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CP 14

Potential pharmacokinetic drug-drug interactions in patients attending medical clinics at Teaching Hospital Jaffna: A prescription analysis

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Abstract

Background and objective: Patients with chronic medical conditions often take multiple medications and are at the risk of developing clinically significant drug-drug interactions (DDI). Many DDI alter pharmacokinetics and thereby the effects of medications. This prescription analysis aimed to describe the potential pharmacokinetic DDI and associated factors among patients attending medical clinics at Teaching Hospital Jaffna.

Methods: This was a descriptive cross-sectional study. As per the sample size recommended by the World Health Organization for prescription analysis, we analysed 600 prescriptions of patients attending medical clinics at Teaching Hospital Jaffna. Systematic sampling was used to select the prescriptions from all clinics. British National Formulary (BNF edition 80) was used as the pharmaceutical reference to identify pharmacokinetic DDI and categorise them as mild, moderate and severe. Chi-square test was used to determine the association between age, sex and polypharmacy (≥5 drugs) and the presence of pharmacokinetic DDI (critical value 0.05).

Results: Of the 600 prescriptions, the majority belonged to females (n= 327; 54.5%). Mean age was 57.5 (SD=14.6) years. A total of 112 potential pharmacokinetic DDI were identified in 86 (14.3%) prescriptions. Of them, 49 (43.8%) were moderate and 63 (56.2%) were severe DDI. Cardiovascular drugs contributed the majority of DDI (85%). The presence of potential pharmacokinetic DDI was statistically associated with age ($p=0.01$) and polypharmacy ($p<0.001$), but not sex. Prescriptions of older patients and those prescribed ≥5 drugs were more likely to contain potential pharmacokinetic DDI.

Conclusion: Patients attending the medical clinics are at risk of developing clinically significant pharmacokinetic DDI. While cardiovascular medications account for a large number of potential pharmacokinetic DDI, elderly patients exposed to polypharmacy may be at greater risk. Raising awareness among doctors, regular prescription review and closely monitoring those at risk may help to reduce the occurrence of clinically significant DDI.

Keywords: Pharmacokinetic interactions, Drug-drug interactions, Polypharmacy, Chronic diseases, Jaffna

Introduction

With the rising burden of chronic non-communicable diseases, many patients are prescribed multiple medications to manage their medical problems. These medications can interact with each other and alter their clinical effects in harmful and beneficial ways. Such interactions between medications are referred to as drug-drug interactions (DDI) [1].

Drug-drug interactions are broadly classified as pharmacodynamic and pharmacokinetic interactions. Pharmacodynamic interactions are those that interfere with the action of the medicines at target organs and pharmacokinetic interactions are those that interfere with the absorption, distribution, metabolism or excretion of medicines [1]. Clinically significant DDI are defined as interactions "associated with either toxicity or loss of efficacy that warrants the attention of healthcare professionals" [2]. Adverse DDI may result in increased hospitalization and prolonged hospital stays, in addition to compromising patient safety [3].

Patients receiving treatment at medical clinics usually have multiple morbidities, are prescribed several medications, and would be at risk of developing clinically significant DDI. Alteration in the kinetics of a medicine may increase or decrease its concentration, resulting in clinically significant DDI and consequent toxic outcomes or therapeutic failures. The aim of the study was to describe potential pharmacokinetic DDI and the association of age, sex and polypharmacy (≥5 drugs) with the presence of potential DDI in the prescriptions of patients attending medical clinics at Teaching Hospital Jaffna.

Methods

This institution-based descriptive cross-sectional study analysed 600 prescriptions of patients attending the medical clinics of Teaching Hospital Jaffna. The World Health Organization recommends a minimum sample size of 600 for prescription analysis [4]. Medical clinics at Teaching Hospital Jaffna were conducted by four medical units at the time of data collection (August 2021). Around 6000-8000 patients were being followed up by each medical unit. We extracted data from 150 prescriptions from each unit using systematic sampling.

Potential pharmacokinetic DDI were identified and categorized using the British National Formulary (BNF edition 80; Appendix 1: Interactions). Pharmacokinetic interactions were categorised as mild, moderate or severe. Age was categorised as <40 years, 40-60 years and >60 years. Polypharmacy was defined as taking five or more medications [5]. Standard descriptive statistics were used to describe key variables. The chi-square test was performed to determine the association between the presence of potential pharmacokinetic DDI and age, sex and polypharmacy. A p value less than 0.05 was considered significant.

Administrative approvals were obtained before commencing data collection. Ethics approval was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Jaffna.

Results

Of the 600 prescriptions, 273 (45.5%) belonged to males and 327 (54.5%) to females. Mean age of the patients was 57.5 (SD=14.6) years. Most were in the >60 years age group (46%, n=276), followed by 40-60 years (42.3%, n=254) and <40 years (11.7%, n=70). Polypharmacy was prevalent in nearly half of the prescriptions (n=294; 49%).

A total of 112 potential pharmacokinetic DDI were identified in 86 prescriptions (14.3%). Of them, 49 (43.8%) were moderate and 63 (56.2%) were severe. There were no minor DDI identified. The number of DDI per prescription ranged from 1 to 3 where the number of prescriptions with one, two and three DDI were 65, 18 and 3, respectively. Potential pharmacokinetic DDI were present more frequently in the prescriptions of females (55.4%, n=62) than males (44.6%, n=50). The presence of potential pharmacokinetic DDI increased with age; the highest proportion was recorded in the >60 years age group (59.8%, n=67), followed by 38.4% (n=43) in the 40-60 years age group and 1.8% (n=2) in those less than 40 years. More than 90% of potential DDI were present in prescriptions with polypharmacy (Table 1).

Table 1. Distribution of DDI by age, sex and polypharmacy (n=112)

		n	%
Age (years)	<40	2	1.8
	40 – 60	43	38.4
	>60	67	59.8
Sex	Female	62	55.4
	Male	50	44.6
Polypharmacy (≥5 drugs)	Yes	103	92.0
	No	9	8.0

A total of 21 drug pairs were implicated in the potential pharmacokinetic DDI. At least one cardiovascular medication was involved in the majority of DDI (85%). The five most frequent drug pairs that could cause DDI were aspirin and hydrochlorothiazide (15.2%), atorvastatin and diltiazem (10.7%), aspirin and metolazone (9.8%), aspirin and beclomethasone (8%), and clopidogrel and omeprazole (7.1%).

Table 2 shows the association of age, sex and polypharmacy with the presence of potential pharmacokinetic DDI. There was a statistically significant association between the presence of potential pharmacokinetic DDI and age group (p=0.01) and polypharmacy (p<0.001).

Table 2. Factors associated with pharmacokinetic drug-drug interactions (n=600)

Factor	**Presence of DDI**		**X^2, df**	**p value**
	Yes	**No**		
	n (%)	**n (%)**		
Age				
<40 years	2 (2.9)	68 (97.1)	9.153, 2	0.01*
40-60 years	37 (14.6)	217 (85.4)		
>60 years	47 (17.0)	229 (83.0)		
Sex				
Male	40 (14.7)	233 (85.3)	0.041, 1	0.839
Female	46 (14.1)	281 (85.9)		
Polypharmacy				
Yes	77	217	66.005, 1	<0.001*
No	9	297		

* Statistically significant (p≤0.05)

Discussion

Potential pharmacokinetic DDI were prevalent in 14.3% of the prescriptions in the present study. For the purposes of comparison, we found only one local study on potential DDI carried out at a pharmacy outlet of the State Pharmaceutical Corporation in Anuradhapura using the Medscape drug interaction checker to identify potential DDI. The study reported that 53% of the prescriptions had DDI [6]. While the methods used in the two studies to identify potential DDI were different, the Anuradhapura study analysed both pharmacokinetic and pharmacodynamic DDI. Studies show that the proportion of pharmacokinetic DDI is generally lower than pharmacodynamic DDI. For instance, a Bulgarian study reported that 12.4% of potential DDI were pharmacokinetic, while a study from Karachi, Pakistan, reported that 37.9% of potential DDI identified were pharmacokinetic [7,8]. The lower prevalence of DDI in our study compared to the Anuradhapura study may be explained by the relatively lower incidence of pharmacokinetic DDI.

The Anuradhapura study found that 19.3%, 73.9% and 6.8% of DDI were minor, significant and serious, respectively [6]. In our study, the majority of DDI were severe (56.2%) and the rest were moderate (43.8%). Indeed, there were no minor DDI in our study. These discrepancies may also be explained by the different methods used as well as our focus on pharmacokinetic DDI.

We found that the five top drug pairs contributing to potential pharmacokinetic DDI at Teaching Hospital Jaffna had at least one cardiovascular medication. A similar finding was reported in a countrywide study conducted on out-hospital drug dispensing centres in France where four out of five of the most represented contraindicated or discommended pairs involved cardiovascular medications [9]. Findings of a study conducted in primary care centres in Brazil also supports this observation [10].

We found that the prescriptions of older patients and those with polypharmacy were more likely to have potential pharmacokinetic DDI. While similar observations are reported in the literature [10-14], our findings suggest that elderly patients with co-morbidities may be at greater risk of exposure to DDI and warrant close monitoring and follow up and frequent prescription reviews.

This study has some limitations. We only assessed potential pharmacokinetic DDI. However, prior research suggests that pharmacodynamic interactions make up a larger proportion of DDI. Therefore, our findings likely underestimate the presence of potential DDI. As we did not assess clinical outcomes, we are unable to comment on the clinical significance of the potential DDI identified. Lastly, the prescriptions we analysed did not contain information on comorbidities. Therefore, the influence of disease condition on the presence of potential DDI was not assessed.

Conclusion

A substantial proportion of prescriptions issued to patients attending medical clinics at Teaching Hospital had potential pharmacokinetic DDI, and the majority of them were in the severe category. Based on our results, the risk of clinically significant adverse outcomes occurring as a result of DDI may be higher among elderly patients, those exposed to polypharmacy and patients on cardiovascular medication. Raising awareness among health professionals, regular prescription review and close monitoring of patients at risk could reduce the adverse outcomes of clinically significant potential DDI.

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Conflict of interest
None of the authors have conflicts of interest that are directly or indirectly relevant to this study.

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CP 15

Knowledge, attitude, and practices related to antenatal care among primiparous pregnant women attending an antenatal clinic in Kopay, Jaffna District, Sri Lanka

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Abstract

Background and objective: Knowledge on antenatal care (ANC) empowers women to be aware of their health status during pregnancy. The objective of this study was to assess knowledge, attitude, and practices related to ANC among primiparous pregnant women in their second and third trimesters visiting an antenatal clinic in Kopay, Jaffna District.

Methods: A clinic-based cross-sectional study was carried out at the antenatal clinic in the office of the Medical Officer of Health (MOH) – Kopay in Jaffna district. An interviewer-administered questionnaire consisting of socio-demographic profile, knowledge on ANC, attitude towards ANC and practices related to ANC was used for data collection. The data were analyzed by using SPSS v23.0. Standard descriptive statistics were applied.

Results: In total, 276 primiparous mothers in their second and third trimesters participated in the study. The mean age of the mothers was 29.0 (±5.2) years. Good and moderate knowledge was recorded among 49.3% (n=136) and 40.9% (n=113) of mothers, respectively; only 9.8% (n=27) had poor knowledge. Positive attitude was recorded among 95.3% (n=263) of mothers, while 4.7% (n=13) had a neutral attitude and none had a negative attitude. The proportion of mothers with good and moderate practice was 56.9% (n=157) and 39.9% (n=110), respectively; only 3.3% (n=9) had poor practice. Notably, 72.5% of mothers had registered with the public health midwife before 8 weeks of gestation.

Conclusion: The study shows that most primiparous mothers have good or moderate knowledge and a positive attitude towards ANC, with commendable early registration for ANC. However, there is a need for targeted interventions to improve ANC education and support for the small percentage of mothers with poor knowledge and practices. These findings