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Title: Comparison of dermatologists and family physicians in terms of prescribing antibiotics for the treatment of acne vulgaris

Running Head: Attitude of prescribing antibiotics

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Key Words: Acne vulgaris, antibiotic resistance, antibiotics, treatment

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Comparison of dermatologists and family physicians in terms of prescribing antibiotics for the treatment of acne vulgaris

Abstract

Background: Acne Vulgaris (AV) is a common skin disease that is treated both with dermatologists and family physicians (FPs) with different strategies.

Objective: To assess the antibiotics that are frequently preferred in AV treatment, and the differences between the FPs and dermatologists in treatment were investigated.

Material-Method: The physicians were informed about the study, and sent over the internet a multiple-choice questionnaire that consists of 29 questions in total. Afterwards the answers provided were compared.

Results: 201 dermatologists and 147 FPs participated in the study. Dermatologists were found to have preferred topical erythromycin, nadifloxacin, clindamycin and tetracycline, and systematically doxycycline and azithromycin in adult patients, whereas the FPs were found to have preferred mupirocin, fusidic acid (FA) and oxytetracycline, and systematically tetracycline. Dermatologists were found to have recommended topical clindamycin and erythromycin in pregnant/breastfeeding AV patients, whereas the FPs were found to have recommended FA. Dermatologists were found to have continued the antibiotics for 8-12 weeks, whereas the FPs were found to have continued for 1-4 weeks. The dermatologists preferred systemic antibiotics in cases with back involvement, moderate to severe AV, and that the FPs preferred them in severe AV. The dermatologists considered that the use of antibiotics alone or long-term were important factors causing antibiotic resistance.

Conclusion: There were significant differences between the approaches of dermatologists and FPs to AV treatment. FPs were found to have insufficient information about prevention of antibiotic resistance. Therefore, we think that the continuous training of FPs on dermatology will be beneficial.

Key words: acne vulgaris, antibiotic resistance, antibiotics, treatment.

Introduction

Acne Vulgaris (AV) is a common chronic inflammatory skin disease in which the antibiotics are used for treatment given their antibacterial and anti-inflammatory properties.¹ However, antibiotics are not effective anymore due to the increasing resistance observed in years, and additionally, this resistance is passed down to microflora and to the persons those have come into contact.

Patients refer to both dermatologists and family physicians (FPs) for AV treatment.² They both prescribe antibiotics for AV but in different prescribing manner.³ The objective of our study was to draw attention to antibiotic resistance and to reveal the differences between the two branches in respect of prescribing antibiotics for AV treatment.

Material and Method

Ethics committee approval (2018/144) was obtained from the University Clinical Research Center Ethics Committee. The study which announced through social media and e-mails was conducted between May and July 2018 in Turkey. 348 physicians (201 dermatologists; 147 FPs) participated. Physicians were sent over the internet a multiple-choice 29 questions (Table I) and afterwards the answers were compared.

Data analyses were performed with the statistical software SPSS for Windows, version 25.0 (SPSS, Inc., Chicago, IL). Significant differences of normally distributed data were assessed using t-test and

significant difference of not normally distributed data were analyzed using Mann-Whitney U test. P value < 0.05 was considered to be statistically significant.

Results

For the number of daily examined AV patients, 98% of the FPs (n=144) examined 0-5 patients every day, 40% of the dermatologists (n=80) examined 0-5, another 40% (n=80) examined more than 10 patients. The remaining 20% of the dermatologists examined 5-10 patients a day. 96% of the dermatologists (n=193) prescribed both topical and systemic antibiotics, while 51% of the FPs (n=75) prescribed both topical and systemic antibiotics and 38% (n=56) prescribed topical antibiotics only. All of the dermatologists prescribed antibiotics and 6% (n=9) of the FPs never prescribed antibiotics for AV.

76.6% of the dermatologists (n=154) preferred topical antibiotics in fixed combinations while 57.1% of the FPs (n=84) preferred topical antibiotics as monotherapy (p=0,000). The antibiotics of choice by dermatologists and FPs are presented in Table II and III.

Dermatologists prescribed systemic antibiotic for the following indications in order of frequency: moderate AV (85%), back involvement (58.2%), severe AV (52.7%), as a supportive treatment (45.8%), for patients refusing topical treatment (23.9%), patients insisting on systemic antibiotics (9%), and mild AV (2.5%). FPs prescribed systemic antibiotics for the following indications in order of frequency: severe AV (69.4%), mild AV (2%), back involvement (44.2%), as a supportive treatment (28.6%), patients refusing topical treatment (7.5%), patients insisting on systemic antibiotics (6.1%) and mild AV (2%).

Dermatologists' choice for systemic antibiotics in cases of moderate and severe AV, back involvement, patients refusing topical treatment and as a supportive treatment were significantly higher than FPs (p=0.000, p=0.001, p=0.007, p=0.000, p=0.001, respectively).

Majority of the dermatologists (88.5%) did not prescribe antibiotics for comedones while 50% of FPs did not prescribe antibiotics and 32% prescribed on occasion ($p=0.000$, $p=0.000$ respectively).

While most of the dermatologists (37.8%) preferred systemic antibiotic treatment for 8-12 weeks, 39.5% of the FPs preferred a duration of 1-4 weeks. 78 of the dermatologists (39%) preferred topical antibiotic treatment for 8-12 weeks and 53 of the FPs (36%) preferred less than 4 weeks and 52 of them (35%) preferred 4-8 weeks. Time to switch the class of the antibiotic due to lack of efficacy was 8 weeks for 45% of dermatologists and 4 weeks for 48% of the FPs.

While dermatologists prescribed fixed combinations of topical antibiotics with benzoyl peroxide (BP), adapalene, isotretinoin and tretinoin, FPs either did not prescribe fixed combinations or stated that they have no idea. Dermatologists' choice for fixed combinations were erythromycin and tretinoin (72.2%), clindamycin and BP (67.6%) and erythromycin and isotretinoin (50%).

72.8% of the answers in favor of BP in fixed combinations was from dermatologists and 27.8% was from FPs ($p=0.000$). For the answers in favor of adapalene and tretinoin in fixed combinations, rate of dermatologists was 85.5% and 86.6%, respectively. ($p=0.000$, $p=0.000$).

Concerns regarding antibiotic resistance were similar among dermatologists and FPs, 88.5% and 79.5%, respectively ($p=0.070$). Regarding the transmission of antibiotic resistant strains, 72.4% of the answers in favor of family contact was from dermatologists and 27.6% from the FPs ($p=0.014$). For the answers in favor of transmission during clinical examination, hand shake, use of common items, the rate of dermatologists were 82.6%, 71.4% and 78.1%, while the FP's rates were %17.4%, 28.6% and 21.9% ($p=0.015$, $p=0.191$, $p=0.015$, respectively) . 54.3% of the answers not considering transmission of the resistant strains were from the dermatologists and 45.7% were from the FPs ($p=0.008$).

When questioned about the highest rates of resistance among antibiotics, dermatologists' concerns were about erythromycin (34.3%), tetracycline (17.9%), doxycycline (7%) and azithromycin (6.7%). FPs'

concerns were 12.2%, 12.2%, 3.4% and 6.1% respectively. 27.2% of the FPs considered trimethoprim-sulfamethoxazole (TMX) as the highest rate of resistance. 23.9% of the dermatologists and 31.9% of the FPs had no idea at all.

Some questions regarding the measures to prevent antibiotic resistance were also asked. Use of antibiotics as monotherapy and longer duration of the treatment were considered as the most important risk factors by the dermatologists. When questioned about the measures to prevent the resistance, most common answers were not prescribing antibiotics as monotherapy, not using antibiotics more than 2-3 months, not switching the group of the antibiotics unless lack of efficacy, not prescribing different groups of antibiotics in combination at the same time and combining with topical BP and topical retinoids. Employment of the measures above by dermatologists was significantly higher than FPs. FPs who did not choose systemic antibiotics for mild and moderate AV were more than dermatologists. (Table IV).

Discussion

The most frequently recommended topical antibiotics are erythromycin and clindamycin while the systemic antibiotics are tetracycline and macrolide groups in AV guidelines.⁴⁻⁶ Topical antibiotics may be preferred for mild papulopustular acne, whereas the systemic antibiotics are indicated for moderate/severe AV.^{7,8} Dermatologists' preferences of antibiotics were in parallel with the guidelines in our study. The rate of dermatologists using nadifloxacin and tetracycline were found to be significantly higher than FPs. On the other hand, antibiotics preferred by FPs were less effective against *P. acnes* like mupirocin, FA or oxytetracycline.

AV patients primarily admit to FPs as primary care physicians since it is hard to book an appointment from the dermatologists throughout the world. Only 15% of the AV patients were reported to be able to reach dermatologists for treatment in the United States.⁸ In contrary, in our study, we have found that

the dermatologists were examining more AV patients than FPs. In our country, patients may directly admit to the dermatologists, and there is no obligation to apply to the primary care physicians beforehand.

FPs are known to prescribe antibiotics at the highest rate compared to other specialties.⁹ However, when all the prescriptions are taken into account, antibiotics prescribed by FPs for skin diseases constitute 8% of the total.¹⁰ FPs were found to prescribe systemic antibiotics to 33-37% of AV patients during initial examination, rising to 43% at repeated examinations within 90 days.¹¹⁻¹⁴

Dermatologists are responsible for 4.9% of total antibiotic prescriptions, although they comprise only 1% of the physicians.¹⁵ The vast majority of the antibiotics prescribed by the dermatologists is due to AV.¹⁶ In our study, it was found that all dermatologists prescribe antibiotics to AV patients, whereas 51% of the FPs prescribe both topical and systemic antibiotics.

Antibiotic resistance *P. acnes* was first reported by Leyden in 1976 and raised from 20% in 1978 to 65% today, even 90% in some countries like China and India.¹⁷⁻²¹ The resistance to macrolides is more pronounced.²¹⁻²³

Topical antibiotics like erythromycin and clindamycin have caused an increase in antibiotic-resistant bacteria both in the applied and other areas.^{21,24,25} On the other hand, systemic antibiotics were found to cause microflora to gain resistance throughout the body.^{21,22,26} This resistance is transmitted not only to the treated patients, but also to their close contacts.^{19,21,27,28} In our study, 79.1% of dermatologists and 89.8% of FPs thought that antibiotic resistant strains were contagious. The routes of transmission were clinical examination, handshake, family contact, and common items. 54.3% of the physicians who think that the antibiotic resistant strains would not be transmitted were dermatologists, 45.7% were FPs. 34.3% of the dermatologists thought that the antibiotic against which resistance have already developed is erythromycin, whereas 27.2% of FPs thought as TMX.

Shaffer *et al* determined resistant *P. acnes* strains on 24% of AV patients who were not treated with antibiotics before. The authors explained this by transmission with human to human contact.²⁹ The transmission of antibiotic resistant strains is possible with all human contacts as well as the family contact.²¹ In an European study done in six countries, 41-86% of the treated AV patients had antibiotic resistant *P. acnes* on their skin. 25 of 39 dermatologist who specifically examine AV patients had also these resistant strains but none of 27 dermatologist who work on the other outpatient clinics of dermatology had resistant *P. acnes*.³⁰ The study showed the possibility of transmission of *P. acnes* strains by patient-doctor contact while examining.

Antibiotic resistance and measures taken to prevent are widely covered in AV treatment guidelines.^{Error!}

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To prevent antibiotic resistance it is recommended to combine antibiotics with BP or retinoids.^{8,31} These combinations may also provide more effective treatment for AV.⁸ In our study, dermatologists stated that it is necessary to prevent using antibiotics alone and for a long time, in order to prevent resistance. They prescribe antibiotics along with BP/retinoids and do not prescribe antibiotics for comedones. FPs stated that they do not prescribe combination therapies or have no idea about what to do to prevent resistance.

Dermatology education of FPs is limited to a few weeks during residency.³² Topical preparations containing antibiotics are reimbursed in our healthcare system which leads the physicians to prescribe more antibiotics and the patients to request antibiotics.

In our study, the FPs' antibiotic preferences do not fully comply with the AV guidelines with insufficient duration and less effective antibiotic choices against *P. acnes*. It can be claimed that the FPs' aforementioned attitude may be an important factor leading to antibiotic resistance. That's why, we think that dermatology trainings intended for FPs as well as awareness of FPs should be increased.

It would be beneficial for the health authorities to include retinoids or BP as single preparations in the reimbursement plans and FPs should also be allowed to prescribe these medications. Dermatologists should support FPs in the treatment methods to be applied in order to limit the use of antibiotics and to prevent development of resistance.

Our study has some limitations such as it is a questionnaire-based study taken in internet, and it was conducted only in Turkey. However, we hope that it will draw attention to the issue of antibiotic resistance. Extending the study so that it can be carried out in different countries will render it possible to reveal any existing differences on a country basis.

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Table I: Categories included in the questionnaire (the subcategories are written in brackets if any)

How many AV patients do you see daily?
Do you prescribe antibiotics for AV? (Topical and systemic, asked separately)
Which antibiotics do you prefer in adult, child and pregnant/lactating patients, respectively? (Topical and systemic, asked separately)
Do you prescribe topical antibiotics alone or together with other treatments?(if so, which ones)
In which cases do you prefer systemic antibiotics (in cases of mild, moderate or severe AV, in cases with back involvement, in cases of patients that do not want to use topical treatment, in cases of patients that insist on using antibiotic treatment, in cases of supportive treatments)
Do you prescribe antibiotics for comedones?
For how long do you recommend the antibiotics be used? (Topical and systemic, asked separately)
Do you switch the antibiotics during treatment?(Topical and systemic, asked separately)
Do you prefer to prescribe antibiotics that are from the same group or that are from different groups, in the same prescription? (Topical and systemic, asked separately)
What is your preference for combined preparations?
In which group of antibiotics the drug resistance is a major concern?
What should be done to prevent antibiotic resistance?
In what ways can antibiotic resistance be transmitted? (through family contact, clinical examinations, handshake, or common items; or it cannot be transmitted through any means)

AV: Acne Vulgaris

Table II: Distribution of topical antibiotic preferences of physicians by patient groups

Topical Antibiotic Preferences of Physicians (%)									
	Adult Patients			Pregnant/Lactating Patients			Pediatric Patients		
	Dermatologist	FP	p value	Dermatologist	FP	p value	Dermatologist	FP	p value
Clindamycin	65.7	34.3	0.000	85.7	14.3	0.000	74.9	25.1	0.000
Tetracycline	62.8	37.2	0.040	-	-	-	66.7	33.3	0.064
Erythromycin	75.9	24.1	0.000	81.9	18.1	0.000	75.9	24.1	0.000
Nadifloxacin	69.8	30.2	0.000	-	-	-	-	-	-

Mupirocin	34.6	65.4	0.013	57.9	42.1	0.985	43.5	56.5	0.151
Fusidic Acid	30.4	69.6	0.000	36	64	0.023	35	65	0.002
Oxytetracycline	16.7	83.3	0.000	-	-	-	75	25	0.318
Nitrofurazone	-	-	-	-	-	-	42.9	57.1	0.462
I do not prescribe topical antibiotics	42.9	57.0	0.460	36	64	0.000	34.8	65.2	0.020
I do not recommend any treatment	-	-	-	37.6	62.4	0.000	23.3	76.7	0.000

FP: Family Physician

Table III: Distribution of systemic antibiotic preferences of physicians by patient groups

Systemic Antibiotic Preferences of Physicians (%)									
	Adult Patients			Pregnant/Lactating Patients			Pediatric Patients		
	Dermatologist	FP	p value	Dermatologist	FP	p value	Dermatologist	FP	p value
Tetracycline	42	58	0.000	-	-	-	72.7	27.3	0.067

Doxycycline	76.3	23.7	0.000	-	-	-	86	14	0.000
Erythromycin	35.3	64.7	0.055	68.4	31.6	0.333	57.1	42.9	0.945
Azithromycin	63.4	36.6	0.000	65.5	34.5	0.377	66.9	33.1	0.000
Trimethoprim-sulfamethoxazole	83.3	16.7	0.201	-	-	-	40	60	0.418
Clindamycin	71.4	28.6	0.191	50	50	0.824	40	60	0.418
I do not prescribe systemic antibiotics	25	75	0.002	56.6	43.4	0.242	35.2	64.8	0.000

Table IV: Distribution of physicians who approves of the measures to be taken in order not to give rise to the development of antibiotic resistance

What do you do to prevent the development of antibiotic resistance?

	not prescribe antibiotics alone	not prescribe antibiotics longer than 2-3 months	prescribe same group for same patient when they are effective	not prescribe different groups of antibiotics simultaneously	Combine antibiotics with benzoyl peroxide	Combine antibiotics with topical retinoids	Not prescribe systemic antibiotics as the first choice in mild/moderate AV
Number of Dermatologists	126	158	89	45	44	18	43
Dermatologists %	82.9	69.9	60.5	70.3	83	78.3	35.5
Number of FP	26	68	58	19	9	5	78
FP %	17.1	30.1	39.5	29.7	17	21.7	64.5
Total Number of Approving Physicians	152	226	147	64	53	23	121
P value	0.000	0.000	0.381	0.043	0.000	0.039	0.000