

A pharmacoepidemiological study of prescription pattern for upper respiratory infections in a tertiary health care center

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Upper respiratory tract infections (URTIs) constitute one of the most common causes of seeking medical advice, both in primary health care and in the hospital environment.<sup>1,2</sup> Most of these infections are caused by viruses, and usually do not require treatment with antibacterial agents. Symptomatic treatment to reduce patient suffering may be all that is required.<sup>1,2</sup> Irrational prescribing of antibacterial agents for URTIs, especially those caused by viruses such as common cold and viral pharyngitis, is a worldwide problem.<sup>3</sup> The excessive and irrational use of antibacterial agents has been implicated as one of the main causes of the emergence of bacterial resistance to antibiotics.<sup>4</sup> Several current clinical practice guidelines for the use of antibiotics in URTIs are available.<sup>1</sup> This work was designed to collect information on the pattern of prescriptions for URTIs in a tertiary health care setting located within the Southwestern part of Saudi Arabia. The purpose of the work was to identify deficiencies and provide suggestions for a more rational prescription behavior for URTIs. All outpatient prescriptions from within the hospital, irrespective of the clinic of origin, received by and kept in the pharmacy were the target of the study. One-year prescriptions during the period 8th April 2000 until 7th April 2001 were analyzed retrospectively. This period was divided into 4 seasons: spring, summer, fall and winter. One week (5 working days) of each season was sampled randomly and systemically as every other prescription. Of these, all prescriptions with a diagnosis of URTI, common cold, influenza, rhinitis, otitis media, sinusitis, tonsillitis, pharyngitis or cough were analyzed for the type and number of drugs prescribed. When a combination product was prescribed, its components are counted as separate entities. The local "Ethics Committee" at Aseer Central Hospital approved the study. The data generated were fed to the SPSS program and simple descriptive statistics were used to analyze the results. A total of 3796 prescriptions were reviewed, 905 (23.8%) of which carried a diagnosis of either an unspecified URTI, common cold, influenza, rhinitis, pharyngitis, otitis media, sinusitis, tonsillitis or cough. The majority of prescriptions (75.6%)

carried the diagnosis URTI without specifying the type, while 15.3% carried the diagnoses otitis media, sinusitis and tonsillitis. The age group distribution of the prescription included 35% for the pediatric age group and 19.2% for adults, while such information was missing in 45.7% of prescriptions. The most frequently prescribed drug groups were in descending order: paracetamol was present in 77.9% of prescriptions, antibacterial agents in 67.5%, histamine H<sub>1</sub>-receptor antagonists in 59.8%, and decongestants (α<sub>1</sub>-adrenoceptor agonists) in 33.1% of prescriptions. Prescriptions of antipyretics for patients with URTI are considered appropriate to alleviate fever and are a reasonable symptomatic treatment. The most frequently prescribed antibacterial agents were penicillins (50.5% of all prescriptions), especially amoxicillin, and in few cases, ampicillin, penicillin V or penicillin G, followed by macrolides (5.3%), cephalosporins (first generation and cefuroxime) (5%), and cotrimoxazole (2.3%). Other antibacterials and various other combinations of antibiotics appeared in 4.4% of all prescriptions. Antibiotics prescribed according to the type of URTI are presented in **Table 1**. Our finding of 65.2% of prescriptions for unspecified URTI containing antibacterial agents is close to the 52% figure reported by Gonzales et al.<sup>3</sup> Prescribing of antibacterial drugs for unspecified URTI, although difficult to assess, does not seem to be appropriate as the site of URTIs can be identified in many cases on clinical ground alone, and it seems that many physicians are not keen on being more specific. Our finding that 17.5% of prescriptions labeled with common cold and other viral causes of URTI as a diagnosis received antibacterial agents is less than percentages of 51% and 40-60% which have been reported by Gonzales et al.<sup>3</sup> and Mainous et al.,<sup>5</sup> respectively. It is not acceptable to prescribe antibacterial drugs for viral causes of URTI. Although some prescribers believe that their use could prevent secondary bacterial infections, it has been shown that amoxicillin/clavulanic acid is ineffective in preventing otitis media in children with viral URTI, even in susceptible patients.<sup>6</sup> Although pharyngitis is mainly caused by viruses, 88.5% of prescriptions labeled with pharyngitis as a diagnosis contained antibacterial agents with amoxicillin (and in few cases ampicillin) being the most frequently prescribed (65.4%). Such antibiotics will be justified for bacterial causes of pharyngitis such as *Streptococcus pyogenes*.

Our finding that 95.1% of prescriptions labeled with otitis media and sinusitis and 97.4% of prescriptions labeled with tonsillitis receiving antibacterial agents is reasonable since these infections are mainly caused by bacteria. In both situations, amoxicillin was the most frequently

prescribed, followed by second generation cephalosporins for otitis media and sinusitis and macrolides for tonsillitis. These findings are in accordance with the recommended clinical practice guidelines.<sup>1</sup> Ochoa et al<sup>2</sup> reported that 69.2% of cases of otitis media and sinusitis and 83% of cases of tonsillitis received the appropriate antibiotic either the first choice or an alternative. Adults, in general, were more frequently prescribed antibiotics (77%) than the pediatric age group (59.3%) (Pearson chi-square value 50.328,  $p < 0.05$ ). Histamine H<sub>1</sub>-receptor antagonists were found in 59.8% of prescriptions. However, in 4.6% of prescriptions, 2 antihistamines were simultaneously prescribed and one prescription contained 3 antihistamines. Histamine H<sub>1</sub>-receptor antagonists were found in 70% of prescriptions with the diagnoses common cold, influenza and rhinitis, 68.8% of those with cough, 65.1% of those with unspecified URTI, 39.3% of those with otitis media and sinusitis, 30.8% of those with tonsillitis, and in 26.9% of those with pharyngitis as diagnoses.

Decongestants (1-adrenoceptor agonists) were found in 33.1% of all prescriptions, while in 3.5% of prescriptions, 2 decongestants were simultaneously prescribed. They were in 57.5% prescriptions for common cold influenza and rhinitis, 36.1% for unspecified URTIs, 31.3% for cough, 18% for otitis and sinusitis, 16.7% for tonsillitis and 3.8% for pharyngitis. Prescription of more than one H<sub>1</sub>-receptor antagonist or more than one decongestant is rather strange. It indicates the unawareness of the prescriber about the identity of the active ingredients of the pharmaceutical products he or she is prescribing, which might put patients on undue

danger regarding the adverse effect of these drugs. It may also indicate the influence of promoters of pharmaceutical products on the prescribing habits of physicians, being apparently the sole source of information for few physicians. The role of the dispensing pharmacist in such cases should be to call the prescriber to discuss the matter with him or her, to be able to prevent such an occurrence. This will have a positive impact, both on patients' health and the financial resources of the hospital. Antitussives were found in 37.5% of prescriptions carrying cough as diagnosis, while expectorants and mucolytics were found in 6.3% of prescriptions with cough as diagnosis. Antitussives was infrequently prescribed being found in 7.8% of prescriptions while expectorants/mucolytics in 1.8% of prescriptions.

In conclusion, most prescriptions contained the diagnosis "URTI" unspecified and some of them only specified the type of URTI. The most frequently prescribed drugs in descending order were: paracetamol, antibacterial agents, histamine H<sub>1</sub>-receptor blockers and decongestants. Antibacterial agents were used for unspecified URTI and viral causes of URTI. Antitussives, expectorants and mucolytics were infrequently used. These results emphasize the need for establishing local clinical practice guidelines for the treatment of URTIs, utilizing local and international experience, training practitioners on rational prescribing and educating them on how to use the guidelines. Establishing a monitoring system to ensure adherence to the guidelines is beneficial. The pharmacist also should be in a position to enhance rational prescribing through professional cooperation with the prescriber.

Table 1 - Antibiotic prescription according to type of upper respiratory tract infection stated in the prescription order.

Antibiotics	Number of patients (%)					
	URTI	Common cold influenza rhinitis	Pharyngitis	Otitis media sinusitis	Tonsillitis	Cough
No antibiotic	238 (34.8)	33 (82.5)	3 (11.5)	3 (4.9)	2 (2.6)	15 (93.8)
Penicillins*	349 (51)	6 (15)	17 (65.4)	28 (45.9)	56 (71.8)	1 (6.2)
FGC, cefuroxime	32 (4.7)	0 (0)	0 (0)	9 (14.8)	4 (5.1)	0 (0)
Macrolides	34 (5)	0 (0)	2 (7.7)	1 (1.6)	11 (14.1)	0 (0)
Co-trimoxazole	17 (2.5)	0 (0)	0 (0)	4 (6.6)	0 (0)	0 (0)
Others or combination	14 (2)	1 (2.5)	4 (15.4)	16 (26.2)	5 (6.4)	0 (0)
Total with antibiotic	446 (65.2)	7 (17.5)	23 (88.5)	58 (95.1)	76 (97.4)	1 (6.2)
<b>Total</b>	<b>684 (100)</b>	<b>40 (100)</b>	<b>26 (100)</b>	<b>61 (100)</b>	<b>78 (100)</b>	<b>16</b>

\*Penicillins are mainly amoxicillin and few, ampicillin, penicillin G or penicillin V.  
URTI - Upper respiratory tract infection, FGC - first generation cephalosporins.

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## Outcomes of penicillin toxicities on DNA in rats

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Penicillin is a non-toxic class of antibiotics, which are used for most infections caused by Gram-negative cocci and majority Gram-positive bacteria. Sodium salt of penicillin G reaches a maximum of plasmatic concentration in 15 or 30 minutes. Although many indication of penicillin derivations are also clinically has toxic and adverse effects. Organ toxicity in urinary bladder,<sup>1</sup> DNA damage in children with rheumatic fever,<sup>2</sup> convulsions induced by penicillin and neurotoxic effects,<sup>2,3</sup> were studied in literature. However, no studies of any kind have investigated the effects of penicillin's toxicity on DNA quantity in muscles and organs. Thus, the purpose of this study was to show effect of penicillin derivates toxicity on DNA quantities in muscles and organs in rats with

meningitis.

The study was conducted in the Faculty of Arts and Sciences, Dumrupinar University, Kutahya, Turkey between the year 2002-2004. This study was approved by the local Institutional Ethic Committee. Experiments were conducted in 160 adult female rats (Sprague Dawley). There were 10 rats in each group (12 experimental and 4 control groups). We tested a well-characterized rat's model of pneumococcal meningitis. Animals were weighed and meningitis was induced by transcutaneous intracisternal injection of 20 µl of  $1 \times 10^7$  colony-forming units (cfu)/ml of *Streptococcus pneumoniae* type 3 after short-term anesthesia with halothane. All infected rats showed clinical signs of meningitis and the following day, penicillin derivatives have been injected as intraperitoneal 100 mg/kg/day to the experimental groups 3 times a week and during 60 day. After an overdose of thiopental, rats were perfused transcardially and the organs and muscles were extracted and rapidly frozen on dry ice. Certain grams (3 gm liver, 2.7 gm lung, 2.4 gm brain, 3.6 gm kidney, 1.02 gm tongue and 2.5 gm ovary, 5 gm from each muscle) of frozen organs or muscles were thawed, and washed in 5 times in 100 ml ice-cold portions of 0.1 M aqueous sodium citrate (pH 7.4) or 0.1 ethylenediaminetetraacetate (EDTA) (pH 7.35). The homogenate is centrifuged for 30 minutes at 1800 x g and the supernatant discarded. The final residue was extracted with 1000 ml of 2 M aqueous NaCl solution and was left at 4°C for 1 day and then centrifuged for 1 hour at 1900 x g. To the opalescent supernatant 2 volume of absolute ethanol is added at a rate of 150 ml/ hr with constant slow swirling of the recipient flask; washed in 75% aqueous ethanol, drained, and redissolved, as described before, in a cooled tissue grinder in 1000 ml of 0.14 M aqueous NaCl solution made 0.015 M with respect to sodium citrate (pH 7.1), hereafter called "standard buffer". To this solution is added 1/9 volume of 5% Duponol in 45% aqueous ethanol and the mixture was stirred for 1 hour at room temperature. The mixture, which contains precipitated Duponol is then centrifuged for one hour at 31.000-x g to the clear supernatant 2 volume of ethanol redissolved in 1000 ml of standard buffer with 1/9 volume of 5% Duponol. Solid NaCl is then added to obtain 5% NaCl solution, and the mixture is stirred, stored, and centrifuged. To the final clear supernatant, 2 volume of absolute ethanol is slowly added, and the fibers are lifted, washed in 75% ethanol, and redissolved in standard buffer to yield a clear, very viscous solution, containing 1 - 2 microgram of DNA /per milliliter. The product is stored in the frozen state at