriate [9]. The impact of training in infectious diseases in our study was higher than that described by other authors [6, 7].

A final point is the partial loss of the formative impact over time. In our study we observed a median 9.7% decrease in correct answers (difference between subgroup 3A and subgroup 3B).

Training in infectious diseases in a medical school is an effective strategy to improve the use of antibiotics. However, as in other published studies, we observed a remarkable margin for improvement in training in infectious diseases and a rapid loss of knowledge one year after training [14]. Enhancing the training in the rationale use of antibiotics in medical schools, should represent an important stimulus for teachers to improve results and probably will have to go through a change in the teaching methodology [15].

We must adopt pedagogical measures to stabilize the knowledge learned in infectious diseases in medical schools and, through continuous medical education, establishing the training of future prescribers. According to pedagogical studies, learning consists in reconstructing knowledge [16]. That is, the new knowledge is built on the existing one. Therefore, to add knowledge, you must have a solid foundation that allows the student to deepen certain aspects [15]. In this way, Spanish students consider that the discussion of clinical cases and rotations in infectious diseases are the most useful among their medical degree [17].

Several studies have investigated how to prevent the decline in the knowledge of students and professionals and others forms of learning such as role-playing, teaching in workshops or e-learning can also be implemented and have shown that they can improve students' knowledge [15, 16].

The opinions-responses expressed by doctors and medical students should help us to propose changes in teaching planning in undergraduate and postgraduate training.

Other measure that could be assumed to improve the safety and rationale use of antibiotics is the “P-drugs method”. This method recommended by the WHO [18] and successfully applied in several countries has shown good acceptance among students and favors an adequate use of antibiotics [19, 20].

Some limitations of this study, despite the high participation, it has been carried out in a single center, participation in the survey depends on class attendance and an unvalidated questionnaire has been used whose degree of discrimination of certain questions is difficult to assess.

In conclusion, in this study training of medical students improved the recognition of antimicrobial resistance as an important problem. But this knowledge decreased after a year of education.

Declarations

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Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jose Ramon Yuste, Andres Blanco-Di Matteo and Fernando Gruber. The first draft of the manuscript was written by Jose Ramon Yuste, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated during and/or analyzed during the current study are not publicly available due to Spanish law for the protection of personal data and digital right but are available from the corresponding author on reasonable request.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University of Navarra.

Consent to participate

Oral informed consent was obtained from all individual participants included in the study.

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22. *The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.*

Figures

Figure 1

Division of students according to year of training and time of survey.

Figure 2

Correct answers between groups and subgroups of students.

Supplementary Files

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