

## PRESCRIPTION RATIONALITY ANALYSIS FOR TONSILLITIS AND HYPERTENSION: EVALUATION OF PRESCRIBING SKILLS OF FINAL YEAR MEDICAL STUDENTS AND GPs, A COMPARATIVE STUDY

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### Summary

*Objective:* Prescribing skills of final year medical students (interns) and general practitioners (GPs) regarding rational use of drugs were evaluated by written scenarios of  $\beta$ -hemolytic streptococcal tonsillitis and essential hypertension cases.

*Study design:* Two groups of interns were invited to participate in the study from medical schools of two different universities where rational pharmacotherapy education (RPE) was given (RPE<sup>+</sup>) and was not (RPE<sup>-</sup>). GPs were also not undergone RPE. The participants were asked to prescribe for written cases of given indications. Rationality of drugs chosen were evaluated according to the national standard guidelines and prescribing rates of antibiotics, analgesics/antipyretics and antihypertensive drugs were compared in all groups.

*Results:* Fifty RPE<sup>+</sup> interns, 54 RPE<sup>-</sup> interns and 53 GPs participated in the study. For antibiotic treatment of  $\beta$ -hemolytic streptococcal tonsillitis, the majority (68 and 64 % for case 1 and case 2, respectively) of RPE<sup>+</sup> interns prescribed penicillin G, which is the most rational choice according to the guidelines, whereas, number of scripts with penicillin G by RPE<sup>-</sup> interns and GPs were lower, the former being significantly different for both cases. Paracetamol was the first analgesic-antipyretic prescribed by all groups, but was more frequently chosen by RPE<sup>+</sup> interns and GPs compared to RPE<sup>-</sup> interns. Concerning essential hypertension cases, although all groups prescribed first-line antihypertensives recommended by the recent guidelines, GPs and RPE<sup>-</sup> interns tended to use more than one antihypertensive drug per patient, which may be called as polypharmacy habit.

*Conclusion:* The present study once more revealed that undergraduate RPE provides a more rational prescribing skill compared to RPE<sup>-</sup> interns and GPs who have not educated accordingly.

**Keywords:** Prescribing Skills, Medical Students, General Practitioners, Rational Pharmacotherapy.

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### Introduction

Traditional undergraduate pharmacology education is being criticized by many medical authorities in Turkey as in many other countries, since traditional pharmacology training does not cover the skills required to make a rational treatment plan and monitor the treatment adequately. Traditionally, a list of certain drugs used in a defined situation, their pharmacological properties and adverse effects are presented, thus making the scope of lectures “drug-centered”. However, in clinical practice, pharmacotherapy should be considered as a rational process starting from diagnosis, until the cure of the disease and/or relieve of symptom(s), and therefore planned as “patient-centered”. Traditional methods supply medical students a loan of theoretical knowledge about drugs, but rational pharmacotherapy skills remain to be developed in future practice [1,2]. As it has been previously documented, traditional education makes the physicians more prone to be affected by the patients, colleagues or drug company representatives and thus resulting in inappropriate prescribing [1-6]. It must always be kept in mind that “bad” prescribing habits lead to ineffective and unsafe treatment causing exacerbation or prolongation of the disease or either give distress or harm to the patients. A well-designed and needs-based rational pharmacotherapy education (RPE) during both undergraduate and continuous medical education could be a solution to prevent irrational use of drugs [1,5,7-11]. World Health Organization – Drug Action Program (WHO-DAP) has provided an interactive rational pharmacotherapy training model (WHO/Groningen Model) [1,2]. Evidence for the effectiveness of this model were presented in our recent studies [12-15]. One of those studies has demonstrated that the final-year medical students who had RPE (RPE<sup>+</sup>) were markedly successful regarding rational pharmacotherapy decision-making competence than the students and general practitioners (GP) who were taught with traditional methods (RPE<sup>-</sup>) [14]. As a complimentary part of this study, in this article we aimed to compare the prescribing skills of

medical students of two different medical schools and also GPs who were and were not exposed RPE for the treatment of  $\beta$ -hemolytic streptococcal tonsillitis and essential hypertension (HT).

### **Materials and methods**

#### *Participants*

Final year students of Istanbul University Cerrahpaşa School of Medicine (RPE<sup>-</sup> interns; n=54) and Marmara University School of Medicine (MUSM) (RPE<sup>+</sup> interns; n=50), and GPs (n=53) working at primary health care centers in Istanbul were the participants of this study. MUSM students had successfully completed problem-based RPE (WHO/Groningen model) during their 5<sup>th</sup> year Clinical Pharmacology Clerkship. All GPs and RPE<sup>-</sup> interns who participated in the study have received undergraduate traditional pharmacology education.

#### *Study Protocol*

Prescription data presented here were collected as a part of the study published recently in which the study protocol was described in detail [14]. Briefly, a written, objective structured clinical examination (OSCE) was given to all participants. The case scenarios were of simple, uncomplicated  $\beta$ -hemolytic streptococcal tonsillitis and mild-to-moderate essential hypertension (Addendum 1); and the cases were prepared as one open ended, one structured question sheet for each indication. The participants were expected to make a treatment plan, explain their proposed treatment plans and write a full prescription for each of the cases.

#### *Prescription analysis*

Number of antibiotic and analgesic or antihypertensive drugs per prescription and the rationality of these drugs for the  $\beta$ -hemolytic streptococcal tonsillitis and the essential hypertension cases, respectively, were evaluated. Essential drugs for the treatments of these

indications were ranked according to the national standard guidelines [16] for the comparison of drug choice of the participant subgroups.

### *Statistical analysis*

The Statistical Package for the Social Sciences (SPSS / Pct, version 11.5) and Graph Pad 3.0 were used for data entry and analysis. Chi-square test was used for the statistical analysis, where  $p < 0.05$  was accepted as the level of statistical significance.

## **Results**

A total of 157 volunteers (50 RPE<sup>+</sup>, 54 RPE<sup>-</sup> interns and 53 GPs) participated in this study. The mean age of the participants were  $23.7 \pm 1.1$ ,  $23.6 \pm 1.7$ , and  $35.8 \pm 6.8$  years, respectively. The mean working experience after graduation of GPs was  $9.8 \pm 5.6$  years.

### *Tonsillitis prescriptions:*

The most preferred antibiotic by the RPE<sup>+</sup> interns was penicillin G for both tonsillitis cases (68.0 % and 64.0 %), whereas, penicillin G were prescribed less frequently by GPs (60.4 and 49.1 %) and particularly by RPE<sup>-</sup> interns (18.5 and 29.6 %). The rate of prescribing penicillin G among RPE<sup>-</sup> interns is significantly lower than RPE<sup>+</sup> interns and GPs for both cases (Table 1 and Figure 1). Even a significant difference between RPE<sup>+</sup> interns and GPs is detected in terms of prescribing penicillin G for one of the tonsillitis cases (Case 2) (Table 1 and Figure 1). While only 12.0 % and 10.0 % of RPE<sup>+</sup> interns prescribed oral penicillins, and 26.0 % and 30.0 % of them chose beta-lactamase + penicillin combinations, these percentages were markedly higher for RPE<sup>-</sup> interns (38.9 % and 29.6 % for oral penicillins; 38.9 % and 33.3 % for beta-lactamase + penicillin combinations) (Table 1). On the other hand, fewer GPs (not significantly different than RPE<sup>+</sup> interns) prescribed oral penicillins (22.6 % and 20.8 %) and beta-lactamase + penicillin combinations (18.9 % and 24.5 %) (Table 1). Interestingly, more

than one antibiotic for a case was given by approximately 1/5th of the GPs (18.9 and 15.1 %), and by 12.0 and 6.0 % of RPE<sup>+</sup> interns, while 3 RPE<sup>-</sup> interns did not recommend any antibiotic for one of the cases (Table 1).

The most frequently prescribed analgesic/antipyretic drug was paracetamol for both tonsillitis cases by all groups and there was no statistically significant difference among them (Table 2 and Figure 1). Surprisingly, 18.9 % and 17.0 % of GPs prescribed a COX-II preferential inhibitor, nimesulide, which was withdrawn from the market later, as the second most frequently prescribed analgesic/antipyretic agent, for Case 1 and 2, respectively. Nimesulide preference among RPE<sup>+</sup> interns were 12 % for both cases. Likely, 7.4 % and 9.3 % of RPE<sup>-</sup> interns preferred nimesulide (Table 2). The most irrational choices were observed among RPE<sup>-</sup> interns regarding the presence of non-selective NSAID (written as either naproxen or ibuprofen, or as NSAID) in their prescriptions for both cases (22.2 % and 20.4 %; Table 2).

**Table 1:** The distribution of antibiotics prescribed for the  $\beta$ -hemolytic streptococcal tonsillitis cases by RPE<sup>+</sup> (n=50) and RPE<sup>-</sup> (n=54) interns, and GPs (n=53).

	Penicillin G			Oral penicillin			Beta- lactamase inhibitor + penicillin			Sefalosporins			Macrolides			Others			Total		
	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *
<i>Case 1</i>																					
RPE + interns	34	60.7	68.0	6	10.7	12.0	13	23.2	26.0	0	0	0	3	5.4	6.0	0	0	0	56	100.0	112.0
RPE <sup>-</sup> interns	10 <sup>a</sup>	18.5	18.5	21	38.9	38.9	21	38.9	38.9	0	0	0	2	3.7	3.7	0	0	0	54	100.0	100.0
GPs	32	50.8	60.4	12	19.1	22.6	10	15.9	18.9	4	6.3	7.6	4	6.3	7.6	1	1.6	1.9	63	100.0	118.9
<i>Case 2</i>																					
RPE + interns	32 <sup>b</sup>	60.4	64.0	5	9.4	10.0	15	28.3	30.0	0	0	0	1	1.9	2.0	0	0	0	53	100.0	106.0
RPE <sup>-</sup> interns	16	31.4	29.6	16	31.4	29.6	18	35.2	33.3	1	2.0	1.9	0	0	0	0	0	0	51	100.0	94.4
GPs	26	42.6	49.1	11	18.1	20.8	13	21.3	24.5	3	4.9	5.7	7	11.5	13.2	1	1.6	1.9	61	100.0	115.1

\*Percentage of number of participants.

<sup>a</sup>p < 0.05, different from RPE<sup>+</sup> and GPs.

<sup>b</sup>p < 0.05, different from RPE<sup>-</sup> and GPs.

**Table 2:** The distribution of analgesics/antipyretics prescribed for the  $\beta$ -hemolytic streptococcal tonsillitis cases by RPE<sup>+</sup> (n=50) and RPE<sup>-</sup> (n=54) interns, and GPs (n=53).

	Paracetamol			Non-selective NSAIDs			Nimesulide			Salicylates			Dipyrrone			Total		
	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *
<i>Case 1</i>																		
<b>RPE<sup>+</sup> interns</b>	26	<b>70.3</b>	<b>52.0</b>	4	<b>10.8</b>	<b>8.0</b>	6	<b>16.2</b>	<b>12.0</b>	1	<b>2.7</b>	<b>2.0</b>	0	<b>0</b>	<b>0</b>	37	<b>100.0</b>	<b>74.0</b>
<b>RPE<sup>-</sup> interns</b>	22	<b>50.0</b>	<b>40.7</b>	12	<b>27.3</b>	<b>22.2</b>	4	<b>9.1</b>	<b>7.4</b>	3	<b>6.8</b>	<b>5.6</b>	3	<b>6.8</b>	<b>5.6</b>	44	<b>100.0</b>	<b>81.5</b>
<b>GPs</b>	28	<b>57.1</b>	<b>52.8</b>	4	<b>8.2</b>	<b>7.6</b>	10	<b>20.4</b>	<b>18.9</b>	4	<b>8.2</b>	<b>7.6</b>	3	<b>6.1</b>	<b>5.7</b>	49	<b>100.0</b>	<b>92.5</b>
<i>Case 2</i>																		
<b>RPE<sup>+</sup> interns</b>	23	<b>62.2</b>	<b>46.0</b>	7	<b>18.9</b>	<b>14.0</b>	6	<b>16.2</b>	<b>12.0</b>	1	<b>2.7</b>	<b>2.0</b>	0	<b>0</b>	<b>0</b>	37	<b>100.0</b>	<b>74.0</b>
<b>RPE<sup>-</sup> interns</b>	22	<b>50.0</b>	<b>40.7</b>	11	<b>25.0</b>	<b>20.4</b>	5	<b>11.4</b>	<b>9.3</b>	4	<b>9.1</b>	<b>7.4</b>	2	<b>4.5</b>	<b>3.7</b>	44	<b>100.0</b>	<b>81.5</b>
<b>GPs</b>	26	<b>59.1</b>	<b>49.1</b>	4	<b>9.1</b>	<b>7.6</b>	9	<b>20.5</b>	<b>17.0</b>	3	<b>6.8</b>	<b>5.7</b>	2	<b>4.5</b>	<b>3.8</b>	44	<b>100.0</b>	<b>83.0</b>

\*Percentage of number of participants.

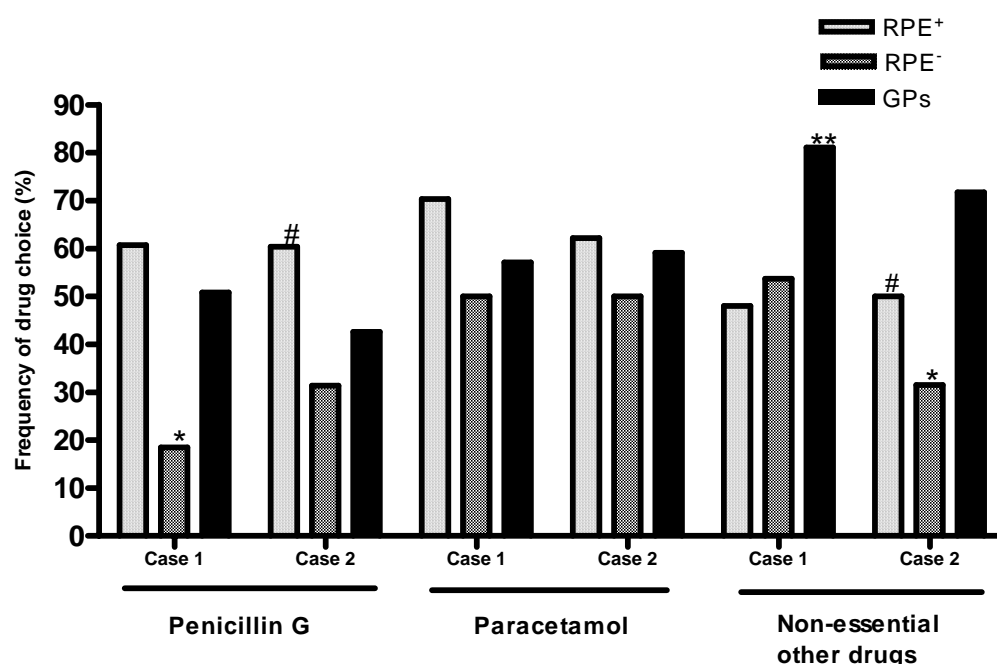
Throat antiseptics, vitamins, decongestants, antitussive and antihistaminic preparations are the other drugs prescribed for tonsillitis cases. Most of the GPs prescribed a third drug other than antibiotics and analgesic/antipyretics (81.1 % and 71.7 % in Case 1 and 2, respectively). The statistical analysis yielded a significant difference between GPs and both intern groups regarding the use of non-essential other drugs like antiseptics, vitamins, etc. in the prescriptions for one of the tonsillitis cases (Case 1) (Table 3 and Figure 1). On the other hand, concerning non-essential other drugs, ratios of 48 % and 50 % were found in RPE<sup>+</sup> interns, and 53.7 % and 31.5 % in RPE<sup>-</sup> interns, for Case 1 and 2, respectively.

The tendency for polypharmacy was high in all 3 groups, being more prominent in the GPs (43 in 53; Table 3 and Figure 1). Twenty-four RPE<sup>+</sup> interns and 29 RPE<sup>-</sup> interns out of 50 prescribed non-essential other drugs (Figure 1), and the difference between two intern groups was not statistically significant. Throat antiseptics and vitamins were the most preferred non-essential remedies (Table 3 and Figure 1).

**Table 3:** The distribution of drugs other than antibiotics and analgesics/antipyretics prescribed for the  $\beta$ -hemolytic streptococcal tonsillitis cases by RPE<sup>+</sup> (n=50) and RPE<sup>-</sup> (n=54) interns, and GPs (n=53).

	Throat antiseptics			Vitamins			Cold remedies			Antitussives			Anti-histamines			Total		
	n	%	%*	n	%	%*	n	%	%*	n	%	%*	n	%	%*	n	%	%*
<i>Case 1</i>																		
RPE <sup>+</sup> interns	16	66.7	32.0	3	12.5	6.0	4	16.7	8.0	1	4.2	2.0	0	0	0	24	100.0	48.0
RPE <sup>-</sup> interns	12	41.4	22.2	11	37.9	20.4	5	17.2	9.3	1	3.5	1.9	0	0	0	29	100.0	53.7
GPs	25	58.1	47.2	14	32.6	26.4	3	7.0	5.7	0	0	0	1	2.3	1.9	43 <sup>a</sup>	100.0	81.1
<i>Case 2</i>																		
RPE <sup>+</sup> interns	17	68.0	34.0	4	16.0	8.0	4	16.0	8.0	0	0	0	0	0	0	25 <sup>b</sup>	100.0	50.0
RPE <sup>-</sup> interns	6	35.3	11.1	8	47.1	14.8	3	17.6	5.6	0	0	0	0	0	0	17 <sup>c</sup>	100.0	31.5
GPs	22	57.9	41.5	12	31.6	22.6	3	7.9	5.7	0	0	0	1	2.6	1.9	38	100.0	71.7

\*Percentage of number of participants. <sup>a</sup>p < 0.05, different from RPE<sup>+</sup> and RPE<sup>-</sup>. <sup>b</sup>p < 0.05, different from RPE<sup>-</sup> and GPs. <sup>c</sup>p < 0.05, different from RPE<sup>+</sup> and GPs.



**Figure 1:** The comparison of frequency of penicillin G, paracetamol and non-essential other drugs chosen in case scenarios of  $\beta$ -hemolytic streptococcal tonsillitis in interns educated with RPE (RPE<sup>+</sup>) or not (RPE<sup>-</sup>) and the general practitioners (GPs).

\* p < 0.05, Chi-square test (different from RPE<sup>+</sup> and GPs regarding penicillin G choice within Case 1; different from RPE<sup>+</sup> and GPs regarding non-essential other drug choice within Case 2).

#p < 0.05, Chi-square test (different from RPE<sup>-</sup> and GPs regarding penicillin G choice within Case 2; different from RPE<sup>-</sup> and GPs regarding non-essential other drug choice within Case 2). \*\* p < 0.05, Chi-square test (different from RPE<sup>+</sup> and RPE<sup>-</sup> regarding non-essential other drug choice within Case 1).

*Hypertension prescriptions (Table 4, Figure 2):*

Angiotensin converting enzyme (ACE) inhibitors were the most frequently prescribed anti-hypertensive agents for essential hypertension Case 2 in all groups (37.5 % in RPE<sup>+</sup> interns; 29.1 % in RPE<sup>-</sup> interns; 27.0 % in GPs groups) and for essential hypertension Case 1 in both RPE<sup>-</sup> interns (29.4 %) and GPs (36.1 %); except that 39.6 % RPE<sup>+</sup> interns prescribed calcium channel blockers for the latter. Diuretics followed ACE inhibitors for both cases in prescriptions by both RPE<sup>-</sup> interns (27.9 % and 29.1 %) and GPs (27.9 % and 27.0). However, RPE<sup>+</sup> interns' second preference was calcium channel blockers (33.2 %) following ACE inhibitors for Case 2.

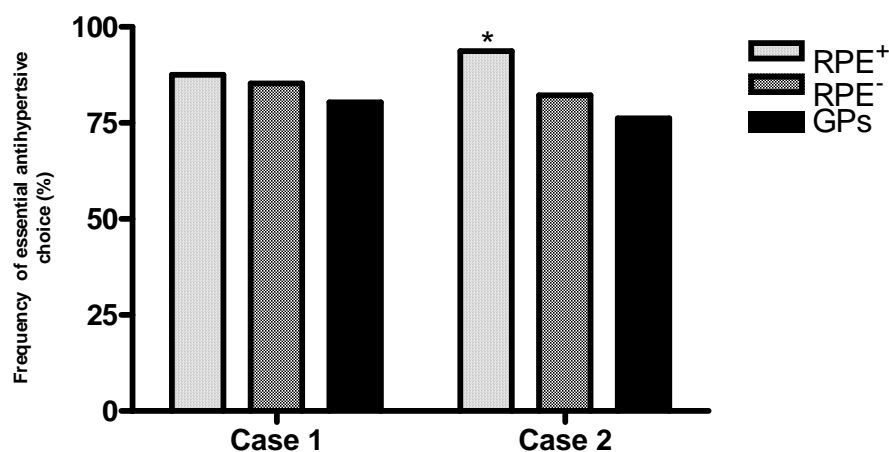
RPE<sup>+</sup> interns prescribed less non-essential antihypertensive drugs compared to RPE<sup>-</sup> interns and GPs, the difference being more apparent in Case 2 (RPE<sup>+</sup> interns: Case 1, 12.5 % and Case 2, 6.3 %; RPE<sup>-</sup> interns: Case 1, 14.7 % and Case 2, 17.8 %; GPs: Case 1, 19.6 % and Case 2, 23.8 %). The number of essential antihypertensive drugs prescribed by RPE<sup>+</sup> for Case 2 was significantly lower than other groups ( $p < 0.05$ ). None of the RPE<sup>+</sup> interns prescribed more than one antihypertensive drug per patient. However, the tendency for polypharmacy was marked in both RPE<sup>-</sup> interns and GPs. The number of the antihypertensives prescribed by RPE<sup>-</sup> interns were 68 drugs / 54 patients and 79 drugs / 54 patients, and by GPs 61 drugs / 53 patients and 63 drugs / 53 patient for Case 1 and 2, respectively.



**Table 4:** The distribution of antihypertensive drugs prescribed for the mild-to-moderate essential hypertension cases by RPE<sup>+</sup> (n=50) and RPE<sup>-</sup> (n=54) interns, and GPs (n=53).

	Essential Antihypertensive Drugs												Other anti-hypertensive drugs			Total		
	Diuretics			β blockers			ACE inhibitors			Calcium channel blockers								
	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *	n	%	% *
<i>Case 1</i>																		
RPE <sup>+</sup> interns	7	14.6	14.0	2	4.1	4.0	14	29.2	28.0	19	39.6	38.0	6	12.5	12.0	48	100.0	96.0
RPE <sup>-</sup> interns	19	27.9	35.2	7	10.3	13.0	20	29.4	37.0	12	17.7	22.2	10	14.7	18.5	68	100.0	125.9
GPs	17	27.9	32.1	0	0	0	22	36.1	41.5	10	16.4	18.9	12	19.6	22.6	61	100.0	115.1
<i>Case 2</i>																		
RPE <sup>+</sup> interns <sup>a</sup>	8	16.7	16.0	3	6.3	6.0	18	37.5	36.0	16	33.2	32.0	3	6.3	6.0	48	100.0	96.0
RPE <sup>-</sup> interns	23	29.1	42.6	11	13.9	20.4	23	29.1	42.6	8	10.1	14.8	7	17.8	13.0	79	100.0	146.3
GPs	17	27.0	32.1	3	4.8	5.7	17	27.0	32.1	11	17.4	20.8	15	23.8	28.3	63	100.0	118.9

\*Percentage of number of participants.

<sup>a</sup>p < 0.05, different from RPE<sup>-</sup> and GPs regarding essential antihypertensive choice.**Figure 2:** The comparison of frequency of essential anti-hypertensives (diuretics, β blockers, ACE inhibitors and calcium channel blockers) chosen in case scenarios of mild-to-moderate essential hypertension in interns educated with RPE (RPE<sup>+</sup>) or not (RPE<sup>-</sup>) and the general practitioners (GPs).\* p < 0.05, Chi-square test (different from RPE<sup>-</sup> and GPs regarding essential antihypertensive choice within Case 2).

**Discussion and conclusions**

The physician is advised to choose the best pharmacotherapy that helps to achieve the goals of treatment according to the efficacy, the safety, the suitability and the cost. The most valid approach to evaluate the drug choice of the physicians is prescription analysis. As these 4 criteria are easily affected by various individual differences, written scenarios based on a standard patient may be used as objective tools for the evaluation of the scripts [1-5, 17, 18]. In the present study, the prescribing habits of the final year medical students and GPs were evaluated by prescription analysis as it was used elsewhere [7, 9, 19, 20]. Tonsillitis and essential hypertension are two important health problems, commonly encountered at primary health care level in Turkey, like in many other countries [16, 21-26]. Therefore, these indications have been chosen to be the study cases as an acute and chronic disease example.

Polypharmacy can be defined as the concurrent use of many drugs together and is an important sign of irrational pharmacotherapy [3,6]. The analysis of tonsillitis cases demonstrated that the GPs are more prone to polypharmacy, where RPE<sup>-</sup> interns tend to prescribe fewer drugs. Fifteen and 18 % of them prescribed more than one antibiotic per patient and most of them (71 and 81 %) prescribed non-essential drugs. This situation may not only reflect the tendency of GPs to polypharmacy, but also the fact that RPE<sup>-</sup> interns knew few drugs to prescribe (Table 1 and Figure 1). The tendency of GPs to prescribe more drugs may be a result of their inadequate education that makes them easily influenced by the patients. It seems likely that the fear of being unable to please the patients may have caused the GPs to adopt the habit of prescribing more medications, as seen in tonsillitis indication..

Collectively, RPE<sup>-</sup> interns prescribed fewer agents than the RPE<sup>+</sup> interns and the GPs in the tonsillitis cases, although there are too many products on the market for that indication. The prescription analysis in essential hypertension cases strongly supported the conclusion that the GPs are more prone to polypharmacy, since 15 and 19 % of them prescribed more

than one antihypertensive drug per case. However, unlike tonsillitis, RPE<sup>-</sup> interns (126 and 146 %) showed greater polypharmacy tendency, making the above explanation of fewer knowledge about drug names irrelevant. On the other hand, particularly regarding non-essential drug recommendation in tonsillitis and prescribing only one or no essential antihypertensive drug for both cases by RPE<sup>+</sup> intern, they seem to be more rational than the other groups in both indications. Furthermore, they have been reported to be significantly better in recommending non-drug treatment as well [14]. As the GPs and RPE<sup>-</sup> interns were in the habit of polypharmacy, it may be deduced that RPE is an important tool to prevent this kind of prescribing behaviour.

The rationality of the drug choice was examined according to the Turkish Ministry of Health's Diagnosis and Treatment Guidelines [16]. Regarding acute tonsillitis, RPE<sup>+</sup> interns were far more rational by prescribing penicillin G with a percentage of higher than 60 %. The difference between the RPE<sup>+</sup> and RPE<sup>-</sup> interns was very striking, indicating the benefit of undergraduate RPE. There is no doubt that the irrational use of antibiotics, including polypharmacy, produces development of antibiotic resistance, increased risk of side effects, economical and psychosocial problems [27-37]. Therefore, the present study supports the role of RPE in the prevention of irrational use of antibiotics by improving physicians' prescribing habits. Non-essential drugs such as throat antiseptics, vitamins, cold remedies, antitussives and antihistaminics have been recommended by 81 % of the GPs, which is significantly higher than both intern groups. This figure strikingly indicates the need of continuous RPE after graduation.

On the other hand, although the first-line analgesic/antipyretic agent was paracetamol in both tonsillitis cases by all groups, almost half of each group prescribed other drugs including non-selective NSAIDs and nimesulide. This number is high enough to pay close attention to the results, since the use of new and expensive COX II preferential inhibitors in

upper respiratory tract infections is accepted to be irrational [16, 38-40], and some COX II selective inhibitors were either withdrawn from the market or strongly restricted using in many countries because of increased death from cardiovascular events [41,42].

The overall evaluation of the results of tonsillitis cases demonstrated that RPE<sup>+</sup> interns behaved more rational, but still below the expected level. Because previously published results of this study showing the prescribing skills of the same subjects other than prescription writing (i.e. defining the diagnosis, informing the patient, etc.) have demonstrated that written objectively structured clinical examination (OSCE) scores as a good sign of thorough evaluation of competence of rational pharmacotherapy were far better than the RPE<sup>-</sup> students [14]. The reason why this significant difference did not project to the scripts may be because the students had their RPE in the 5<sup>th</sup> year of their medical education, and they had very limited medical practice experience until the day of this evaluation. This again, may be taken as an indicator of the need for continuous RPE throughout the medical education and afterwards.

Prescription analysis for essential hypertension cases regarding polypharmacy were in the favor of RPE<sup>+</sup> interns as it was discussed above. As a positive result of this study, the majority of all participants prescribed a diuretic, beta-blocker, ACE inhibitor or calcium channel blocker, which are considered as first-line antihypertensives according to the recent guidelines [16, 21, 22, 43]. Unfortunately, the percentage of RPE<sup>-</sup> interns and GPs who prescribed nonessential antihypertensive drugs were significantly higher than that of RPE<sup>+</sup> interns.

In conclusion, data presented here showed that RPE<sup>+</sup> interns were more successful concerning their rational prescribing skills compared to other groups who did not receive a formal RPE neither during nor after medical school years. Furthermore, we have reported that the cost of the prescriptions for both tonsillitis and hypertension cases was significantly higher in GP [14]. Therefore, continuous education of GPs about the principles of rational

pharmacotherapy is highly recommended in addition to undergraduate RPE in the medical schools.

### **Acknowledgements**

This study was supported by a grant from Marmara University Scientific Research Projects Commission (2000-Sağlık HEA-078/131200).

### **Addendum:**

#### **Written cases scenarios**

#### ***Uncomplicated $\beta$ -hemolytic streptococcal tonsillitis cases scenarios***

**Case 1:** Mrs. M.G. (68 kg and 163 cm), who is a 32 year-old bank officer, admitted to the primary health center you are working at, with the complaints of a mild fever, headache and loss of appetite that started 2 days ago. She also mentioned that her body temperature did not decrease below 38.5°C. In your physical examination, you found hypertrophic and hyperemic tonsils with crypts over them. Your diagnosis is beta hemolytic streptococcal tonsillitis. Please manage the patient.

**Case 2:** Mr. H.D. (75 kg and 175 cm) is a 29 year-old primary school teacher. He came to your clinic with the complaints of headache, mild fever, lack of appetite, and fatigue for three days. In physical examination, you found that his body temperature was 39°C and his tonsils were hypertrophic and hyperemic. Laboratory results revealed leucocytosis in hemogram, and beta hemolytic streptococci in throat culture. Please manage the patient.

*Mild-to-moderate essential hypertension cases scenarios*

**Case 1:** Mrs A.S. is a 62 year-old housewife (159 cm and 82 kg). Her blood pressure has been found to be high sometimes in the last 5 years. When she visited another doctor last year, life style modifications have been suggested. Although she has tried to change her life style, her blood pressure was 158/98 mmHg in average during in the last month. She had given up smoking two years ago, but she started smoking 5-10 cigarettes daily in the last three months. In your physical examination, there were no abnormalities. Please manage the patient.

**Case 2:** Mr. M.K. is a 64 year-old retired officer (167 cm and 87 kg). He has a history of high blood pressure sometimes since he retired 3 years ago. The family doctor has suggested life style modifications such as modifying his diet when he first introduced with this problem, but Mr. M.K. could not manage to do these. He smokes 10-15 cigarettes daily and takes alcohol rarely. He had checked his blood pressure regularly last week and it was 156/96 mmHg in average. In physical examination, you found no abnormalities. Please manage the patient.

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