



ORIGINAL ARTICLE

Awareness of Physicians Working in Kayseri of the Age Limits Related to the Use of Cough and Cold Medicines in Children

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Abstract

Introduction: The purpose of this study is to examine the awareness of physicians concerning the age limit regulations related to the use of cough and cold medicines (CCM) in children.

Methods: A questionnaire including 12 questions was distributed to 180 pediatricians in Kayseri. In the first part of the questionnaire, the questions were covering demographic characteristics. In the second part, physicians were asked about the drugs they were prescribing and that were among 30 drugs for which the age limits were changed.

Results: Of the 180 practitioners who participated in the study, 91 (50.56%) were aware of a new regulation on the age limits and CCM use. However, only 5 physicians involved in the study (2.77%) preferred the new arrangement where the appropriate age for all the drugs was determined.

Discussion and Conclusion: Physicians' awareness about the new regulations regarding the age limits and CCM use was at a low level. Integrating up-to-date drug guidelines into hospital and family medicine information management systems will contribute significantly to the elimination of such shortcomings.

Keywords: Awareness; common cold; medicine; physician.

Common cold is an acute viral infection of the upper respiratory tract with prominent symptoms of nasal discharge and obstruction. Young children are exposed to common cold 6–8 times a year on average. However, 10%–15% of these children contract this disease 12 times a year [1]. In the symptomatic treatment of common cold, antihistamines, antitussives, decongestants, and expectorants are used intensively [2].

The use of over-the-counter cough and cold medicines (CCM) has become controversial [3, 4]. Indeed, studies have demonstrated that although CCM are effective in adults, benefits of such drugs cannot be proven in children, and

they have serious adverse effects. In the United States, 20 deaths related to the use of CCM between 2000 and 2007 were reported [4]. Drugs containing more than one of the active ingredients such as phenylephrine, dextromethorphan, pseudoephedrine, guaiphenesin, and diphenhydramine agents have been held responsible for most of these cases.

Regulations with regard to the age limits of CCM use in our country have been implemented by the Ministry of Health (MoH) in 2008, 2011, and 2013 [5–7]. The purpose of this study is to determine physicians' awareness of the regulations regarding the age limitations of their use in children.

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Materials and Methods

This study was carried out between July 1, 2017, and October 30, 2017, and it included 220 physicians (pediatricians, general practitioners, and family medicine specialists), who actively provided services for the pediatric age group in the province of Kayseri. An approval of the Kayseri Training and Research Hospital Clinical Research Ethics Board was obtained for this study (2017/315). A questionnaire consisting of 12 questions was distributed to the physicians who submitted their consent forms. The data in the questionnaire forms were collected for the study. Physicians and assistants who did not provide active outpatient services were excluded from the study.

In the first part of the questionnaire, in addition to demographic characteristics of the participants, questions were asked about whether the physicians knew about the amendments in regulations implemented by the MoH concerning the age limitations in CCM use in children, and if they had been informed, they were asked from where, and for which active ingredients they got this information. In the second part, they were asked about from what age they preferred to prescribe, and which CCMs among 30 drugs in the market containing active ingredients singly or in combination. To facilitate their recall, commercial drug names containing these active ingredients were listed. According to the Anatomical Therapeutic Chemical Classification (ATC) code, CCMs for which the participants were asked questions about the age limitations in their use were divided into four groups (Table 1).

Statistical Analysis

The SPSS version 24 program was used to evaluate data obtained in the study. The distribution of responses given to the questions with more than one alternative (questions for which the participant could select more than one option) was determined by the ticked options. The consistency coefficient (Cronbach's alpha) was tested to test the reliability of the questionnaire used. A chi-square test was used to evaluate the intergroup discontinuous data. Continuous data that did not fit a normal distribution pattern were assessed by the Kruskal–Wallis H test. A p value <0.05 was considered statistically significant.

Results

Initially, 220 physicians were included in the study. Due to various reasons (physicians who did not fill out the forms completely or who did not want to participate, participants who did not deliver the forms, etc.), we ended up with 180

Table 1. List of drugs containing active ingredients, singly or in combination, for which the info on the age of application was changed by the Ministry of Health

1. Cold Medicines (ATC Code R05X)
 - *triprolidine+pseudoephedrine+dextromethorphan
 - *paracetamol+chlorpheniramine
 - *paracetamol+chlorpheniramine+pseudoephedrine
 - *paracetamol+chlorpheniramine maleate+oxolamine citrate
 - *dextromethorphan+pseudoephedrine+chlorpheniramine maleate
 - *terbutaline+guaiphenesin
 - *ephedrine+guaiphenesin
 - *ibuprofen+chlorpheniramine maleate+pseudoephedrine
 - *paracetamol+chlorpheniramine maleate+phenylephrine
 - *pseudoephedrine+guaiphenesin
 - *diphenhydramine+ammonium chloride+sodium citrate +menthol
 - *dextromethorphan+guaiphenesin+pseudoephedrine
 - *ibuprofen+chlorpheniramine
 - *paracetamol+chlorpheniramine+pseudoephedrine
 - *paracetamol+guaiphenesin+pyrilamine maleate +chlorpheniramine
 - *phenylephrine+guaiphenesin+diphenhydramine
 - *pseudoephedrine+chlorpheniramine+dextromethorphan +paracetamol
 - *pseudoephedrine+dextromethorphan+paracetamol +doxylamine succinate
2. Cough-Suppressant Drugs (ATC Code R05DB27)
 - *levodropropizine
 - *levodropropizine (drops)
 - *levodropropizine+chlorpheniramine
 - *oxolamine phosphate
 - *butamirate citrate
3. Systemic Nasal Decongestants (ATC Code R01BA52)
 - *triprolidine Hcl+pseudoephedrine
 - *pseudoephedrine
4. Topical Nasal Decongestants (ATC Code R01AA05)
 - *oxymetazoline 0.01%
 - *oxymetazoline 0.025%
 - *oxymetazoline 0.05%
 - *xylometazoline 0.05%
 - *xylometazoline 0.1%

ATC: Anatomical therapeutic chemical classification.

physicians. To test the reliability of the questionnaire applied to participants, the Cronbach's alpha coefficient was checked, and the Cronbach's alpha value was found to be 0.931 (>0.7). The demographic characteristics of the physicians involved in the study are shown in Table 2.

The first five questions asked the information about the

Table 2. Demographic characteristics of physicians participating in the study

1. Distribution of physicians according to their specialties	
Specialty	n (%)
General practitioner	123 (68.3)
Family medicine specialist	12 (6.7)
Pediatrician	45 (25)
Total	180 (100)
2. Age range	
Age range (years)	n (%)
24-35	55 (30.6)
36-45	65 (36.1)
46-55	46 (25.6)
>55	14 (7.7)
Total	180 (100)
3. For how long have the physicians worked in their field of medicine?	
Duration (years)	n (%)
0-5	43 (23.9)
6-10	28 (15.5)
11-15	39 (21.7)
>16	70 (38.9)
Total	180 (100)

CCMs prescribed by the physicians taking part in the study. The physicians' responses are shown in Table 3.

Ninety-one physicians who knew about the amendments in the relevant regulations concerning the age limits in the use of CCMs were asked about their knowledge about ingredients, and they indicated that they most frequently got the information about pseudoephedrine, chlorpheniramine, and ephedrine (Table 4).

When the answer to the question "I do not prescribe" was accepted correctly among the 30 drugs for which the age limits were examined, only 5 physicians (2.77%) out of the 180 participants preferred to prescribe the drug fully in compliance with the new amendment in the regulation. On the other hand, it was found that drugs listed in the 1–5 (n=70; 38.8%); 6–10 (n=56; 31.1%); 11–15 (n=25; 13.8%); 16–20 (n=19; 10.5%); and ≥21 (n=5; 2.7%) rows of the questionnaire were not prescribed by the respective number of physicians. It was found that pediatricians prescribed 85%, general practitioners 71.81%, and family medicine specialists 66.68% of the drugs in compliance with the new amendment in the regulation. The prescribing rates of common cold medicines, cough suppressants, and systemic and nasal decongestants by pediatricians in compliance with the new amendment in the regulation concerning CCMs were statistically significantly higher relative to

Table 3. Responses of the physicians to the questions about prescribed cough and common cold medicines (CCM)

1. Types of the sources of information about prescribed CCM	
Sources of Information	n (%)
Drug guides	61 (20.7)
Internet	115 (39.1)
Short product information	61 (20.7)
Representative of the pharmaceutical firm	30 (10.2)
I don't have the need to be informed	27 (9.3)
Total	294 (100)
2. The number (%) of physicians who faced parental objection or opposition with regard to the age limitations of the prescribed CCM	
	n (%)
Yes	62 (34.4)
No	118 (65.6)
Total	180 (100)
3. The number (%) of physicians who had information available about the age limitations with regard to CCM application	
	n (%)
Yes	91 (50.6)
No	89 (49.4)
Total	180 (100)
4. Sources of information on age limitations with regard to CCM	
Sources of Information	n (%)
Pharmaceutical firms	45 (34.1)
Others	33 (25)
Instructions for use	32 (24.2)
The institute where the physician was employed	17 (12.9)
Letters from the Ministry of Health addressed to physicians	5 (3.8)
Total	132 (100)

Table 4. Active ingredients that information was obtained for their age limits of use by indicated number (%) of physicians

Active ingredient	n (%)
Pseudoephedrine	74 (55.6)
Chlorpheniramine	20 (15)
Phenylephrine	8 (6)
Ephedrine	7 (5.3)
Butamirate	3 (2.3)
Guaifenesin	3 (2.3)
Pheniramine maleate	3 (2.3)
Dextromethorphan	2 (1.5)
Oxolamine	1 (0.8)
Others	12 (9.1)
Total	133 (100)

general practitioners and family physicians. However, the difference was not statistically significant for topical nasal decongestants (Table 5).

The rates of physicians' non-preference among 30 medicines investigated in the survey differed among family physicians (12.25%), general practitioners (13.6%), and pediatricians (20.17%). The rate of non-prescribing, excluding topical nasal decongestants, by pediatricians was statistically significantly higher when compared with family physicians and general practitioners (Table 6).

Seventy-four participants who stated that they were informed about the age limitations of pseudoephedrine application were further evaluated for 11 drugs that included this ingredient. Although they got information about these drugs, it was revealed that an average of 34% of these 11 drugs was still prescribed in accordance with the previously determined age limit.

Discussion

All of the physicians involved in this study had a lower level of awareness of the new regulations regarding the age limitations of CCM application.

However, the awareness of pediatricians was relatively higher when physicians participating in the study were divided into groups.

In 2007, the US Food and Drug Administration took an action to limit the use of CCMs sold as over-the-counter for small children [8]. On top of this, drug manufacturers in the United States voluntarily withdrew their medications from

the marketplace in 2007 to make a label change stating that the drug should not be applied under 2 years of age [9]. In 2008, a changed product label of these drugs prohibited the use of CCMs under the age of 4 years [10]. In this process, the American Academy of Pediatrics, went even further, suggesting that these drugs should not be used under the age of 6 [11]. The Canadian MoH also reported in 2009 that they decided to ban the use of these drugs in children under 6 years of age because of the following four reasons. First, the weight of some children between the ages of 2 and 6 can be as low as those under 2 years of age. Second, Canadian and foreign experts have reported the harmful effects of these medicines. Third, children under 6 years of age are more likely to have a cold and therefore more likely to be exposed to these medications. Fourth, children under 6 years of age are less able to communicate with their parents about the medication side effects [12].

The initiation of label changes in CCMs has resulted in fewer adverse events associated with these drugs in the United States and side effects associated with the use of these drugs in emergency departments [13–17]. There are studies in the literature about health professionals' attitudes toward CCMs. Mazer-Amirshahi et al. [18] conducted a study comparing the attitudes of health personnel using CCMs between 2005 and 2006 and between 2009 and 2010. These limitations and recommendations showed that the rates of drug use did not change in children under 2 years of age in emergency services and out patient clinics.

However, the number of common cold prescriptions written for patients after their discharge was significantly re-

Table 5. Prescription rates of cold and cough medicines according to medical specialties

Drugs	General Practitioner, %, n=123	Family Medicine Specialist, %, n=12	Pediatricians, %, n=45	p
Cold medicines (18)	69.3 (1536) ^a	61.5 (133) ^a	82.3 (667) ^b	0.000
Cough-suppressant drugs (5)	75.6 (465) ^a	79.0 (49) ^a	94.2 (214) ^b	0.000
Systemic nasal decongestants (2)	64.6 (159) ^a	54.1 (13) ^a	81.1 (73) ^b	0.022
Topical nasal decongestants (5)	76.4 (470) ^a	71.6 (43) ^a	71.6 (190) ^a	0.313

A statistically significant difference exists between the groups labeled with superscript ^a and ^b.

Table 6. Non-preference rates of cold and cough medicines according to medical specialties

Drugs	General Practitioner, %, n=123	Family Medicine Specialist, %, n=12	Pediatricians, %, n=45	p
Cold medicines (18)	46.2 (1025) ^a	44.4 (96) ^a	65.4 (530) ^b	0.000
Cough-suppressant drugs (5)	50.7 (312) ^a	53.2 (33) ^a	83.7 (190) ^b	0.000
Systemic nasal decongestants (2)	40.2 (99) ^a	41.6 (10) ^a	75.5 (68) ^b	0.000
Topical nasal decongestants (5)	30.8 (190) ^a	20.0 (12) ^a	35.8 (95) ^a	0.207

A statistically significant difference exists between the groups labeled with superscript ^a and ^b.

duced in both groups. In a study by Şen et al. [19] realized in Italy and in the Netherlands in 2010, the prescribing rates of CCMs were examined in children under 2 years after the announcement of national and international warnings. In Italy, a slight decrease in the prescribing rates of all CCMs was detected; however, an increase in the prescribing rates of these drugs was noted in the Netherlands. As a result, it has been stated that drug companies should clearly indicate that the use of these medicines in small children is dangerous to raise awareness among health care professionals.

In parallel with the discussions in the world, in Turkey, the General Directorate of Pharmaceuticals and Pharmacy sent a letter to pharmaceutical companies and the unions dated March 31, 2008, concerning an arrangement related to the prescription of CCMs [5]. In this letter, there was an addition to the statement in the warnings/precautions section of the instructions of the short product information for drugs containing brompheniramine, chlorpheniramine and diphenhydramine, dextromethorphan, pholcodine, guaiphenesin, ipecacuanha, phenylephrine, pseudoephedrine, ephedrine, oxymetazoline that prohibited the use of these drugs in children without absolute and compulsory indications.

After a while, on November 18, 2011, the General Directorate of Pharmaceuticals and Pharmacy declared that "based on the decisions made by the Advisory Commission on Pharmacology of the Ministry of Health and the Advisory Commission on Licensing Regulation on Human Medicinal Products for Human Use in consideration of its possible risks and adverse effects, for pharmaceutical preparations containing pseudoephedrine singly or in combination the following statements should be added, and required changes should be made in the relevant sections of the SPC/SPO" [6].

Accordingly, they proposed four basic recommendations. Proprietary drugs in liquid forms that contain a combination with an antipyretic agent (such as paracetamol, ibuprofen) must not be used in patients aged younger than 6 years, and the formulations in liquid forms combined with other agents must not be used in children younger than 12 years of age. Liquid preparations containing only pseudoephedrine alone should not be used in patients younger than 6 years of age. Preparations in solid forms containing pseudoephedrine singly or in combination should not be used in children younger than 12 years.

Turkey's Pharmaceuticals and Medical Devices Agency issued an update on July 23, 2013, regarding CCMs currently in use [7]. The age limits for the use of the prepa-

rations containing a single active ingredient including levodropropizine, guaiphenesin, brompheniramine, chlorpheniramine, phenylephrine, xylometazoline, diphenhydramine, butamirata citrate, dextromethorphan, oxymetazoline, pentoxyverine, oxolamine, noscapine, and cloperastine were increased.

In our study, only 2.77% of the participants prescribed CCMs in compliance with new arrangements in regulations, while 49.4% of the respondents were not aware of the changes, indicating that physicians' awareness of this issue was not at a satisfactory level. In addition, 50.6% of the physicians who were informed about the changes were knowledgeable about the age limits related to very few active ingredients. Physicians who received information about pseudoephedrine were evaluated separately, and it was also found that approximately 34% of them preferred to prescribe these drugs considering previous age limits. This situation suggests that physicians do not benefit from current sources.

Physicians prescribing these drugs without definitely established absolute indications for patients beyond the defined age limits can present serious problems in terms of patient health and may expose physicians to serious legal troubles. Some (34.4%) proportion of the physicians face the parental objection about the age limits of prescription drugs, which can be evaluated as steps toward possible legal problems.

The strength of our study, as far as we know, is that it reveals the first batch of data in our country on his issue, to the best of our knowledge. The limitations of the study are the low number of physicians in the family physician group (the number in the province is low) and its local frame.

As a result, integrating both the hospital and family medicine information management systems into the current drug guidelines will make a significant contribution to the elimination of such malpractices. Where integration is not possible, physicians should reexamine their current sources of CCMs. In addition, sending letters by MoH to relevant physicians may be a significant contribution to the elimination of this problem.

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