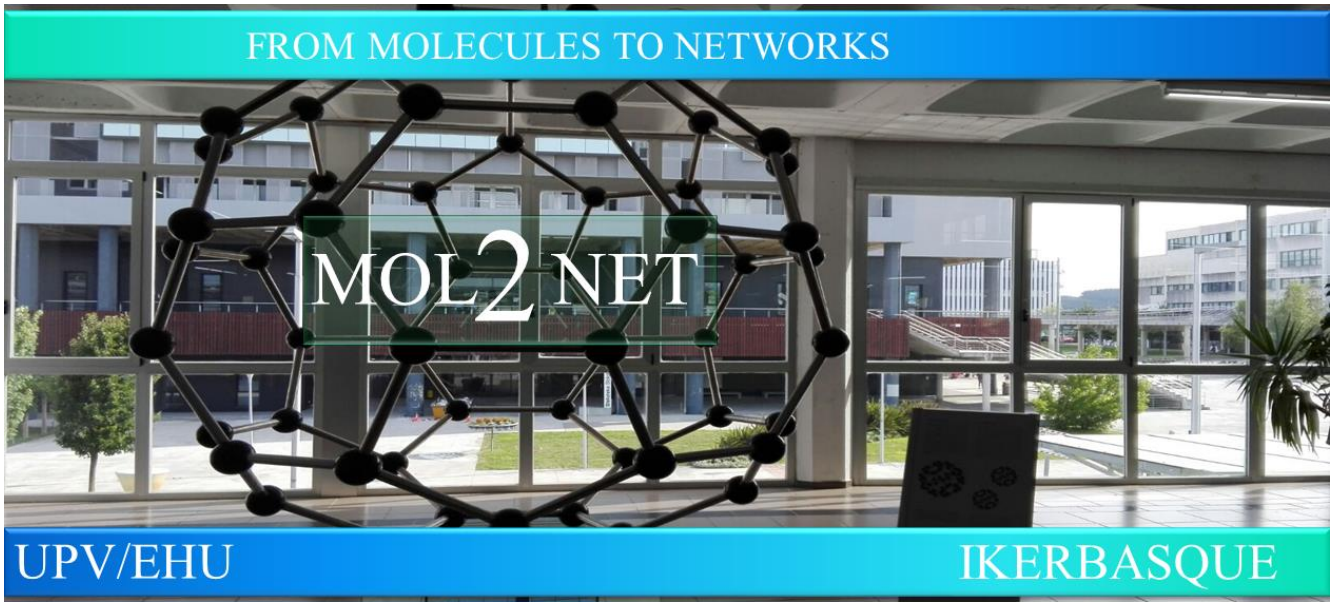
MOL2NET'23, Conference on Molecular, Biomedical, Computational, & Network Science and Engineering, 8th ed.



Assessing the situation of drug interactions at the Hospital of Traditional Medicine - Ministry of Public Security

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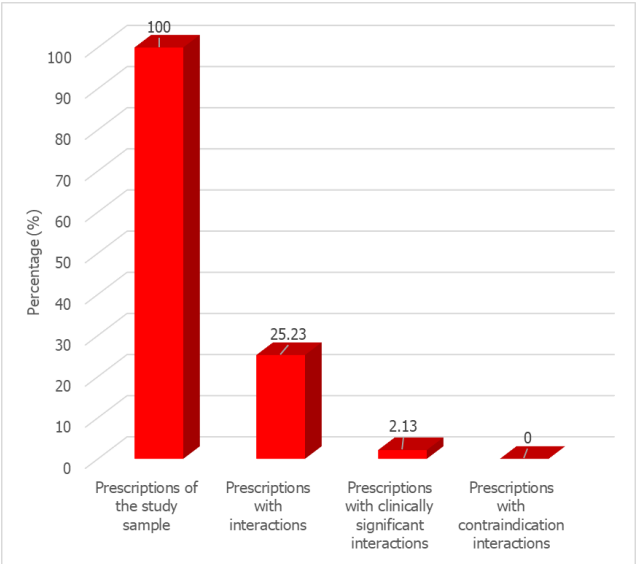
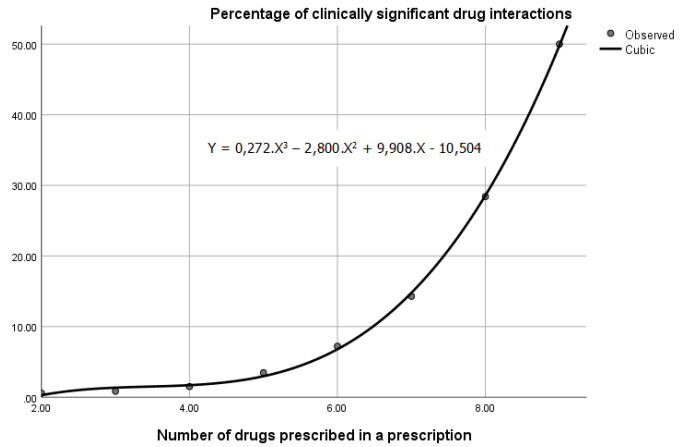
Graphical Abstract



Abstract.

Drug-drug interactions occur when one drug adds to or diminishes the effect of another drug or affects the absorption, distribution, metabolism, or excretion of another drug. A survey of 14,341 prescriptions corresponding to 14,341 patients at the traditional medicine hospital of the Ministry of Public Security showed that the average age of the patients was 58.77±13.83, the male/female ratio was 45.54/54.95. The number of patients treated for cardiovascular disease and metabolic endocrine disease accounted for the highest proportion, 46.24%. The average



number of drugs per prescription was 3.5±1.36 (drugs) in which the most commonly prescribed drugs were antidiabetic drugs (A10, 22.79%), drugs acting on the renin-angiotensin system (C09, 12.27%), calcium blockers (C08, 8.57%). The rate of prescriptions detected with drug interactions was 25.23%, the number of drug interactions calculated according to the total number of prescriptions with drug interactions was 1.74%. The frequency of occurrence of two pairs drug interactions perindopril - spironolactone, aspirine - hydrochlorothiazide is the largest, reaching values > 3/1000 prescription. The percentage of clinically significant drug interactions that increase sharply with the number of drugs used in a prescription is represented by the regression equation $Y = 0.272.X^3 – 2,800.X^2 + 9,908.X - 10,504$. *Patients prescribed more than 3 drugs were 5.86 times more likely to experience DICS than patients prescribed less than 3 drugs. Male patients when using the drug, the likelihood of developing DI is 1.90 times greater than that of female patients. The probability of occurrence of DICS in patients aged > 60 years is 1.44 times higher than in patients aged ≤ 60 years. There are 13/20 drugs that have a statistically significant effect on the occurrence of DICS. Strong influence on DI are other metabolic endocrine diseases (OR=1.34), other cardiovascular circulatory diseases (OR=2.89), and hypertension (OR=1,4).*

Introduction

Drug interactions, common problems in clinical practice, are one of the leading causes of adverse drug events, including toxicity or adverse reactions during use, failure to treatment, and can even lead to death [5]. The combination of drugs is inevitable, especially in the case of multiple diseases, multiple symptoms. In most cases, physicians actively combine drugs to maximize effectiveness and minimize side effects, or in some cases combine drugs after carefully weighing benefits and risks. However, adverse drug interactions can be prevented by special precautions or by taking interventions to reduce the risk. Therefore, in order to give appropriate warnings to help doctors weigh the benefits/risks of drug combinations, the research team assessed the current situation of drug-drug interactions at the Department of Medical Examination Traditional - Ministry of Public Security from which to make recommendations and attention in prescribing practices at hospitals.

Keyword: drug interactions (DI), drug interactions clinically significant (DICS)

Materials and Methods

Research subjects

The study was conducted on outpatient prescriptions prescribed at the clinic at the Traditional Medicine Hospital of the Ministry of Public Security. Prescriptions selected for the survey only include pharmaceutical drugs with the number of drugs in the prescription greater than or equal to 2, not using traditional medicine, prescribed from June 1, 2020 to August 31. 2020 (patients do not use dietary supplements during the time of taking prescription drugs).

Methods

Non-interventional cross-sectional description through retrospective data collection on patient applications. Based on data collected from outpatient prescriptions and results of interaction review, survey and analysis of patient characteristics, assessment of adverse drug interactions, factors affecting the likelihood of occurrence of drug interactions clinically significant.

Browse prescription drug interactions on the Micromedex Drug Interactions database (online version).

Statistical processing

Collected data were statistically processed using SPSS 26.0 software and Microsolf Excell 365.

Results and Discussion

Results

Patient characteristics

During the period from June 1, 2020 to August 31, 2020, the collected data extracted from the software was 25,296 prescriptions. These prescriptions were reviewed and then included in the study sample of 14,341 prescriptions corresponding to 14,341 patients.

Table 1. Patients characteristics in the study sample

No	Patient characteristics	Number (%) (n=14.341)
1	Gender: Male, n (%) Female, n (%)	 6.460 (45,05) 7.881 (54,95)
2	Age	58,77±13,83
3	Characteristics of disease group according to ICD 10 code	
3.1	Endocrine, nutritional and metabolic diseases	8.646 (23,78)
3.2	Diseases of the circulatory system	8.165 (22,46)
3.3	Diseases of the eye, ear	4.713 (12,97)

No	Patient characteristics	Number (%) (n=14.341)
3.4	Diseases of the musculoskeletal system and connective tissue	2.818 (7,75)
3.5	Diseases of the digestive system	5.099 (14.03)
3.6	Other diseases	2.243 (6,17)
3.7	Diseases of the genitourinary system	1.648 (4,53)
3.8	Mental and behavioural disorders	1.135 (3,12)
3.9	Diseases of the skin and subcutaneous tissue	767 (2,11)
3.10	Diseases of the respiratory system	389 (1,07)
3.11	Neoplasms	380 (1,05)
3.12	Certain infectious and parasitic diseases	253 (0,70)
3.13	Diseases of the nervous system	95 (0,26)

Patients in the study sample had an average age of 58.77±13.83 (year) with the proportion of men accounting for about 45.05% (Table 1). The proportion of patients with endocrine, nutritional and metabolic diseases and diseases of the circulatory system was 23.78% and 22,46%, respectively, the highest among 14,341 patients surveyed. In general, the results of the analysis of the disease group structure are relatively consistent with the hospital's disease model.

Characteristics of prescribed drugs

The average number of drugs per prescription was 3.5±1.36 (drugs). In which, the most commonly prescribed drugs are antidiabetic drugs (A10, 22.79%), drugs acting on the renin-angiotensin system (C09, 12.27%), calcium blockers (C08, 8.57%), lipid modifiers (C10, 7.81%), beta blockers (C07, 6.19%) and systemic antibacterials (J01, 5.53%) (Figure 1). Specifically, the most commonly prescribed active ingredients were metformine, gliclazide, amlodipine, perindopril and telmisartan with a prescription rate of 9.69%; 8.79%; 8.18%; 5.71% (Figure 2). This is also consistent with the survey of patient characteristics in which the prevalence of endocrine, nutritional and metabolic diseases and diseases of the circulatory system is the most common and highest.

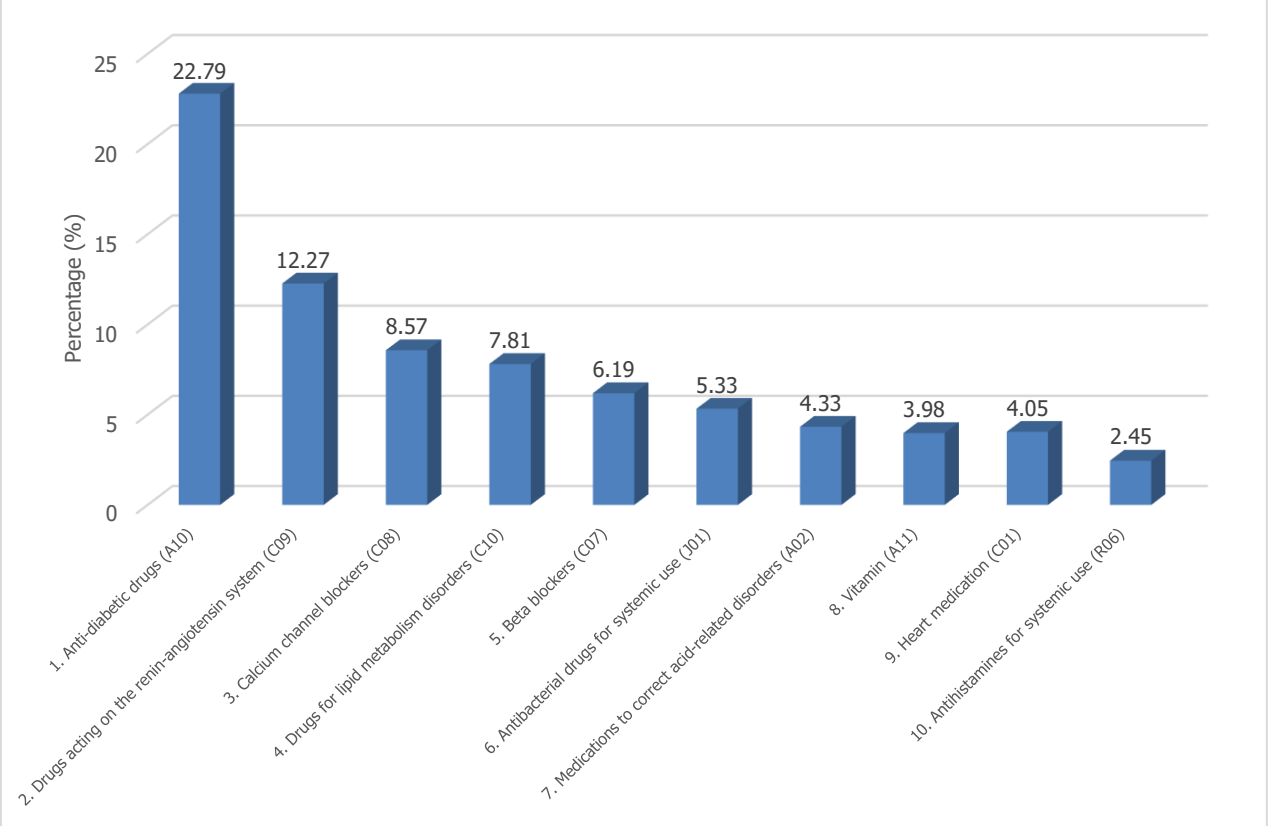


Figure 1. Top 10 most prescribed drug groups

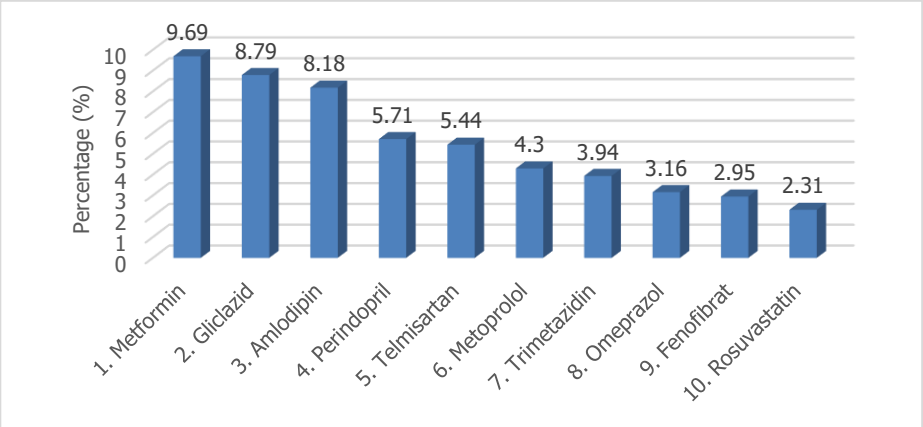


Figure 2. Top 10 most prescribed active ingredients

Assessment of adverse drug interactions

Prescriptions with drug interactions and drug interactions clinically significant drug

The survey results showed that 3,619 prescriptions had interactions ranging from major to moderate. In which, there were 307 prescriptions with DICS (Table 2). The ratio of prescriptions detected with drug interactions was 25.23%. In which, the ratio of prescriptions with DICS was 2.13%, no prescriptions with contraindicated interactions were detected (Figure 3).

Table 2. Number of drug interactions in the study

Drug interactions	Quantity			Total (%)
	Month 6	Month 7	Month 8	
Contraindications	0	0	0	0 (0)
Major	522	564	499	1.585 (25,13)
Moderate	1.447	1.629	1.647	4.723 (74,87)

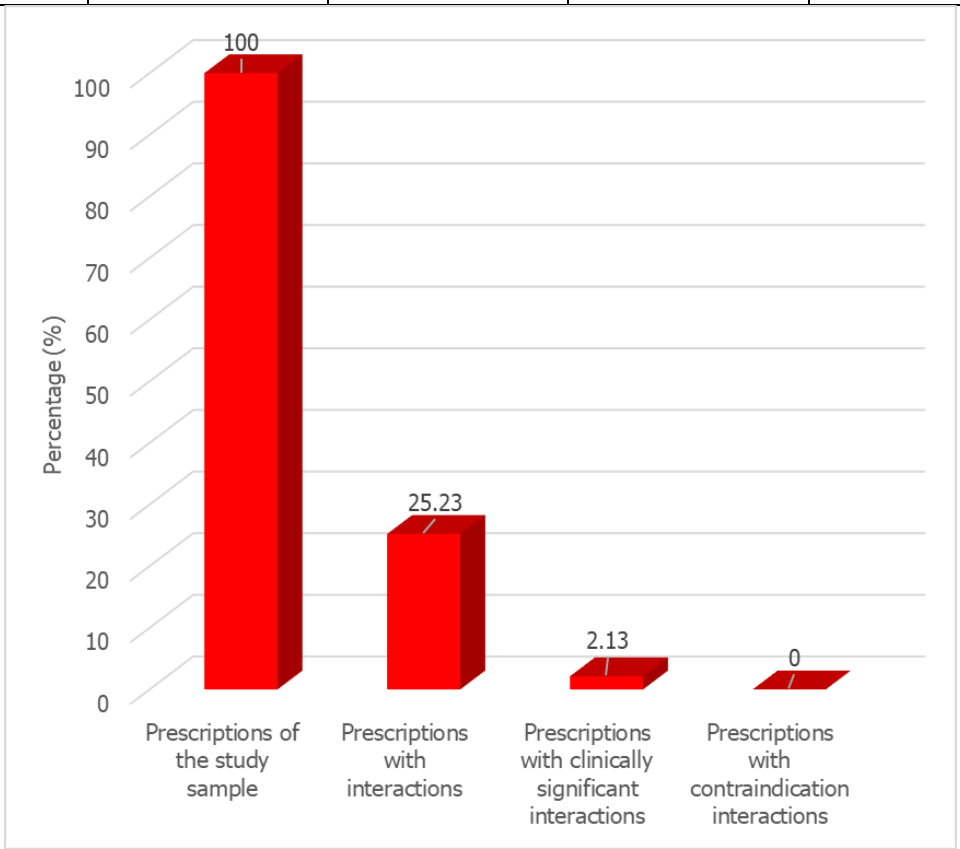


Figure 3. Prevalence of prescriptions with drug interactions and clinically significant drug interactions

Number of drug interactions, clinically significant interactions in prescriptions

The number of DI in the three months of June, July and August were quite similar, of which the major accounted for 25.13%, the rest was the moderate (74.87%). The survey results show that: the number of DI calculated according to prescriptions with DI is 1.74 interactions, about 4 times higher if calculated according to the total number of prescriptions. Besides, on average, a prescription has 1.16 DICS based on the number of prescriptions with DICS, and according to the total number of prescriptions in the research sample, the result is 0.03 (Table 3).

Table 3. Mean number of interactions and clinically significant interactions per prescription

Parameter	Number of prescription	Number of drug interactions in a prescription
General interactions		
- Calculated according to the total prescription	14.341	0,44
- Calculated by prescription with drug interactions	3.619	1,74
Clinically significant interactions		
- Calculated according to the total prescription	14.341	0,03
- Calculated by prescription with drug interactions	307	1,16

Common pairs of clinically significant drug interactions

Based on the results of interaction browsing, 36 pairs of interactions were determined to have clinical significance, of which 10 pairs of interactions are common with a frequency of more than 1000 orders from 0.91 to 3.70 (Figure 4). The frequency of occurrence of two drug interactions perindopril - spironolactone, aspirine - hydrochlorothiazide was the largest, reaching values > 3/1000 prescriptions with 53 and 45 occurrences, respectively. Among the drugs that interact, aspirine, spironolatone, clopidogrel or perindopril, meloxicam has many interactions with other drugs. Regarding drug interaction mechanism, mainly pharmacokinetic mechanism, increase/decrease pharmacological effects or increase toxicity/side effects of concomitant drugs.

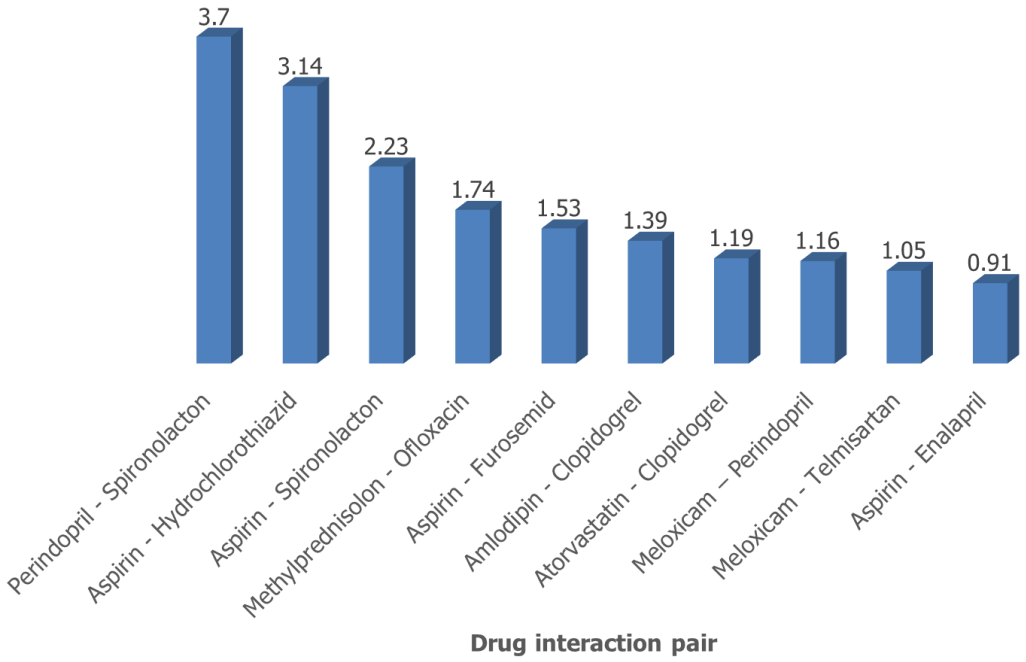


Figure 4. Frequency of occurrence of 10 drug interactions in 1000 prescriptions

Factors affecting the likelihood of drug interactions

Effect of drug quantity

Processing and calculating the number of drugs prescribed in a prescription and the number of DICS from 14,341 prescriptions, making a table showing the relationship between the number of drug interactions with DICS and the number of drugs prescribed in a prescription (Table 4).

Table 4. Relationship between number of drugs and number of clinically significant drug interactions in prescriptions

Number of drugs prescribed in a prescription	No drug interactions	Number of clinically significant drug interactions			Total prescriptions for clinically significant drug interactions	Total prescriptions	Percentage of clinically significant drug interactions
		1	2	3			
2	3.919	22	0	0	22	3.941	0,56
3	4.030	34	0	0	34	4.064	0,84
4	3.316	47	3	1	51	3.367	1,51
5	1.614	52	6	0	58	1.672	3,47
6	824	45	17	2	64	888	7,21
7	252	34	7	1	42	294	14,29
8	63	22	3	0	25	88	28,41
9	11	9	0	2	11	22	50,00
10	1	0	0	0	0	1	-
11	1	0	0	0	0	1	-
12	1	0	0	0	0	1	-
14	1	0	0	0	0	1	-
15	1	0	0	0	0	1	-
Total	14.034	265	36	6	307	14.341	2,14

As the number of drugs increased from 2 to 9 in a prescription, the percentage of DICS prescriptions compared to prescriptions increased from 0.56 to 50%, respectively. This shows that when increasing the number of drugs in a prescription, the rate of DICS increases sharply. To determine the relationship between the rate of DICS and the number of drugs in a prescription, regression curve estimation analysis was used (Table 5, Figure 5).

Table 5. Model Summary and Parameter Estimates

Dependent Variable: Percentage of clinically significant drug interactions

	Model Summary					Parameter Estimates			
Equation	R Square	F	df1	df2	Sig.	Constant	b1	b2	b3
Linear	.760	19.021	1	6	.005	-21.155	6.262		
Logarithmic	.585	8.441	1	6	.027	-28.440	26.075		
Inverse	.404	4.069	1	6	.090	32.682	-84.839		
Quadratic	.979	118.081	2	5	.000	20.864	-12.226	1.681	
Cubic	**.999**	**2617.748**	**3**	**4**	**.000**	**-10.504**	**9.908**	**-2.800**	**.272**
Compound	.996	1399.331	1	6	.000	.122	1.960		
Power	.937	89.521	1	6	.000	.035	3.100		
S	.796	23.347	1	6	.003	4.155	-11.177		
Growth	.996	1399.331	1	6	.000	-2.101	.673		
Exponential	.996	1399.331	1	6	.000	.122	.673		
Logistic	.996	1399.331	1	6	.000	8.177	.510		

The independent variable is number of drugs in a prescription.

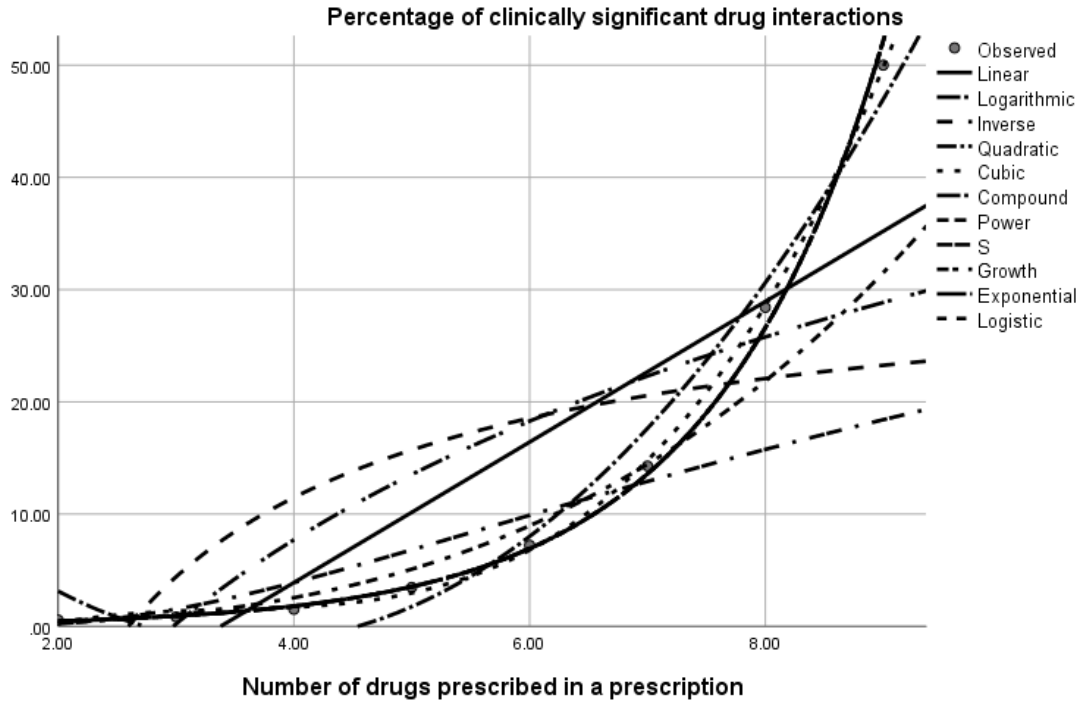


Figure 5. Graph of the correlation analysis between the number of drugs and the percentage of clinically significant drug interactions in the prescription

In 11 survey models, the third-order model has the largest adjusted R^2 coefficient of 0.999 with the correlation coefficient R approximately equal to 1. Thus, the percentage of DICS has a positive and close relationship with the ratio of number of drugs used in a prescription according to the regression equation $Y = 0.272.X^3 – 2,800.X^2 + 9,908.X - 10,504$ ($P<0.05$). The survey results show that increasing X (number of drugs in a prescription) strongly increases Y (ratio of DICS) (Figure 5). Continue to compare two proportions of prescriptions with DICS/prescriptions without DI when the number of drugs on the prescription is less than or equal to 3 and greater than 3, the test when squared is used. The results show that patients who are prescribed more than 3 drugs in a prescription are 5.86 times more likely to experience DICS than patients who are prescribed less than 3 drugs in a prescription. The 95% confidence interval ranges from about 4.37 to 7.84 (P=0.000) (Table 6).

Table 6. Number of clinically significant drug interactions and no clinically significant drug interactions when prescribing greater than and less than 3 drugs per prescription

Number of drugs in prescription	Number of prescriptions (%)		Total	OR (95%CI)	P
	Clinically significant drug interactions	Drug interactions of no clinical significance			
> 3	251 (3,96)	6.085 (96,04)	6.336	5,86 (4,37 - 7,84)	0,000
≤ 3	56 (0,70)	7.949 (99,3)	8.005		
Tổng	307	14.034	14.341		

Effect of gender

Gender has an effect on the likelihood of appearing DICS. When surveying over 14,341 prescriptions, it was found that male patients using the drug were 1.90 times more than female patients. The confidence interval ranges from 1.51 to 2.40 (P < 0.001) (Table 7). There are many possible causes for the difference in the likelihood of DICS occurrence related to sex factors, including the average number of prescription drugs of the male and female patients. The number of drugs in a prescription used in male and female patients is 3.49 and 3.51, respectively. The results of comparison of variance showed that P = 0.12 > 0.05, showing that the variance of 2 different samples was not statistically significant. With this result, two mean values of the number of drugs used for 2 groups of male and female patients were analyzed in the case of equal variance. Using T test shows that P = 0.36 > 0.05. This result can conclude that the mean value of the 2 samples is not statistically significant (the number of drugs in a prescription is not the cause of the difference in the likelihood of the occurrence of DICS related to sex).

Table 7. Effect of sex on the likelihood of clinically significant drug interactions

Gender	Number of prescriptions (%)		Total	OR (95%CI)	P
	Clinically significant drug interactions	Drug interactions of no clinical significance			
Male	186 (2,88)	6.274 (97,12)	6460	1,90 (1,51 – 2,40)	0,000
Female	121 (1,54)	7.760 (98,46)	7881		
Total	307	14.034	14.341		

Effect of the age

The average age of patients is 58.77 ± 13.83, so the age to assess the influence on DI is divided into 2 ranges: older than 60 years old and younger than 60 years old. Compare the rate of occurrence of drug interactions of two groups of patients older than 60 and younger than 60 years old. The results show that, the older the age, the greater the likelihood of drug interactions. The likelihood of DICS occurrence in patients older than 60 years old is 1.44 times greater than that in patients younger than 60 years old (P < 0.05). The confidence interval (95%) of the odds ratio ranges from 1.14 to 1.83 (Table 8).

Table 8. Effect of the age on the likelihood of clinically significant drug interactions

Age	Number of prescriptions (%)		Total	OR (95%CI)	P
	Clinically significant drug interactions	Drug interactions of no clinical significance			
> 60	200	7.920	8.120	1,44 (1,14 – 1,83)	0,002
≤ 60	107	6.114	6.221		
Tổng	307	14.034	14.341		

Continue to compare the average value of the number of drugs used in a prescription of two groups of subjects older than 60 years old (G>60) and younger than 60 years old (G<60). The results showed that the number of drugs in a prescription used in groups G>60 and G<60 were 3.62 and 3.35, respectively. This difference is statistically significant (P<0.05). This result can conclude that the reason for the possibility of DICS occurrence in patients G>60 is 1.44 times greater than that in patients G<60 due to the larger number of prescription drugs.

Effect of active ingredients

Of the 20 drugs analyzed, 07/20 drugs that affect the likelihood of DICS occurrence are not statistically significant (P>0.05), 13/20 drugs that affect the likelihood of DICS occurrence have statistical significance (P<0.05). In which, some drugs have quite large odds ratio such as spironolactone, clopidogrel or aspirine, ranging from 24.66 to 66.29.

Drug	Number of prescriptions (%)		OR (95%CI)	P
	Clinically significant drug interactions	Drug interactions of no clinical significance		
Amlodipine Yes No	3.774 (26,73) 10.345 (73,27)	24 (10,76) 199 (89,24)	0,33 (0,22-0,51)	P>0,05
Aspirine Yes No	430 (3,05) 13.649 (96,95)	115 (43,73) 148 (56,27)	24,66 (18,98-32,05)	**P<0,05**
Atorvastatine Yes No	285 (2,03) 13.773 (97,97)	26 (9,15) 258 (90,85)	4,87 (3,20-7,41)	**P<0,05**
Celecoxib Yes No	242 (1,71) 13.794 (98,28)	6 (1,96) 300 (98,04)	1,14 (0,50-2,58)	P>0,05
Clopidogrel Yes No	43 (0,31) 14.008 (99,69)	55 (13,40) 252 (86,60)	50,41 (32,11-79,14)	**P<0,05**
Colchicine Yes No	59 (0,42) 13.980 (99,58)	8 (2,64) 295 (97,36)	6,43 (3,04-13,57)	**P<0,05**
Enalaprile Yes No	214 (1,52) 13.826 (98,48)	20 (6,62) 282 (93,38)	4,58 (2,85-7,35)	**P<0,05**
Fenofibrate Yes No	1.351 (9,61) 12.703 (90,39)	18 (6,25) 270 (93,75)	0,63 (0,38-1,01)	P>0,05
Furosemide Yes No	197 (1,40) 13.858 (98,60)	25 (8,71) 262 (91,29)	6,71 (4,35-10,36)	**P<0,05**
Hydrochlorothiazide Yes No	415 (2,95) 13.631 (97,05)	51 (17,23) 245 (82,77)	6,84 (4,99-9,39)	**P<0,05**

Drug	Number of prescriptions (%)		OR (95%CI)	P
	Clinically significant drug interactions	Drug interactions of no clinical significance		
Levofloxacine Yes No	42 (0,30) 13.993 (99,70)	6 (1,95) 300 (98,05)	6,64 (2,80-15,74)	**P<0,05**
Losartan Yes No	175 (1,25) 13.874 (98,75)	1 (0,34) 292 (99,66)	0,27 (0,04-1,95)	P>0,05
Meloxicame Yes No	476 (3,39) 13.563 (96,61)	38 (12,54) 265 (87,46)	4,09 (2,87-5,81)	**P<0,05**
Methylprednisolone Yes No	338 (2,41) 13.697 (97,59)	31 (10,10) 276 (89,90)	4,55 (3,09-6,70)	**P<0,05**
Ofloxacine Yes No	531 (3,78) 13.511 (96,22)	25 (8,33) 275 (91,67)	2,31 (1,52-3,51)	**P<0,05**
Omeprazole Yes No	1.456 (10,34) 12.628 (89,66)	12 (4,65) 246 (95,35)	0,42 (0,23-0,76)	P>0,05
Perindopril Yes No	2.581 (26,79) 11.495 (73,21)	71 (26,69) 195 (73,31)	1,62 (1,23-2,13)	**P<0,05**
Pravastatine Yes No	844 (6,00) 13.224 (94,00)	9 (3,28) 265 (96,72)	0,53 (0,27-1,04)	P>0,05
Spironolactole Yes No	79 (0,56) 13.966 (99,44)	81 (27,27) 216 (72,73)	66,29 (47,29-92,93)	**P<0,05**
Telmisartane Yes No	2.498 (17,71) 11.611 (82,29)	27 (11,59) 205 (88,41)	0,61 (0,41-0,91)	P>0,05

Effect of the disease group

Among the 15 groups of diseases analyzed, there were 9/15 groups of diseases that had a statistically significant effect on the occurrence of DICS (P<0.05). The risk of drug interactions in hypertension, circulatory and cardiovascular diseases is higher than in other disease groups. Compared with the hospital disease model, these are complex, high-risk diseases and often use a combination of different drugs.

Disscustion

Evaluation of drug interactions clinical significance in the study sample

The number of prescriptions with DICS was 307 (2.14%). This rate is lower than the rate of 6.7% in the study of Nguyen Thi Hien when surveying over 5,338 outpatients at Hue University of Medicine and Pharmacy Hospital [1]. This difference may be due to the fact that the list of drugs used in hospitals is relatively different due to the specific disease patterns in each hospital. The second reason may be the

sample size in each study and the criteria for identifying drug interactions with different clinical significance. The number of prescriptions with major and moderate drug interactions, studied was 9.94% (1,426/14,341), lower than that of Nguyen Thi Hue (2020) at Bach Mai Hospital (19.3%) [2]. The reason may be that the Hospital of Traditional Medicine mainly manages chronic diseases such as hypertension, diabetes, lipid metabolism disorders or musculoskeletal diseases with the main strength of using traditional medicine, which is different from Bach Mai Hospital - a special-class general hospital in the country with a wide variety of diseases and a wide range of drugs. In addition, each study can use different drug interaction search software, in which there are some disagreements between the software. The average number of DICS per prescription based on the number of prescriptions with DI is 1.16. In which, the lowest number of DIs in prescription is 01 (86.32%) and the highest number is 03 (1.95%). This result is similar to the study of Nguyen Thi Hien (2018) when surveying over 5338 outpatient prescriptions at the hospital of Hue University of Medicine and Pharmacy [1].

During the interaction browsing process, the Micromedex database identified 36 pairs of DICS related to 27 active ingredients, including drugs/drugs belonging to different pharmacological groups such as cardiovascular, diuretics, antibiotics, anti-inflammatory pain reliever, proton pump inhibitor .... Including 6 drugs belonging to the cardiovascular group such as clopidogrel, AT1 receptor blockers, ACE inhibitors, fenofibrate, statins and aspirine. These drugs interact not only with drugs of the same class (fenofibrate-statin group, AT1 receptor blockers - ACE inhibitors) but also with other drugs. The survey shows that there are 10 pairs of moderate interactions with the frequency of over 1000 prescriptions from 0.91 to 3.77. No pair of contraindicated drug interactions were detected. The pair of perindopril-spironolactone interactions with severity is the most common DI pair, which can be explained because hypertension is the disease accounting for the largest proportion in the study sample. The ratio of drugs/drug groups that appear commonly in interaction pairs include: meloxicam (7 pairs), aspirin (5 pairs), clopidogrel (5 pairs), atorvastatin (4 pairs)… Serious interactions such as spironolactone-ACE inhibitor/receptor blocker, clopidogrel-proton pump inhibitor is similar to the study of Nguyen Thi Hue (2020) [2]. However, the number of pairs of DI contraindicated and serious DI at Bach Mai Hospital is much higher than this study, because the number of active ingredients prescribed at Bach Mai Hospital's Department of Examination is nearly 500 active ingredients, much higher compared with traditional medicine hospital. From the above 36 drug interaction pairs, the number of similar interactions are grouped, resulting in the highest number of interactions between aspirin and diuretics (106/355 times), followed by enzyme inhibitors switch-diuretic drugs (57/355 times), followed by glucocorticoid-quinolone-antibiotic interaction pairs (31/355 times), NSAID-receptor blocker interactions with the number of detections 24/355 ranked 4^{th} and 5^{th} is a pair of Ca-clopidogrel channel blocker interactions (23/355 turns).

Regarding the mechanism of interaction, NSAIDs inhibit prostaglandin-mediated vasodilation and increase salt and water retention in the body. Both of these mechanisms contribute to the partial antagonism of NSAIDs to antihypertensive agents, especially those whose mechanism of action is via prostaglandin, renin or sodium-water balance such as diuretics, ACE inhibitors, receptor blockers or beta blockers. This may also reduce the effectiveness of antihypertensive agents, reduce the effectiveness of the prevention of cardiovascular events and the need for blood pressure control in patients. In addition, in a recent large study, the simultaneous use of three drugs including: one of NSAID, one of thiazide diuretic and one of ACE inhibitor or receptor blocker could increase the risk of injury by 31% acute kidney injury [6]. Therefore, the European Society of Cardiology (ESC) and the American Heart

Association both recommend and avoiding the use of NSAIDs if possible in patients with congestive heart failure. In addition, many elderly patients often have chronic diseases such as high blood pressure, osteoarthritis, etc., often have to use more anti-inflammatory pain relievers such as NSAIDs or aspirin to prevent cardiovascular complications. The risk of drug interactions is so great that care must be taken to manage these interactions actively. In addition to using aspirin to prevent cardiovascular events, clopidogrel is also widely used. In the study sample, the frequency of clopidogrel interactions with Ca blockers is also quite large (23/355 times), it is necessary to pay attention to the interactions of clopidogrel with PPIs (omeprazol/esomeprazole) (12/355 times). The mechanism of this interaction is related to metabolism due to inhibition of the CYP2C9 enzyme by PPIs, resulting in decreased concentrations of the active metabolite of clopidogrel and a decrease in the antiplatelet effect of clopidogrel. This is one of the interactions that needs to be carefully managed when the research results show that the rate of using PPIs in hospitals is also quite large. An interaction that was considered serious, with very good evidence, was an interaction between corticosteroids and fluoroquinolone antibiotics (ofloxacine, levofloxacine) that was also observed in a study with an interaction count of 31/355. The consequence of the interaction is the cumulative risk of tendonitis, tendon rupture. From the data in the study sample, it is shown that this pair of interactions mainly occurs in the otolaryngology examination table.

Factors affecting the likelihood of drug interactions

Using χ^2 test with odds ratio (OR) to analyze some influencing factors (age, gender, disease group, prescription drugs) and the likelihood of occurrence of DICS. Regarding age, the research sample was divided into 2 groups of subjects: over 60 years old and younger than/equal to 60 years old, the analysis showed that the probability of occurrence of DICS in patients aged 60 years and older was 1,44 times greater compared to patients with age less than 60 years ($P < 0.05$). This result is similar to the study of Nguyen Duy Tan (2015) [3] when investigating the influence of age on the likelihood of DI occurrence at the National Hospital of Hematology and Blood Transfusion (comparing 02 age groups > 65 and older). <=65, p=0.021; OR=2.22) or research by Nguyen Thi Hien (2018) [1]. This can be explained because patients over 60 years old often have chronic diseases or have many diseases at the same time, so they use many drugs regularly leading to DI. Regarding gender, the analysis shows that the chance of having DI in male patients is 1.90 times higher than in female patients. According to previous studies, the influence of gender on the likelihood of DI occurrence and for different results. However, the majority of the results showed that gender did not affect the likelihood of DI occurrence. Conducting analysis to further clarify, the mean of drugs prescribed for two groups of male/female subjects in the study sample was not statistically significant ($P > 0.05$), so the number of prescribed drugs was not statistically significant in a single application is not the cause of the above result. The cause may be due to the group of male patients who often suffer from cardiovascular diseases such as hypertension, lipid disorders ... and will be prescribed cardiovascular drugs, drugs to regulate blood lipid disorders ..., this is drugs that cause more DI when used with other drugs.

Regarding the type of prescription drugs, the drugs in the 10 most common pairs of DI have an effect on the probability of occurrence of DI ($P<0.05$). In which aspirine, clopidogrel and spironlactone have quite large OR compared to other drugs. These drugs interacted with many other drugs in the sample. In addition, amlodipine with an odds ratio OR=0.33 ($P>0.05$) is also consistent with the recommendation to use amlodipine as a first-line drug and is relatively safe for hypertensive patients. For celecoxib with

an OR=1.14 (P>0.05), a drug that is metabolised by the liver by CYP2C9, so it has little interaction with other drugs and is a drug with high safety in the NSAID class.

The number of drugs is a risk factor affecting the likelihood of drug interactions in patients [1], [7], [8]. The patient's risk of adverse drug interactions increases sharply with the total number of medications the patient takes. Research by Doan et al. [4] indicates that the risk of drug interactions is 50% when patients take 5-9 drugs and this risk increases to 100% when patients take 20 or more drugs. Therefore, for prescriptions with a large number of drugs, it is necessary to take measures to eliminate unnecessary drugs and reduce the number of drugs in the prescription. At the same time, it is also necessary to proactively detect, monitor, manage and handle drug interactions in order to minimize adverse interactions and improve treatment efficiency for patients. From the analysis results, when the number of prescription drugs increased from 2 to 9 drugs, the percentage of prescriptions with DICS/total prescriptions increased by about 89 times. With prescriptions of more than 10 drugs, accounting for a very small amount, the DICS was not recorded because these prescriptions were mainly prescribed as vitamin and mineral supplements.

Regarding the influence of disease group on the likelihood of drug interactions, the results showed the risk of drug interactions in hypertension, other metabolic endocrine diseases (except diabetes), circulatory-cardiac diseases. pulse rate higher than other disease groups. Compared with the hospital disease model, these are complex, high-risk diseases and often use a combination of different drugs. Therefore, a strategy is needed to manage drug interactions in these patients.

Conclusions

The current situation of drug interactions has been assessed at the medical examination department of the Traditional Medicine Hospital of the Ministry of Public Security: the rate of prescriptions with DICS at the Department of Medical Examination is relatively low, accounting for 2.13%, the frequency occurrence of DICS in 1000 prescriptions ranges from 3.37 to 0.91, the lowest number of DICS in a prescription is 1 and the largest is 3, when the number of drugs is greater than 3, the probability of having DICS 5.86 times higher for patients prescribed less than 3 drugs, 1.44 times more likely to occur DICS in patients with age 60 than in patients with age younger than 60, when using aspirin, spironolactone or clopidogrel... the probability of experiencing DICS is 24.66 to 66.29 times higher than that of patients who do not prescribe these drugs.

Based on the above results, the following recommendations are proposed to reduce clinically significant drug interactions that contribute to improving the effectiveness of safe and effective drug use:

Firstly, the number of prescription drugs should not exceed 3 drugs in a prescription

Second, pay special attention to patients over 60 years old who have many comorbidities, the risk of drug interactions increases sharply when using high-risk drug groups such as spironolactone, clopidogrele, aspirine…

Third, it is necessary to develop a list of drug interactions that need attention when prescribing in hospital treatment. Warn and guide doctors when prescribing in the treatment of diseases.

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