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## EVALUATION OF DRUG-DRUG INTERACTIONS IN PATIENTS ADMITTING TO THE EAR NOSE AND THROAT CLINIC

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### Research Article

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### Abstract

Drug interactions are defined as the situation that occurs when two drugs are used together, as a result of the pharmacological effect of one of the drugs being changed by the other. Drug interactions can cause serious consequences such as the development of adverse events, ineffectiveness of the treatment, or mortality. The prescriptions of 106 patients who applied to the ear, nose, and throat outpatient clinic between January and December 2021 were examined retrospectively. 106 prescriptions were included in the study. Twelve major, 19 moderate, and 9 minor interactions were detected in 106 prescriptions. Although there are relatively few interactions compared to studies conducted with other patient groups, interactions can affect the clinical status of the patient. More attention should be paid to drug interactions in these patients, especially physicians and pharmacists.

**Keywords:** Drug interactions, Ear-nose-throat diseases, Antihistamines.

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## Özet

İlaç etkileşimleri, iki ilacın birlikte kullanılması durumunda bir ilacın farmakolojik etkisinin diğer ilaç tarafından değiştirilmesi sonucu ortaya çıkan durumu ifade eder. İlaç etkileşimleri, advers olayların gelişimi, tedavinin etkisizliği veya mortalite gibi ciddi sonuçlara yol açabilir. Ocak-Aralık 2021 tarihleri arasında kulak, burun, boğaz polikliniğine başvuran 106 hastanın reçeteleri retrospektif olarak incelendi. Çalışmaya 106 reçete dahil edildi. 106 reçetede 12 majör, 19 orta ve 9 minör etkileşim tespit edildi. Diğer hasta gruplarıyla yapılan çalışmalara kıyasla nispeten daha az etkileşim olmasına rağmen, etkileşimler hastanın klinik durumunu etkileyebilir. Bu hastalarda ilaç etkileşimlerine daha fazla dikkat edilmeli, özellikle hekimler ve eczacılar tarafından.

**Anahtar Kelimeler:** İlaç etkileşimleri, Kulak-burun-boğaz hastalıkları, Antihistaminikler.

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## 1. Introduction

Ear, nose, and throat (ENT) diseases affect people of all ages and often cause significant changes in the health of patients. They are responsible for many hospital visits worldwide, significant morbidity, and rarely mortality. A wide variety of medications, from antibiotics to antihistamines, can be used in the treatment of ENT diseases. Many infectious diseases have been controlled through improving living conditions, public health measures, and the use of antimicrobial agents (Bhat, 2015).

Although preventable, drug-drug interactions (DDI) can have harmful effects on the patient, including mortality. Adverse effects can be seen as toxicity resulting from increased drug effect or therapeutic failure resulting from decreased drug effect. Drug interactions should also be considered in the differential diagnosis of symptoms. Interactions with the use of drugs are known to be the most common type of complications that develop during hospital treatment. The rate of preventable DDI among DDI is around 3-5% (Yunes, 2011). Allergic reactions or unpredictable adverse effects due to drug use are around 25%. During the treatment, Situations encountered in the management of treatments and dose calculations of drugs administered to the patient constitute 70% of the complications (Seynaeve, 2011). Today, drug interactions are a major problem globally. In a study conducted in the United States, 30.3% of outpatients were potentially at risk of DDI (Delafuente, 2003).

In this study, the prescriptions of patients who applied to the ENT outpatient clinic were retrospectively examined. The study aimed to examine the interactions of drugs prescribed in ear, nose, and throat outpatient clinics, which are frequently treated as outpatients, and to increase awareness that they can cause serious problems in this field.

## **2. Material and Methods**

In our study, the prescriptions of patients who applied to the ear, nose, and throat outpatient clinic between January 2021 and December 2021 were examined retrospectively. Demographic data of the patients, such as age and gender, were collected from electronic patient files within the hospital system. Patients over the age of 18 and with at least 2 medications prescribed were included in the study. Drug-drug interactions were analyzed using RxMediaPharma™, a software program available only to healthcare professionals. The reason why this database was chosen is that it is easier to access than other databases. Because the cost of accessing other databases is quite high. The database used at our hospital is RxMediaPharma. In clinical practice, its classification is guiding.

In this licensed program, drug interactions are divided into three levels: "Low", "Moderate" and "Major" according to the clinical severity of the interaction.

### *2.1. Statistical analysis*

Statistical Package for the Social Sciences (IBM SPSS) 21.0 program was used for statistical evaluation. A P value of less than 0.05 was considered statistically significant. Data are given as numbers or %. The chi-square test was used to compare categorical variables.

## **3. Results and Discussion**

Of the 106 prescriptions included in the study, 52.8% (n=56) belonged to women and 47.2% (n=50) belonged to men. The average number of drugs in prescriptions was 2.5 (minimum 2, maximum 5). The average age of prescription holders is 40.4 years. The average age of female patients is 40 (minimum 21, maximum 81); The average age of male patients was found to be 40.9 years (minimum 19, maximum 78). There was no significant difference between the average ages of men and women ( $p = 0.078$ ).

In the study, a total of 12 major, 19 medium, and 9 low-level interactions were detected. The average interaction per prescription was found to be 0.4. The interaction contents are shown in Table 1. When all interactions were examined, it was seen that the most frequently interacting drug group was classified according to group, with antihistamines in the first place, nonsteroidal anti-inflammatory drugs (NSAIDs) in the second place, and antibiotics in the third place.

**Table 1.** Drug Interactions and Classification

<b>Interaction</b>	<b>Number of interactions</b>	<b>The ratio of total interactions</b>
<b><i>Major</i></b>	<b>12</b>	<b>30</b>
Diclofenac x Naproxen	8	20
Azithromycin x Moxifloxacin	4	10
<b><i>Moderate</i></b>	<b>19</b>	<b>47.5</b>
Dimenhydrinate x Hydroxyzine	9	22.5
Cetirizine x Hydroxyzine	6	15
Hydroxyzine x Clarithromycin	4	10
<b><i>Low</i></b>	<b>9</b>	<b>22.5</b>
Ceftriaxone x Diclofenac	9	22.5

In our study, a total of 40 interactions were observed in 106 prescriptions. In prevalence studies conducted on malignancy patients in 2011, the average number of potential drug interactions per patient was found to be 1.4 in 278 outpatients, and the average number of potential drug interactions per 100 patients in inpatients was determined to be 8 (Van, 2011). In a study conducted by Mutluay in 2023, 199 interactions were detected in 94 prescriptions belonging to kidney transplant patients. In Taiwan, Fang Lin et al. conducted in 2011, an unnamed internet-based database was used and the prescriptions of 81650 patients who applied to a medical center were evaluated. (Lin, 2011.). The reason for relatively few interactions may be that patients applying to the ear, nose, and throat outpatient clinic are treated with fewer drugs. Because, as the number of drugs in the prescription increases, the frequency of drug interactions also increases. Nevertheless, ignoring drug-drug interactions can have a major impact on the

medical treatment of patients. DDI increases in direct proportion to the number of medications used in the treatment. It is known that the increase in the number of drugs ordered is a risk factor for DDI (Andrade 2017). The small number of drugs in the prescriptions included in our study may also have caused the number of interactions to be low.

In our study, the drug group with the most interactions was antihistamines. Agents with anticholinergic properties may cause additive effects when used in combination. Because patients are often unaware of the extent to which their performance is impaired, it is possible that they may not exercise adequate caution when performing potentially hazardous activities such as driving or operating heavy machinery while under the influence of antihistamines. Adults who work in jobs that require attention and concentration are likely to be adversely affected by antihistamines. These additive effects are not limited to driving and operating hazardous machinery but can also adversely affect the performance of clerical work. Additionally, since drug-food interactions in patients were not examined due to study limitations, taking this group of drugs together with alcohol increases the risk of toxicity (Kay, 2000; Kaferelli, 2023). In addition, with so many medications being used today, it is impractical for healthcare professionals to rely solely on their knowledge to prevent potential drug interactions. It is known that some interactions and side effects reduce patient compliance with treatment. Therefore, physicians' monitoring of databases when prescribing and prescribing drugs within the framework of appropriate prescribing rules can reduce the risks of interactions.

In our study, two nonsteroidal anti-inflammatory drug interactions were observed in 8 prescriptions. Collateral use of a nonsteroidal anti-inflammatory drug (NSAID) may increase the potential for serious toxicity, including subjective side effects such as heartburn, bleeding in the gastrointestinal tract, ulceration, and perforation. These events can occur at any time during NSAID use, even without symptoms. This risk depends on both the dose and duration of treatment. Therefore, toxicity increases with concurrent use. In addition, advanced age, alcohol, and cigarette use also cause increased toxicity and should be questioned in prescribing. The most common NSAID side effects occur in a large proportion of patients and may cause patients to discontinue. In addition, chronic use of NSAIDs causes serious gastroduodenal ulcerations and the associated mortality rate is significant (Hunter, 2011; Bindu, 2020). In the data of the Ministry of Health of the Republic of Turkey published in 2016, it was said that more than 2 billion boxes of medicine were consumed in Turkey. According to these data, NSAIDs are in the first place and

antibiotics are in the second place (Ministry of Health, 2016). When this consumption is taken into consideration, the importance of interaction becomes evident.

In our study, the most common drug group with drug interactions was antibiotics. Turkey ranks first in the world in antibiotic consumption, according to 2021 data from the Organization for Economic Co-operation and Development (OECD, 2021). Nonsteroidal anti-inflammatory drugs may increase the effectiveness of antibiotics through pharmacokinetic interactions, as shown in experimental studies by Joly et al. In a study, it was stated that diclofenac caused a significant decrease in biliary ceftriaxone excretion in rabbits, although there was no significant decrease in bile flow. Alvim et al. In the study conducted by et al., it was determined that 46% of the drug-drug interactions were related to antimicrobial drugs and that the interaction between 51% of these drugs was significantly severe in patients who were hospitalized in the intensive care unit for a long time and used 15 antimicrobial agents. (Alvim, 2015; Wang, 2022)

The limitation of our study is that, due to the retrospective design of the study, over the counter and plant-derived medications used by the patients could not be included in the study. Since the study was planned retrospectively, patients' demographic information, smoking, and alcohol consumption could not be examined. This is also a limitation of our study. Prospective studies can provide access to larger samples and information.

#### **4. Conclusion**

As a result, the most important step in preventing drug interactions and the problems they cause is awareness. To improve patients' quality of life and ensure patient safety, multiple drug use should be avoided. In this way, both side effects and interactions can be kept to a minimum, and healthcare costs can be reduced.

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