

Evaluation of Symptomatic Treatment Approaches of Pediatricians for Pediatric Patients with Upper Respiratory Tract Infection Regarding to Rational Drug Use

Pediatristlerin Üst Solunum Yolu Enfeksiyonu Olan Çocuk Hastalarda Semptomatik Tedavi Yaklaşımlarının Akılcı İlaç Kullanımı Açısından Değerlendirilmesi

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Abstract

Introduction: Prescribing a large number of drugs for symptomatic treatment of upper respiratory tract infection (URTI) can cause more frequent drug interactions and an increase in undesirable side effects in pediatric patients. The aim of this retrospective study is to evaluate the drug prescriptions for symptomatic treatment to pediatric patients diagnosed with URTI in terms of rational drug use.

Materials and Methods: Fourteen pediatric outpatient clinics of Şanlıurfa Training and Research Hospital were included in the study. The number of samples was determined as 1064. The first 76 prescriptions of the pediatricians written for patients diagnosed as URTI were selected retrospectively by using the Hospital Information Management System.

Results: There was an average of 4 and a maximum of 9 drugs, whereas the number of active substances was between 6 and 19 in prescriptions. Analgesics-antipyretics (86.7%) and antibiotics (69.1%) were most prescribed, followed by decongestants (47.9%) and antihistamines (47.1%). Analgesic-antipyretics (36.4%) was the most preferred drug group among the drugs used in symptomatic treatment whereas antiseptics was the least (0.9%). Active ingredients prescribed more than once due to combined preparations were analgesics (36.2%), expectorants (18.7%), decongestants (16.5%), antihistamines (8.8%) vitamins (5%) respectively. Antihistamines (21.8%), decongestants (21.2%), and cough suppressants (16.8%) were used at inappropriately high doses. Decongestants were used mostly in inappropriate dosing interval, compared to other groups (20.8%). When assessed according to physician prescriptions, drugs used in symptomatic treatment, drug combinations from the same group, preference for local or systemic use, and inappropriate doses of antihistamines and decongestants were statistically different among physicians.

Conclusion: This study shows that some of the specialist physicians currently prescribe incompatible with the principles of rational drug use in the symptomatic treatment of children with a diagnosis of URTI. Continuous in-service training could increase the awareness of physicians on this subject and keep their knowledge up-to-date. Additionally, establishing a warning system or making limitations during e-prescription may also be useful.

Keywords

Pediatricians, drug prescriptions, retrospective study, upper respiratory tract infection

Anahtar kelimeler

Pediatristler, ilaç reçetesi, retrospektif çalışma, üst solunum yolu enfeksiyonu

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Öz

Giriş: Pediatrik hastalarda üst solunum yolu enfeksiyonunun (ÜSYE) semptomatik tedavisi için çok sayıda ilacın reçete edilmesi ilaç etkileşimlerinin daha sık olmasına ve istenmeyen yan etkilerin artmasına neden olabilmektedir. Bu çalışmanın amacı, ÜSYE tanısı almış çocuk hastalara semptomatik tedavi amacıyla reçete edilen ilaçları akılcı ilaç kullanımı açısından değerlendirmektir.

Gereç ve Yöntem: Şanlıurfa Eğitim ve Araştırma Hastanesi'ndeki 14 çocuk polikliniği çalışmaya dahil edildi. Örnek sayısı 1064 olarak belirlendi ve çocuk doktorlarının ÜSYE tanısı almış hastalar için yazdığı ilk 76 reçetesi Hastane Bilgi Yönetim Sistemi kullanılarak geriye dönük olarak tarandı.

Bulgular: Reçetelerde ortalama 4, maksimum 9 ilaç bulunurken, etken madde sayısı 6 ile 19 arasındaydı. En çok analjezik-antipiretikler (%86,7) ve antibiyotikler (%69,1) reçete edilirken, bunu dekonjestanlar (%47,9) ve antihistaminikler (%47,1) takip etti. Semptomatik tedavide en çok analjezik-antipiretikler (%36,4) tercih edilirken, en az antiseptikler (%0,9) tercih edildi. Kombine preparatların reçete edilmesinden dolayı analjezikler (%36,2), ekspektoranlar (%18,7), dekonjestanlar (%16,5), antihistaminikler (%8,8) ve vitaminler (%5) için aynı etken maddenin tekrarı var idi. Uygun olmayan dozlarda en çok antihistaminikler (%21,8) kullanılmış, bunu dekonjestanlar (%21,2) ve öksürük kesiciler (%16,8) izlemiştir. Dekonjestanlar diğer gruplara göre en çok uygun olmayan doz aralığında kullanılmıştı (%20,8). Çocuk hekimlerinin reçetelerine göre değerlendirildiğinde, semptomatik tedavide kullanılan ilaçlar, aynı gruptan ilaç kombinasyonları, lokal veya sistemik kullanım tercihi, uygun olmayan dozda antihistaminik ve dekonjestan tercihleri hekimler arasında istatistiksel olarak farklı bulundu.

Sonuç: Bu çalışma, günümüzde uzman hekimlerin bir kısmının ÜSYE tanılı çocukların semptomatik tedavisinde akılcı ilaç kullanımı ilkelerine uymayan reçeteleme yaptığını göstermektedir. Sürekli hizmet içi eğitimler hekimlerin bu konudaki farkındalıklarını artırabilir ve hekimlerin bilgilerini güncel tutabilir. Ayrıca e-reçete sırasında uyarı sistemi kurulması veya kısıtlama getirilmesi de faydalı olabilir.

Introduction

Upper respiratory tract infection (URTI) is the most common reason for applications to outpatient treatment centers and the most common infectious disease encountered by practitioners and pediatricians worldwide (1). The data from Turkey Health Survey conducted by Turkey Statistical Institute also shows that URTI is the most common disease in Turkey, with a prevalence of 35.9% in children aged 0-6 years and 29.1% in children aged 7-14 years (2).

It is of great importance to determine whether the origin of URTI is viral or bacterial, for the correct selection of drugs. In symptomatic treatment, analgesic-antipyretics, antihistamines, systemic and topical decongestants, antitussives, mucolytics, expectorants, antiseptics, and vitamin C are used (3,4). Rational drug use (RDU) is more important in the pediatric age group because the pharmacodynamics and the pharmacokinetics are not the same in adults and children, and this may cause more toxicity and adverse effects for some drugs (1). The high number of drug groups used in the symptomatic treatment of URTI and the over-prescribing of these drugs by physicians increase the importance of determining the treatment in accordance with RDU principles. The most commonly used over the counter (OTC) drug were reported as cold medicines (5). According to the Turkish Pharmaceutical Industry 2021 report,

cold medicines have been the 6th best-selling medicine group per box, despite the appearance of diseases and the decrease in hospital access due to the effect of coronavirus disease-2019 (COVID-19) pandemic limitations (6).

Rational drug use is necessary to prevent drug ineffectiveness, bacterial resistance to antibiotics, drug side effects, and financial losses. Rational drug use will increase the strength of healthcare systems (7).

The aim of this study is to evaluate the drugs prescribed by specialist physicians for symptomatic treatment of patients diagnosed with URTIs in terms of rational drug use in pediatric patients.

Materials and Methods

The study was initiated after obtaining institutional permission from the Chief Physician of Şanlıurfa Training and Research Hospital and approval from the Non-Invasive Clinical Research Ethics Committee of Harran University Faculty of Medicine (no: 2016-07-10).

This study was carried out in Şanlıurfa Training and Research Hospital, which has the highest number of pediatric outpatient clinics located in Şanlıurfa, the province with the largest child population in Turkey according to the 2017 Turkey Statistical Institute data.

Fourteen pediatric outpatient clinics at the Şanlıurfa Training and Research Hospital in the city center of

Şanlıurfa were included in the study. It was found to reach at least 1064 prescriptions based on the rates of the estimated use level of decongestants (47%) and possible mistakes (3%) in the pilot study. We evaluated the prescriptions of 14 pediatricians, and 76 (7.1%) prescriptions written by each pediatrician and scanned to reach the total of 1064 prescriptions with a diagnosis of URTI (ICD code: J.06) for the 0-18 age were included.

Data Collection

The computer printouts of the prescriptions selected through the Hospital Information Management System were taken and stored. Analgesic-antipyretics, antihistamines, decongestants, antitussives, expectorants, mucolytics, antiseptic throat sprays and mouthwashes, and vitamin C were accepted as drugs used in symptomatic treatment (4).

Statistical Analysis

The data were analysed with the SPSS (20.0 version, IBM Company, SPSS Inc.) package program and percentage of distributions were examined. Descriptive statistics (number, percentage, average) were given for categorical variables while evaluating the study data. Chi-square test was used to compare categorical variables. A value of $p < 0.05$ was considered statistically significant.

Results

The age and other comorbidities of patients with URTI in 1064 prescriptions included in the study are given in Table 1. It was determined that 1010 (95%) of prescriptions included the drugs for the symptomatic treatment of URTI. The active substances were in the range of 1-19 with an average of 6. The number of

drugs only specific for local use was 271 (53.1%), for both local and systemic use was 78 (15.3%), and specific for only systemic application was 161 (31.6%) in the prescriptions.

Analgesics-antipyretics (86.7%) and antibiotics (69.1%) were the most prescribed. This was followed by decongestants (47.9%) and antihistamines (47.1%). Antiseptics which have a place in symptomatic treatment, were the least prescribed group (2.1%) and chlorhexidine was preferred in all of these prescriptions. A total of 583 (54.8%) prescriptions included also additional drugs that are not related to the treatment of URTI and lower respiratory tract infections (Table 2). Among the drugs used in symptomatic treatment, analgesic-antipyretics (36.4%) were the most preferred drug group followed by decongestants (20.1%), antihistamines (19.8%) as the least preferred group (0.9%) (Table 3).

Paracetamol alone (36.4%), ibuprofen (32.3%) and ibuprofen/paracetamol combination (30.9%) were the mostly prescribed analgesic-antipyretics. Naproxen, acetylsalicylic acid, and metamizole was prescribed totally 0.3%.

The distribution of single and combined drug groups was also determined. Oxymetazoline was the highest with a rate of 63.3%, followed by phenylephrine (25.5%) and pseudoephedrine (22%), and others such as sodium chloride and xylometazoline (4.9%) among decongestants. The most prescribed antihistamine was chlorpheniramine maleate (56.7%), followed by pyrilamine maleate (22.1%) and desloratadine (7.4%). Chlorpheniramine + desloratadine combination (4.8%) was the most prescribed among the combined preparations. Drugs for cough symptoms were included in 379 (36%) of the prescriptions, such as expectorants (45.3%), antitussives (42.3%), and mucolytics (12.4%) (Table 4).

Age	n (%)	Comorbid disease	n (%)	
0-2	427 (40.1)	Concerning the lower and upper respiratory tract	Acute bronchitis	22 (2.1)
			Acute pharyngitis	2 (0.2)
3-6	485 (45.6)	Concerning the lower and upper respiratory tract	Acute tonsillitis	6 (0.6)
			Asthma	1 (0.1)
			Pneumonia	2 (0.2)
7-17	152 (14.3)	Others	Vitamin deficiency, Down syndrome, growth retardation, etc.	276 (25.9)
Total			309 (29.1)	

Vitamins were preferred alone or in combination and vitamin deficiency was presented as an additional diagnosis in 17 (8.4%) of the prescriptions. Vitamin C (66.4%) was mostly included in prescriptions whereas vitamin B complex (B1, B2, B6, B5, B3, B12) (0.5%) was at least. Bronchodilator was prescribed to 126 (11.8%) of the patients with a diagnosis of URTI and 85 of these prescriptions did not include any additional diagnosis. Salbutamol (99.2%) and salmeterol (0.8%) inhaled forms were only preferred. Steroids were prescribed for 130 (12.9%) patients diagnosed with URTI. A total of 104 patients had no additional diagnosis, 15 had additional diagnoses unrelated to URTI, and 11 had an additional diagnosis of acute bronchitis. Budesonide

Pharmaceutical group	n (%)
Analgesics-antipyretics	922 (86.7)
Antibiotics	735 (69.1)
Decongestants	510 (47.9)
Antihistamines	501 (47.1)
Vitamins	202 (19.0)
Expectorants	172 (16.2)
Antitussives	161 (15.1)
Steroids	130 (12.9)
Bronchodilators	126 (11.8)
Mucolytics	46 (4.3)
Antiseptics	22 (2.1)
Other drugs*	583 (54.8)

*Prescription of drugs not associated with upper respiratory tract infection and lower respiratory tract infection treatment

Pharmaceutical group	n (%)
Analgesic-antipyretic	922 (36.4)
Decongestant	510 (20.1%)
Antihistamine	501 (19.8)
Vitamin	202 (7.9%)
Expectorant	172 (6.8%)
Antitussive	161 (6.3%)
Mucolytic	46 (1.8%)
Antiseptic	22 (0.9%)

was the most prescribed steroid (38.2%) as alone or combined with methylprednisolone-fluticasone whereas mometasone was the least (0.8%). Steroids were preferred by inhaled and intramuscular routes.

The drugs were also prescribed in combination for symptomatic treatment as analgesic-antipyretics (36.2%) followed by expectorants (18.7%) and antihistamines (8.8%).

We determined that the dose and dosing interval of drugs were inappropriate in some prescriptions. The prescription of different preparations containing the same active ingredient was one of the reasons. Antihistamines (21.8%) were used at the most inappropriate doses, followed by decongestants (21.2%) and antitussives (16.8%). The drug group with the highest use in the inappropriate dosing interval was decongestants (20.8%) and mucolytics (8.5%) (Table 5). Although steroids are not included in the symptomatic treatment of URTI, they were prescribed inappropriate doses (14.6%) and dosing intervals (13.9%) in some prescriptions.

When the prescriptions of the pediatricist included in the study are evaluated separately, the prescribing rates for each drug were different (Table 6).

Considering the physicians' approach to the treatment of patients with a diagnosis of URTI, there was difference among physicians in prescribing single antibiotics ($\chi^2=195.244$; $p=0.001$), combined antibiotics ($\chi^2=174.573$; $p=0.001$), analgesic-antipyretics ($\chi^2=61.179$; $p=0.004$) analgesics in combination with other drugs ($\chi^2=211.921$; $p=0.001$); antihistamines ($\chi^2=167.007$; $p=0.001$), antitussives ($\chi^2=157.738$; $p=0.001$), vitamins ($\chi^2=77.971$; $p=0.001$), expectorants ($\chi^2=198.388$; $p=0.001$), decongestants ($\chi^2=159.400$; $p=0.001$), bronchodilators ($\chi^2=128.305$; $p=0.001$), steroids ($\chi^2=217.035$; $p=0.001$) inappropriate doses of antihistamines ($\chi^2=91.016$; $p=0.001$), contraindicated use of antihistamines ($\chi^2=70.264$; $p=0.001$); inappropriate doses of decongestants ($\chi^2=196.038$; $p=0.001$), and prescribing locally or systemically ($\chi^2=328.386$; $p=0.001$).

Discussion

This study differs from current studies that focus on the irrational use of antibiotics in the treatment of URTI. We evaluated the drugs used in the symptomatic treatment of URTI in pediatric patients in terms of rational drug use and we found that there are irrational

drug uses.

This is the first study, evaluating the pediatricians' approach to symptomatic treatment for URTI in children in Turkey. The drugs for symptomatic treatment were included in 95% of the prescriptions written by pediatricians with the diagnosis of URTI and we evaluated the prescribed drugs for symptomatic treatment according to the principles of rational drug use.

We found that analgesic-antipyretics (86.7%) were mostly prescribed in the symptomatic treatment of URTI. In the studies conducted in India, the use

of analgesic-antipyretics in children with URTI was low (18.8% and 20.95 %, respectively) compared to our study (8,9). However, in a study conducted in North Trinidad, paracetamol was the most frequently prescribed drug (40.1%) among symptomatic agents for URTI in pediatric patients (10). We determined that very few of the prescribed analgesics were in inappropriate doses.

We found that decongestants (47.9%) were the most prescribed drug group after analgesic-antipyretics in the symptomatic treatment of URTI. It was reported that the efficacy of topical decongestants in reducing

Table 4. Distribution of single or combined drug groups used for symptomatic treatment in prescriptions

Decongestants	n (%)	Antihistamines	n (%)	Drugs used to treat cough	n (%)	
Oxymetazoline	249 (48.8)	Chlorpheniramine maleate	285 (56.7)	Expectorants	Guaifenesin	91 (52.9)
Pseudoephedrine	83 (16.3)	Pyrilamine maleate	111 (22.1)		Terbutaline + guaifenesin	80 (46.5)
Phenylephrine	77 (15.1)	Desloratadine	37 (7.4)		Ambroxol	1 (0.6)
Phenylephrine + oxymetazoline	51 (10)	Chlorpheniramine maleate + desloratadine	24 (4.8)		Total	172 (45.3)
Pseudoephedrine + oxymetazoline	23 (4.5)	Azelastine	11 (2.2)	Antitussives	Levodropozin	51 (31.7)
Sodium chloride	21 (4.1)	Cetirizine	10 (2.0)		Dextromethorphan	44 (27.3)
Pseudoephedrine + xylometazoline	4 (0.8)	Chlorpheniramine maleate + desloratadine + pyrilamine maleate	9 (1.8)		Butamirate citrate	33 (20.5)
Phenylephrine + pseudoephedrine	2 (0.4)	Pyrilamine maleate + azelastine	4 (0.8)		Oxolamine angelini	33 (20.5)
-	-	Tripolidin	4 (0.8)		Total	161 (42.3)
-	-	Chlorpheniramine maleate + cetirizine	4 (0.8)	Mucolytics	Acetyl cysteine	40 (87)
-	-	Pyrilamine maleate + cetirizine	1 (0.2)		Erdostein	6 (13.0)
-	-	Cetirizine + azelastine	1 (0.2)		Total	46 (12.4)

Table 5. The distribution of inappropriate dose and dosing interval in the drug groups used for symptomatic treatment

Pharmaceutical groups	Inappropriate dose n (%)	Inappropriate dosing interval n (%)
Antihistamine	109/501 (21.8)	32/501 (6.4)
Decongestant	108/510 (21.2)	106/510 (20.8)
Antitussive	27/161 (16.8)	8/161 (5.0)
Mucolytic	5/46 (10.8)	4/46 (8.5)
Expectorant	14/172 (8.2)	12/172 (7.0)
Analgesic-antipyretic	16/922 (1.8)	16/922 (1.8)
Vitamin	2/202 (1.0)	1/202 (0.5)

nasal congestion in adults suffering from the common cold. A modest (6%) but statistically significant decrease was found in patient-reported symptoms after a single dose of intranasal decongestant compared with a placebo in a meta-analysis study (11). We observed that the physicians mostly preferred the local application of oxymetazoline (63.3%), the systemic application of phenylephrine (25.5%), and pseudoephedrine (22%). We think the reason why oxymetazoline is so preferred may be that the risk of rebound congestion is relatively lower with oxymetazoline or locally used decongestants can quickly relieve nasal congestion and allow nasal breathing (12). Additionally, we observed that 21.2% of the decongestants prescribed in inappropriate doses and 20.8% in inappropriate dosing intervals.

The use of decongestants is not recommended in the treatment of URTIs if the patient does not have an

allergic history. Although there are not enough studies showing the effectiveness of many decongestant agents in reducing nasal congestion in adults and children, it is also known that these agents cause tachycardia, high diastolic blood pressure, palpitations (13,14). The use of systemic decongestants in children under six years of age and local decongestants in children under two years of age is not recommended (15). Cases with cardiac arrhythmia, convulsions and psychosis have been reported due to overdose (16-18). In line with these reports 86.1% of decongestants were used in contraindicated situations in this study. However, it is noteworthy that the use of these agents is higher than in other studies (8-10).

Isotonic and hypertonic saline solutions are effective for nasal congestion in children especially. These solutions are suggested as a good choice to reduce the use of antihistamines, decongestants, antibiotics and

Table 6. Number and percentage of drug groups prescribed by each physician

Pharmaceutical group	A	B	C	D	E	F	G	H	I	J	K	L	M	N
	n (%)													
Analgesics-antipyretics	62 (81.6)	69 (90.8)	76 (100)	68 (89.5)	54 (71.1)	70 (92.1)	72 (94.7)	71 (93.4)	73 (96.1)	61 (80.3)	64 (84.2)	61 (80.3)	64 (84.2)	57 (75.0)
Decongestants	27 (35.5)	28 (36.8)	67 (88.2)	27 (35.5)	37 (48.7)	50 (65.8)	51 (67.1)	51 (67.1)	17 (22.4)	49 (64.5)	23 (30.3)	33 (43.4)	14 (18.4)	36 (47.4)
Local	27 (100)	16 (57.1)	8 (11.9)	16 (59.3)	5 (13.5)	42 (84)	19 (37.3)	48 (94.1)	15 (88.2)	40 (81.6)	22 (95.7)	8 (24.2)	0 (0.0)	5 (13.9)
Systemic	0 (0.0)	12 (42.9)	28 (41.8)	11 (40.7)	29 (78.4)	1 (2.0)	17 (33.3)	3 (5.9)	1 (5.9)	1 (2.1)	0 (0.0)	16 (48.5)	14 (100)	28 (77.8)
Local + systemic	0 (0.0)	0 (0.0)	31 (46.3)	0 (0.0)	3 (8.1)	7 (14.0)	15 (29.4)	0 (0.0)	1 (5.9)	8 (16.3)	1 (4.3)	9 (27.3)	0 (0.0)	3 (8.3)
Antihistamines	35 (46.1)	59 (77.6)	49 (64.5)	29 (38.2)	33 (43.4)	50 (65.8)	42 (55.3)	2 (2.6)	39 (51.3)	15 (19.7)	32 (42.1)	46 (60.5)	20 (26.3)	50 (65.8)
Vitamins	32 (42.1)	21 (27.6)	4 (5.3)	15 (19.7)	12 (15.8)	8 (10.5)	10 (13.2)	18 (23.7)	11 (14.5)	10 (13.2)	8 (10.5)	11 (14.5)	31 (40.8)	11 (14.5)
Expectorants	4 (5.3)	9 (11.8)	24 (31.6)	2 (2.6)	43 (56.6)	5 (6.6)	25 (32.9)	3 (3.9)	1 (1.3)	22 (28.9)	1 (1.3)	14 (18.4)	17 (22.4)	2 (2.6)
Antitussives	3 (3.9)	4 (5.3)	15 (19.7)	19 (25.0)	4 (5.3)	21 (27.6)	1 (1.3)	0 (0.0)	19 (25.0)	0 (0.0)	16 (21.1)	15 (19.7)	6 (7.9)	38 (50.0)
Steroids	1 (1.3)	3 (3.9)	1 (1.3)	8 (10.5)	41 (53.9)	1 (1.3)	8 (10.5)	22 (28.9)	0.0 (0.0)	25 (32.9)	12 (15.8)	1 (1.3)	7 (9.2)	6 (7.9)
Bronchodilators	4 (5.3)	3 (3.9)	1 (1.3)	9 (11.8)	13 (17.1)	2 (2.6)	8 (10.5)	22 (28.9)	1 (1.3)	32 (42.1)	11 (14.5)	12 (15.8)	3 (3.9)	5 (6.6)
Mucolytics	0 (0.0)	1 (1.3)	10 (13.2)	0 (0.0)	3 (3.9)	1 (1.3)	0 (0.0)	15 (19.7)	1 (1.3)	2 (2.6)	3 (3.9)	0 (0.0)	10 (13.2)	0 (0.0)
Antiseptics	1 (1.3)	4 (5.3)	1 (1.3)	0 (0.0)	2 (2.6)	4 (5.3)	0 (0.0)	0.0 (0.0)	4 (5.3)	4 (5.3)	0 (0.0)	2 (2.6)	0 (0.0)	0 (0.0)

Each letter represents a physician involved in the study.

corticosteroids in the treatment of URTI since they are well tolerated (19-22). But, in our study prescription of saline drops and sprays was very low (4.1%) in the symptomatic treatment of URTI. Contrary to our data in a study conducted with pediatric patients diagnosed with URTI in Spain, it was stated that saline preparations were among the five most commonly prescribed drugs for symptomatic treatment (10). And also in a study conducted in India, only 2% of the nasal preparations were nasal decongestants such as oxymetazoline, 98% of them were isotonic saline drops (8).

The physicians mostly prefer first-generation antihistamines. It is considered that preferring the first generation is a rational choice since second-generation antihistamines are ineffective on symptoms such as cough, nasal congestion, and sneezing in URTIs, but sedation and anticholinergic side effects of drugs in this group are seen mostly (23). It is reported that antihistamine drugs are not suitable for use because they reduce ciliary activity and mucus excretion and may cause drying in the mucosa and impair sinus drainage with their anticholinergic effects, so they are not very suitable for use. These drugs may cause side effects such as dry mouth, blurred vision, dizziness, drowsiness, hallucinations, arrhythmia, respiratory depression, and urinary retention (23-25). In a study, including randomized controlled trials using antihistamines as monotherapy for the common cold, it was reported that antihistamines have only a limited short-term beneficial effect in reducing the severity of general symptoms, and there is no evidence of the effectiveness of antihistamines in children (25). In addition, according to the information on the instructions for use, it is stated that these drugs should not be used under the age of two. However, in this study, 35.5% of antihistamines were prescribed under this age.

Cough, sore throat and itching sensation are typical symptoms frequently encountered in URTI. Cough affects the quality of life and makes worry the families and causes them to consult a physician (26). It is a reflex mechanism of the body. It is recommended to be treated when it starts to affect the quality of life in URTIs. It is reported that children are more likely to experience URTI-associated acute cough than adults and severe adverse events frequently occur related to cough medications, especially in children (27). In a

study investigating the use of antibiotics in URTIs in Mongolia, it was reported that the first reason for non-prescription antibiotic use in children was cough (84%) (28). The results of the studies on the efficacy of cough suppressants in children vary, and the differences in the duration of treatment in these studies cannot reveal a definite conclusion about the effectiveness of these drugs (29). In this study, antitussive, expectorant, and mucolytic drugs which are used in cough symptom were preferred in 36% of prescriptions. Among these groups, expectorants were the most prescribed (16.2%), but 8.2% of them were at an inappropriate dose and 7% at an inappropriate dosing interval.

Antitussives were preferred with a rate of 15.1% after expectorants, but 16.8% of them were found at an inappropriate dose and 5% at an inappropriate dosing interval.

The other drug group prescribed for cough symptoms in URTI was mucolytics with a lower rate (4.3%). The inappropriate dose and dosing interval was as 10.6% and 8.5% for this group, respectively. United States Food & Drug Administration (FDA) does not recommend the use of any cough or cold medication in children younger than two years of age, because they could cause serious and potentially life-threatening side effects.

In the study of Das et al. (8) expectorants was mostly prescribed for cough as in our study and the rate of non-opioid antitussives (13.5%) was similar. But, mucolytic prescription rate was higher (18.7%) compared to our study. Also in a study conducted in two hospitals of Indonesia including patients under-five years, mucolytics were prescribed higher (21.9% and 71.1% respectively) compared to our study (30). Although many drugs are used clinically as mucoactive, the data partially support the therapeutic efficacy of these drugs (31). Acetylcysteine and carbocysteine, the frequently used mucolytic agents, are effective in reducing the frequency, intensity and duration of cough in acute URTI and lower respiratory tract infections. They are not recommended for children under two years of age due to safety concerns (32).

In this study, 19% of the prescriptions contained vitamins, mostly multivitamins including vitamin C. The diagnosis of vitamin deficiency was in only 8.4% of these prescriptions. Although there is no clear information about other vitamins in the literature, it is stated that vitamin C may be an appropriate approach

in terms of reducing the duration of URTI (33). There is not enough information in the literature about the protective effect of vitamins in URTIs and also how to use and doses. However, it has been reported that antioxidant vitamins A, C and E take part in the immune system and if these vitamins are low the incidence of URTIs increases (34). A relationship between vitamin D deficiency and the incidence of URTI was found (35) whereas routine use of high-dose vitamin D supplementation was not found effective for the prevention of viral URTIs in children (36).

We have observed that antiseptic sprays and mouthwashes were the least common drugs (2.1%) and preparations containing chlorhexidine were preferred in all of these prescriptions. In a study conducted in Japan, water gargling and povidone-iodine gargling were evaluated in URTI and it was reported that simple water gargling was effective to prevent URTIs among healthy people (37). It is also reported that gargling is beneficial in respiratory tract infections and does not have any serious side effects. However, some agents used for mouthwash can damage the epithelium and the use of mouthwash should not be preferred in children under the age of six years (38).

Although the main purpose of this study was to evaluate the symptomatic treatment in URTI, it is noteworthy that the rate of antibiotic prescribing was so high. In developing countries, antibiotic treatment is applied often even in cases of viral origin in URTI, especially in the pediatric age group and it has been observed that almost half of the prescriptions included antibiotics for treatment of outpatients with URTI (8,30,39,40). Physicians tend to prescribe more antibiotics to pediatric patients because they are afraid of URTI complications (40). It is important to prevent the unnecessary use of antibiotics, as not being used in the appropriate indication causes the development of antibiotic-resistant strains and also increases treatment costs.

Polypharmacy leads to negative consequences such as an increase in the adverse effects of drugs, an increase in drug interactions, a decrease in patient compliance with treatment, and an increase in treatment costs. In many studies, polypharmacy in pediatrics has been defined as at least two drugs with or without specified duration (41). We determined that specialist physicians prescribed between 1-9 drugs, with an average of 4 with the diagnosis of URTI. However,

the number of active ingredients in prescriptions was between 1-19 with an average of 6, depending on the use of preparations containing combined drugs. This value shows that there is polypharmacy in the treatment given by pediatricians for URTI in children. Similarly, in the studies of Das et al. (8) and Sankhla et al. (9) polypharmacy was found in pediatric patients with URTI, but the drug average was lower compared to our study, at 2.37 and 3.28, respectively.

This study had some limitations like any other study. It was conducted in only one hospital in Şanlıurfa. However, it is important that Şanlıurfa Training and Research Hospital has the highest number of pediatric clinics in Şanlıurfa and Şanlıurfa is the city that has the highest pediatric population in Turkey according to recent data.

Conclusion

The results of this study showed that the number of drugs and active substances in the symptomatic treatment of URTI in children was high. In some prescriptions, the limitations of drug intake according to age are not taken into account, and also incorrect doses and dosing intervals were chosen. We think that it is necessary to organize in-service training in order to follow the prescriptions of the drugs used in symptomatic treatment, making arrangements in this regard may increase the awareness of physicians on this issue. In addition, alerts in the Hospital Information Management System can increase the awareness of physicians and reduce the number of irrational prescriptions.

Ethics

Ethics Committee Approval: Ethical approval was received for this study from the Non-Invasive Clinical Research Ethics Committee of Harran University Faculty of Medicine (decision no: 2016-07-10, date: 01.09.2016).

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References

1. Gonzales R, Bartlett JG, Besser RE, Hickner JM, Hoffman JR, Sande MA. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults background. *Ann Intern Med* 2001;134:490-4.

2. Turkish Statistical Institute. Turkey Health Survey (TurkStat-THS). (cited 20 April 2021). Available from: <https://data.tuik.gov.tr/Bulten/Index?p=Turkey-Health-Survey-2019-33661>
3. Jain N, Lodha R, Kabra SK. Upper respiratory tract infections, *Indian J Pediatr* 2001;68:1135-8.
4. Collett CA, Pappas DE, Evans BA, Hayden GF. Parental knowledge about common respiratory infections and antibiotic therapy in children. *South Med J* 1999;92:971-6.
5. Tomić M, Pecikoza U. Medications and non-pharmacological measures to alleviate the symptoms of respiratory tract infections in the pediatric population. *Archives of Pharmacy* 2022;72:300-19.
6. Türkiye İlaç Sektörü 2021 Raporu. İlaç Endüstrisi İşverenler Sendikası (İEİS). (cited 23 November 2022). Available from: <https://www.ieis.org.tr/tr/bizden-haberler/turkiye-ilac-sektoru-2021-raporu>
7. Mekonnen BD, Ayalew MZ, Tegegn AA. Rational Drug Use Evaluation Based on World Health Organization Core Drug Use Indicators in Ethiopia: A Systematic Review. *Drug Healthc Patient Saf* 2021 Jul 27;13:159-70.
8. Das B, Sarkar C, Majumder AG. Medication use for pediatric upper respiratory tract infections. *Fundam Clin Pharmacol* 2006;20:385-90.
9. Sankhla S, Kanwar S, Mahawar DK. A retrospective study of prescribing pattern for acute respiratory infections in children in a tertiary care teaching hospital. *Int J Pharm Sci Res* 2017;8:3911-6.
10. Mungrue K, Brown T, Hayes I, Ramroop S, Thurston P, Pinto Pereira L. Drugs in upper respiratory tract infections in paediatric patients in North Trinidad. *Pharm Pract (Granada) [Internet]*. 2009 Mar 4 [cited 2021 Dec 31];7(1):29-33. Available from: <https://www.pharmacypractice.org/index.php/pp/article/view/188>
11. Taverner D, Latte J. Nasal decongestants for the common cold. *Cochrane Database Syst Rev* 2007;24:CD001953.
12. Hayden FG, Diamond L, Wood PB, Korts DC, Wecker MT. Effectiveness and safety of intranasal ipratropium bromide in common colds. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1997;125:89-97.
13. Morales-Carpi C, Torres-Chazarra C, Lurbe E, Torro I, Morales-Olivas FJ. Cold medication containing oral phenylephrine as a cause of hypertension in children. *Eur J Pediatr* 2008;167:947-8.
14. Atan Şahin ON, Gülen F. Approach to Common Cold in Children. *The Journal of Pediatric Research* 2015;2:1-6.
15. Kliegman MD, Stanton MD, Geme MD, Schor MD. The Common Cold In Robert M, Kliegman MD, Bonita M.D, Stanton MD, Joseph St, Geme MD, Nina F, Schor MD, (Eds). *Nelson Textbook Of Pediatrics E-Book*. 20th ed. 2015. p.2948-51.
16. Elshershari H. Pseudoephedrine-Induced Tachycardia and hypertension in an infant misdiagnosed as supraventricular tachycardia: A case report. *Ibnosina Journal of Medicine and Biomedical Sciences* 2010;2:42-5.
17. Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Pseudoephedrine use among us children, 1999-2006: Results from the slone survey. *Pediatrics* 2008;122:1299-304.
18. Singh Rehan H, Chopra A, Kumar S. To Study the Utilization Pattern of Nasal Decongestants and their Effects on Heart Rate and Blood Pressure. *AJCR* 2012;5:91-4.
19. Heikkilä P, Renko M, Korppi M. Hypertonic saline inhalations in bronchiolitis-A cumulative meta-analysis. *Pediatr Pulmonol* 2018;53:233-42.
20. González Bellido V, Velázquez Baza V, Esteo MDCJ, Carballo RG, Colombo A, Zaldívar JNC, et al. Safety of airway clearance combined with bronchodilator and hypertonic saline in non-hospitalized infants with acute bronchiolitis. *Arch Pediatr* 2021;28:707-11.
21. Chirico G, Quartarone G, Malfet P. Nasal congestion in infants and children: a literature review on efficacy and safety of non-pharmacological treatments. *Minerva Pediatr* 2014;66:549-57.
22. Simasek M, David A. Treatment of the Common Cold. *Am Fam Physician* 2007;75:15-20.
23. Johnson EC, Kelley P, Friedman N, Chan K, Berman S. Ear, nose and Throat, Respiratory tract and mediastinum. In William W, Hay J, Myron JL, Robin RD, Mark JA, (eds). *Current Pediatric Diagnosis and Treatment 16th ed*. New York: MCGraw-Hill; 2018. p.459-501.
24. Low DE, Desrosiers M, McSherry J, Garber G, Williams JW Jr, Remy H, et al. A practical guide for the diagnosis and treatment of acute sinusitis. *CMAJ* 1997;156:1-14.
25. De Sutter AI, Saraswat A, van Driel ML. Antihistamines for the common cold. *Cochrane Database Syst Rev* 2015;2015:CD009345.
26. Marchant JM, Newcombe PA, Juniper EF. What is the burden of chronic cough for families? *Chest* 2008;134:303-9.
27. Murgia V, Manti S, Licari A, De Filippo M, Ciprandi G, Marseglia GL. upper respiratory tract infection-associated acute cough and the urge to cough: New insights for clinical practice. *Pediatr Allergy Immunol Pulmonol* 2020;33:3-11.
28. Togoobaatar G, Ikeda N, Ali M, Sonomjams M, Dashdemberel S, Moria R, et al. Survey of non-prescribed use of antibiotics for children in an urban community in mongolia. *Bull World Health Organ* 2010;88:930-6.
29. Manti S, Tosca MA, Licari A, Brambilla I, Foidadelli T, Ciprandi G, et al. Cough remedies for children and adolescents: Current and future perspectives. *Pediatr Drugs* 2020;22:617-34.
30. Anggraini A, & Wirasmi S. Treatment patterns of acute respiratory tract infection in children under-fives in Bogor, Indonesia. *Health Science Journal of Indonesia* 2020;1:9-14.
31. Rubin BK. Mucolytics, expectorants, and mucokinetic medications. *Respir Care* 2007;52:859-65.
32. Duijvestijn YC, Mourdi N, Smucny J, Pons G, Chalumeau M. Acetylcysteine and carbocysteine for acute upper and lower respiratory tract infections in paediatric patients without chronic broncho-pulmonary disease. *Cochrane Database Syst Rev* 2009:CD003124.
33. Vorilhon P, Arpajou B, Vaillant Roussel H, Merlin É, Pereira B, Cabaillet A. Efficacy of vitamin C for the prevention and treatment of upper respiratory tract infection. A meta-analysis in children. *Eur J Clin Pharmacol* 2019;75:303-11.
34. Fondell E. Vitamin C, Vitamin E, and URTI. In: *Web-based studies of lifestyle factors and immune function*. Karolinska Institutet, From the Department of Medical Epidemiology and Biostatistics and Osher Center for Integrative Medicine. Stockholm: Karolinska Institutet; 2011. p.48-52.
35. Science M, Maguire JL, Russell ML, Smieja M, Walter SD, Loeb M. Low serum 25-hydroxyvitamin D level and risk of upper respiratory tract infection in children and adolescent. *Clin Infect Dis* 2013;57:392-7.

36. Aglipay M, Birken CS, Parkin PC, Loeb MB, Thorpe K, Chen Y, et al. Effect of high-dose vs standard-dose wintertime vitamin d supplementation on viral upper respiratory tract infections in young healthy children. *JAMA* 2017;318:245-54.
37. Satomura K, Kitamura T, Kawamura T, Shimbo T, Watanabe M, Kamei M, et al. Prevention of upper respiratory tract infections by gargling: a randomized trial. *Am J Prev Med* 2005;29:302-7.
38. Ahmad L. Impact of gargling on respiratory infections. *All Life* 2012;14:147-58.
39. Li Song X, Yang T, Chen Y, Gong Y, Yin X, Lu Z. A systematic review of antibiotic prescription associated with upper respiratory tract infections in China. *Medicine (Baltimore)* 2016;95:3587-94.
40. AbRahman N, Teng CL, Sivasampu S. Antibiotic prescribing in public and private practice: a cross-sectional study in primary care clinics in Malaysia. *BMC Infect Dis* 2016;16:208-16.
41. Bakaki PM, Horace A, Dawson N, Winterstein A, Waldron J, Staley J, et al. Defining pediatric polypharmacy: A scoping review. *PLoS One* 2018;13:e0208047.