Retrospective Analysis of Possible Drug Interactions in Prescriptions Written by Branch and Emergency Physicians

○ Kasım Turgut[1], ○ Ali Gür[2], ○ Abdullah Keyfo Kama[3], ○ Muhammet Gökhan Turtay[4], ○ Hakan Oğuztürk[5]

[1]Department of Emergency Medicine, Adıyaman University Faculty of Medicine, Adıyaman, Turkey
[2]Department of Emergency Medicine, Atatürk University Faculty of Medicine, Erzurum, Turkey
[3]Department of Emergency Medicine, Elazığ City Hospital, Elazığ, Turkey
[4]Department of Emergency Medicine, Inonu University Faculty of Medicine, Malatya, Turkey
[5]Department of Emergency Medicine, Ankara City Hospital, Ankara, Turkey

Abstract

Objectives: Drug-drug interactions may occur when more than one drug is taken by the same patient. These interactions can result in increasing, decreasing or preventing the effectiveness of drugs. In this study, prescriptions given by branch and emergency physicians were examined in terms of possible drug interactions.

Materials and Methods: Patients over 65 years of age who received a prescription from both the emergency department and the internal medicine or cardiology outpatient clinic were screened over a period of six months from July to December 2019. For the selected patients, information on the name and number of drugs prescribed, age, and gender were recorded. Then, the interactions between the drugs included in the prescriptions were investigated using Drug Interaction Checker-Medscape software.

Results: The study included 93 patients (57% females), with a mean age of 73.5 years. A total of eleven serious interactions, with the highest number belonging to the interaction of aspirin-ramipril were observed in the prescriptions given by branch physicians. Comparing the prescriptions of the branch and emergency physicians, 33 serious interactions, mostly that of ibuprofen-aspirin, were detected. Among the prescriptions of branch physicians, the majority of interactions were observed between aspirin and B blockers. For the emergency physicians, the highest number of interactions were seen in NSAID-NSAIDs. In the comparison of the prescriptions of the branch and emergency physicians, the highest number of interactions was 28, observed between NSAID and beta-blockers.

Conclusion: Emergency physicians should take a detailed history of elderly patients, especially concerning their regularly renewed prescriptions when prescribing NSAID-group drugs.

Key words: emergency, aspirin, drug interaction, NSAIDs

Özet

Amaç: Aynı hasta tarafından birden fazla ilaç aynı anda alındığında ilaç-ilaç etkileşimleri oluşabilir. Bu etkileşimler ilaçların etkinliğini arttırma, azaltma veya engelleme şeklinde olabilirler. Bu çalışmada, branş ve acil hekimlerinin yazdığı reçeteler incelenerek olası ilaç etkileşimleri incelendi.

Gereç ve Yöntem: Temmuz 2019 - Aralık 2019 arasını kapsayan 6 aylık sürede hem acil servisten hem de dahiliye veya kardiyoloji poliklinikten reçete düzenlenen 65 yaş üstü hastalar belirlendi. Belirlenen hastalara, yazılan ilaçların isimleri, ilaç sayısı, hastalara ait yaş, cinsiyet gibi bilgiler kaydedildi. Sonrasında Drug Interaction Checker- Medscape programı kullanarak yazılan reçetelerdeki ilaç etkileşimleri araştırıldı.

Bulgular: Çalışmaya 93 hasta dahil edildi. Dahil edilen hastaların yaş ortalaması 73,5 yıldı. Hastaların 57%'si kadındı. Branş hekimlerinin yazdığı reçetelerde aspirin-ramipril arasında en yüksek sayıda olmak üzere toplam 11 ciddi etkileşim görüldü. Acil ve branş hekimlerinin reçeteleri arasında en fazla ibuprofen-aspirin olmak üzere 33 ciddi düzeyde etkileşim tespit edildi. Branş hekimlerinin reçetelerinde en fazla aspirin-B bloker arasında etkileşim görüldü. Acil hekimlerinin reçetelerinde en fazla NSAID-NSAID arasında etkileşim vardı. Acil ve branş hekimlerinin reçeteleri arasında ise 28 etkileşim ile ne yüksek NSAID-B bloker arasında görüldü.

Sonuç: Acil hekimleri, ileri yaş hastalara özellikle NSAID grubu ilaçları yazarken hastanın kullandığı raporlu ilaçlarla ilgili ayrıntılı öykü almalıdır.

Anahtar kelimeler: acil, aspirin, ilaç etkileşimi, NSAID

Introduction

Polypharmacy, which is defined as the simultaneous use of multiple drugs by an individual, refers to the use of two or more drugs in some definitions while four or more drugs in others. The most important reason for polypharmacy is the need to prescribe drugs by more than one branch due to the increasing number of chronic problems with advancing age, such as diabetes, coronary artery disease, and hypertension. Another cause is the irregular and incorrect use of

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drugs due to the patient being elderly or negligent behavior of caregivers[1]. In studies conducted, the rate of polypharmacy in prescriptions has been reported to be 29% in the USA, mostly seen over the age of 75 years, 50% in Canada, and 53% in Italy[2].

Some patients need to use more than one drug at the same time, even if it is undesirable. In such cases, interactions between the two drugs can be seen. This interaction can sometimes be in the form of increasing the effect of one drug while at other times, a reduction or inhibition occurs. As the number of drugs used increases, the probability of interactions also increases. While the probability of developing an adverse effect is approximately 40% in patients using five drugs at the same time, this risk reaches 80% in those simultaneously taking seven or more drugs. In the literature, these interactions have been classified as serious, moderate, and minor. Being aware of these interactions in advance can prevent adverse effects by adjusting the dose or changing the drug if necessary[3,4].

In this study, drug-drug interactions were investigated by examining the prescriptions given by physicians working in internal medicine, cardiology and emergency clinics. Our aim was to raise awareness of drug-drug interactions and prevent adverse effects in elderly populations in which polypharmacy is frequently seen.

Materials and Methods

This retrospective study was carried out in the emergency medicine clinic of a tertiary hospital. Patients over 65 years of age who presented to our emergency department between July and December 2019 and received a prescription from an emergency physician for any reason were identified. Then, the previous year prescriptions of these patients were examined from the hospital system, and it was investigated whether the same patients had been given any prescription report by branch physicians in the internal medicine or cardiology outpatient clinic. Thus, patients who received a prescription from both the emergency department and an outpatient clinic within the past year were identified. In Turkey, branch physicians usually prepare prescription reports that cover a one to two year period. In our study, we limited the history of drugs prescribed for the duration of one year from the emergency presentation. In order to detect the interactions between the drugs prescribed by two physicians, we assumed that the patient was using the drugs that s/he had been given by the branch physician at the time that the emergency physician wrote a prescription for the same patient. Patients who were given three or more drugs in the same prescription were included in the study. Information on the names and numbers of the drugs, and patient age and gender was recorded.

After the prescriptions given to the patients were compiled, the presence of interactions between the drugs was investigated using Drug Interaction Checker, Medscape software. First, the presence and levels of interaction were investigated for each patient in the prescriptions written by the branch physicians. Then, the prescriptions written by emergency physicians were examined. Finally, all the drugs prescribed by the branch and emergency physician were entered into the software, and the number and level of interactions between the prescriptions of the two physicians were determined. In addition, drugs or drug groups that were involved in the interaction were identified.

According to the results of the software, the interaction levels were determined as serious, moderate (close follow-up), and minor. According to the software, an example of a serious drug-drug interaction is the use of aspirin and ibuprofen at the same time. In this situation, ibuprofen may increase the anticoagulant effect of aspirin and cause bleeding. An example of a moderate interaction is the use of candesartan-flurbiprofen, in which flurbiprofen may reduce the effect of candesartan through pharmacological antagonism. Lastly, an example of a minor interaction is that of diltiazem-aspirin, in which the former may increase the antiaggregant effect of the latter[5].

Statistical Analysis

The study was carried out using SPSS v. 17.0. Descriptive statistics were given as mean ± standard deviation and percentages. For percentages, decimals were rounded to the nearest whole number where necessary.

Results

In this study, it was determined that a prescription containing three or more drugs was prepared for 157 patients in the emergency department over a period of six months. After examining these patients through the hospital system, 93 were determined to have also been prescribed drugs from the outpatient clinics within the past year, and thus were included in the study. The mean age of the patients was 73.5 years, and the majority were female (n = 53). When the prescriptions written by the branch physicians for these patients were examined, it was observed that there were 11 serious interactions in nine patients, 145 moderate interactions in 73 patients, 40 minor interactions in 17 patients, and no interaction in 11 patients. The prescriptions written by the emergency physicians revealed no serious interaction in any of the patients, 21 moderate interactions in 21 patients, six minor interactions in six patients, and no interaction in 66 patients. Examining the interactions of the drugs prescribed by two physicians, it was determined that there were 33 different serious interactions in 27 patients, 109 moderate interactions in 45 patients, and four minor interactions in

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four patients, while 29 patients did not have any drug-drug interaction (Figure 1).

Figure 1. Number of patients receiving prescriptions according to the working area of physicians
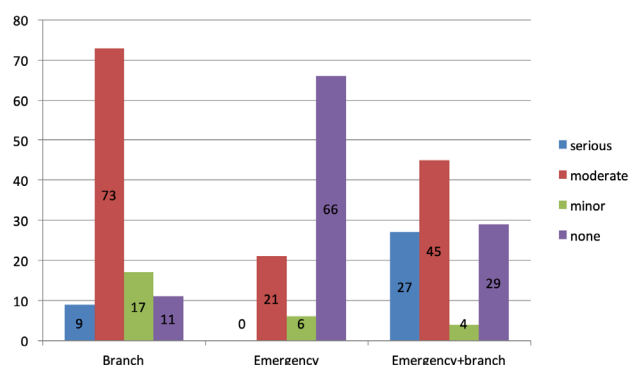
The drug that caused the highest number of interactions in the prescriptions written by the branch physicians was aspirin (85 interactions), followed by beta-blockers (70 interactions) and angiotensin II receptor blockers (ARBs) (35 interactions). In the prescriptions of emergency physicians, flurbiprofen (n = 10), ibuprofen (n = 9) and etodolac (n = 3) mostly caused interactions. Drug-drug pairs with the highest number of interactions were aspirin-beta-blockers (n = 33) among the branch physicians, NSAID-NSAIDs (non-steroidal anti-inflamatory drug) (n = 15) among the emergency physicians, and beta-blockers-NSAIDs (n = 28) and aspirin-NSAIDs (n = 25) in the comparative evaluation of the branch and one emergency physicians (Table 1).

Table 1. Drug groups with the highest number of interactions

Physician	Number of interactions
Branch	
Aspirin-Beta-blockers	33
Aspirin-Clopidogrel	16
Aspirin-ARBs	15
Emergency	
NSAIDs-NSAIDs	15
Caffeine-Pseudoephedrine	5
Chlorpheniramine-Codeine	2
Brach + emergency	
NSAIDs-Beta-blockers	28
NSAIDs-Aspirin	25
NSAIDs-ARBs	21

ARB= angiotensin II receptor blockers, NSAID= non-steroidal anti-inflammatory drug

Considering the drug groups that caused serious interactions, aspirin-ramipril was the most common in the prescriptions of the branch physicians, while there was no serious interaction in those of emergency physicians. When the prescriptions of the branch and emergency physicians were comparatively evaluated, it was seen that the most common drug pair that created serious interactions was ibuprofen-aspirin (Table 2).

Table 2. Number of interactions for drug pairs causing serious interactions

Physician	Number of interactions
Branch	**11**
Aspirin-ramipril	8
Valsartan-ramipril	3
Emergency + branch	**33**
Ibuprofen-aspirin	10
Ibuprofen-ramipril	6
Clarithromycin-clopidogrel	5
Ketoprofen-ramipril	3
Moxifloxacin-indapamide	3
Prednol-silodosin	2
Aspirin-ramipril	2
Clarithromycin-rosuvastatin	1
Clarithromycin-atorvastatin	1

Discussion

Drug-drug interactions and their side effects are important reasons for hospital admission and mortality. Farooqui et al. determined that an average of 4.6 drugs were given per prescription, and most were prescribed for diabetes at a rate of 28.4%[3]. In the literature, the results concerning the number of drugs included in one prescription vary, with one study reporting 7.8 drugs[6] while another observing 9 drugs[7] per prescription. In another study examining drug-drug interactions among the elderly, it was determined that 39% of the prescriptions written included 11 or more drugs[8]. In our study, the number of drugs per prescription was 3.9 among the branch physicians and 3.35 among the emergency physicians.

The geriatric population and patients with depression, HIV positivity, diabetes and hypertension constitute the groups in which polypharmacy is most commonly seen[9]. In a study by Obreli-Neto et al., it was stated that drugs were mostly prescribed due to hypertension and diabetes. In the same study, the drugs that caused the highest number of interactions were reported to be warfarin, NSAID, digoxin, and diuretics [10]. In another study, aspirin, NSAIDs, diuretics, and beta-blockers were identified as the drugs that most caused interactions[4]. In our study, we observed that aspirin, beta-blockers and the ARB-group drugs were most commonly prescribed by branch physicians and the NSAID-group drugs by emergency physician. Beta-blockers and NSAID also had the highest number of adverse effects in the prescriptions comparatively evaluated between the branch and emergency physicians. It was also seen that most prescriptions were for cardiovascular diseases.

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Limitations

In this study, only the information on the prescriptions was used and it was assumed that the patients used all the prescribed drugs. In addition, it was not investigated whether the patients presented to the hospital again after an adverse reaction and needed treatment. A multi-center study that will cover all health institutions in a city and examine hospital admission after adverse effects can yield more valuable results.

Conclusion

It was determined that the prescriptions of branch physicians had more drug-drug interactions than those of emergency physicians. The drug that caused the highest number of interactions was aspirin among the branch physicians and NSAIDs among the emergency physicians. Before prescribing NSAID-group drugs to patients on regularly renewed prescriptions, emergency physicians should investigate possible drug-drug interactions to significantly reduce the number of adverse effects.

References

1. Yıldırım AB, Kılınç AY. Yaşlıhastalarda polifarmasi ve ilaç etkileşimi [Polypharmacy and drug interactions in elderly patients]. Turk Kardiyol Dern Ars. 2017;45(Suppl 5):17 21. doi:10.5543/tkda.2017.92770

2. Jetha S. Polypharmacy, the Elderly, and Deprescribing. Consult Pharm. 2015;30(9):527 532. doi:10.4140/TCP.n.2015.527

3. Farooqui R, Hoor T, Karim N, Muneer M. Potential Drug-Drug Interactions among Patients prescriptions collected from Medicine Out-patient Setting. Pak J Med Sci. 2018;34(1):144 148. doi:10.12669/pjms.341.13986

4. Bucşa C, Farcaş A, Cazacu I, Leucuta D, Achimas-Cadariu A, Mogosan C, et al. M. How many potential drug-drug interactions cause adverse drug reactions in hospitalized patients?. Eur J Intern Med. 2013;24(1):27 33. doi:10.1016/j.ejim.2012.09.011

5. Drug Interactions Checker, Medscape Online Resources. Available from: https://reference.medscape.com/drug-interactionchecker

6. Soherwardi S, Chogtu B, Fazal P. Surveillance of the potential Drug-Drug Interactions in the Medicine Department of a Tertiary Care Hospital. J Clin Diag Res. 2012;6(7):1258-1261.

7. van Leeuwen RW, Swart EL, Boven E, Boom FA, Schuitenmaker MG, Hugtenburg JG. Potential drug interactions in cancer therapy: a prevalence study using an advanced screening method. Ann Oncol. 2011;22(10):2334 2341. doi:10.1093/annonc/mdq761

8. Kashyap M, D'Cruz S, Sachdev A, Tiwari P. Drug-drug interactions and their predictors: Results from Indian elderly inpatients. Pharm Pract (Granada). 2013;11(4):191 195. doi:10.4321/s1886-36552013000400003

9. Roblek T, Vaupotic T, Mrhar A, Lainscak M. Drug-drug interaction software in clinical practice: a systematic review. Eur J Clin Pharmacol. 2015;71(2):131 142. doi:10.1007/s00228-014-1786-7

10. Obreli-Neto PR, Nobili A, de Oliveira Baldoni A, Guidoni CM, de Lyra Junior DP, Pilger D, et al. Adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. Eur J Clin Pharmacol. 2012;68(12):1667 1676. doi:10.1007/s00228-012-1309-3