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Original Research

The prevalence of major potential drug-drug interactions at a University health centre pharmacy in Jamaica

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ABSTRACT[*]

Objective: To identify major potential drug-drug interactions (DDIs) on prescriptions filled at the University Health Centre Pharmacy, Mona Campus, Jamaica.

Methods: This investigation utilised a cross-sectional analysis on all prescriptions with more than one drug that were filled at the Health Centre Pharmacy between November 2012 and February 2013. Potential DDIs were identified using the online Drug Interactions Checker database of Drugs.com.

Results: During the period of the study, a total of 2814 prescriptions were analysed for potential DDIs. The prevalence of potential DDIs found during the study period was 49.82%. Major potential DDIs accounted for 4.7 % of the total number of interactions detected, while moderate potential DDIs and minor potential DDIs were 80.8 % and 14.5 % respectively. The three most frequently occurring major potential DDIs were amlodipine and simvastatin (n=46), amiloride and losartan (n=27) and amiloride and lisinopril (n=16).

Conclusion: This study has highlighted the need for educational initiatives to ensure that physicians and pharmacists collaborate in an effort to minimise the risks to the patients. These interactions are avoidable for the most part, as the use of online tools can facilitate the selection of therapeutic alternatives or guide decisions for closer patient monitoring and thus reduce the risks of adverse events.

Keywords: Drug Interactions; Medication Errors; Patient Safety; Pharmacists; Jamaica

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INTRODUCTION

Adverse events (AE), as was established by the International Conference on Harmonisation can be any unfavourable and unintended sign, symptom or disease temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product.[1] Patients using multiple drug therapy are at a greater risk of being predisposed to AEs associated with drug-drug interactions (DDIs).

The presence of potential DDIs can be determined using the Drug Interactions Checker within the Drugs.com database. This database classifies DDIs into three categories: major, moderate and minor. Major interactions are highly clinically significant and these combinations should be avoided because the risk of the interaction outweighs the benefits; moderate interactions are moderately clinically significant and should be avoided, but may be used only under special circumstances; minor interactions are minimally clinically significant. Alternate online drug interactions checkers include the medscape reference, the WebMD.com database, the rxlist.com database and the Caremark.com Gold standard database. Computer software or applications that may be used to check drug interactions include PocketPharmacist, Micromedex, Medscape and Epocrates.

A study done in Greece between November 2007 and January 2008 assessed a total of 1,553 prescriptions collected from three community pharmacies in the region and identified that 13.7% had major potential DDIs.[2] Sepehri *et al*. in a study from data retrieved from the pharmacy of a general hospital (200 beds) in Iran during a one year period reported that major interactions had a prevalence of 10.8%.[3] The prevalence of major potential DDI increases in the elderly (at least 60 years old) as identified by Neto et al in a Brazilian study done between November 2010 and April 2011 the data from 12,343 elderly patients, which showed a 33.3 % prevalence of major potential DDIs.[4]

Pharmacists play an important role in protecting patients from the harmful effects that may be experienced due to these interactions. Peng et al. (2003) assessed a drug claims database with more than 30 million prescriptions for approximately 2.9 million patients to determine the incidence of clinically relevant potential DDIs. They found that the use of electronic software reduced the incidence of DDI alerts by 70.8% and that review by clinical pharmacists reduced the incidence of potentially serious DDIs by an additional 80.6%.[5]

Moura *et al*. did a similar study where they evaluated the impact of a drug-drug interaction screening software combined with pharmacist intervention in preventing drug interactions. The results showed a reduction of 24% in the average number of DDIs per patient after the intervention. There was also a 71% reduction in high-severity DDIs. They therefore concluded that the performance of the software combined with pharmacist intervention was positive with a reduction in the risks of DDIs.[6]

Clinical Pharmacy is not practiced at the University Health Centre Pharmacy, as this is an out-patient facility. Pharmacists, however, are consulted from time to time by physicians in medication decision-making functions as part of the patient's health care team.

The aim of this study is to determine the prevalence of potential DDIs among prescriptions filled at the University Health Centre Pharmacy with the secondary aim of assessing clinically significant potential DDIs.

METHODS

The study protocol followed the guidelines set out by the Declaration of Helsinki; it was reviewed and ethical approval was granted by the University Hospital of the West Indies/ University of the West Indies/ Faculty of Medical Sciences (UHWI/UWI/FMS) Ethics Committee prior to the commencement of the study. The study was exempted from patient consent since there was no direct involvement with patients. The study was conducted at the University Health Centre (UHC) at the University of the West Indies, Mona Campus. The Health Centre provides a wide range of primary and secondary health care services to members of the university community. Members include staff and their dependents, retirees and their spouses, students, and some residents of surrounding communities. There is no inpatient or medical specialty services offered at the University Health Centre. These services are provided by the University Hospital of the West Indies which is in close proximity to the UHC. Currently this campus serves a combination of residential and commuter students totalling 14,000. The Health Centre however provides some 40,000 consultations annually.

The profiles of patients who utilise the services of the University Health Centre pharmacy are stored electronically and are available for review by the pharmacists. This profile includes the date of birth, age, and contact information for each patient as well as their medication history. All prescriptions with more than one item that were filled at the pharmacy during November 1, 2012 to February 28, 2013 were assessed for potential DDIs using the Drug Interactions Checker within the Drugs.com database. The assessment was not done at the time of dispensing, but at the end of each day and the previous drug history was not factored in the study. Analysis by descriptive statistics was performed with the SPSS statistical software program (version 17.0). Data was expressed in terms mean, standard deviation, median, inter-quartile range (IQR), mode or percentage frequency as appropriate.

RESULTS

A total of 2814 prescriptions qualified for review; 1093 (38.84%) were missing information on the age of the patient. The mean age of the patients was 43 (SD=22) years (range 1-94 years); the median age was 40 years (IQR 22 -61 years). The mean number of drugs on each prescription was 4 (SD=2), and the mode was 2. The number of drugs on each prescription ranged from two to a maximum of eighteen, with 782 prescriptions having two drugs (27.8%) and 211 prescriptions (7.5%) having between 8 and 18 drugs (Table 1).

One thousand four hundred and two (1402) out of 2814 prescriptions (49.8%) had potential DDIs. Further examinations of these prescriptions revealed 4693 pairs of active agents with potential DDIs, of which 3792 (80.8%) were moderate potential DDIs and 222 (4.7%) were major DDIs (Table 1).

The 10 most frequently occurring major potential DDIs were combinations involving simvastatin with amlodipine (20.7%), followed by amiloride with angiotensin receptor blockers (ARBs) (13.5%) and amiloride with angiotensin converting enzyme inhibitors (ACEIs) (11.3%). Table 2 shows the major potential DDIs grouped by the possible AEs stated on Drugs.com. Of the most frequently occurring major potential drug interactions, there were trends with particular classes of drugs. The classifications of these drugs, the frequency of their occurrence, along with the potential clinical consequences as a result of these combinations are listed in Table 2. Most of the major potential DDI identified were associated with increased risk of hyperkalemia (36.9%), followed by simvastatin induced rhabdomyolysis/hepatotoxicity (20.7%).

Table 1. Demographic data

Age (years)	Number of patients
0-9	42
10-19	140
20-29	528
39-39	133
40-49	176
50-59	213
60 and over	489
Number of drugs on prescription	**Number of prescriptions**
2	782
3	699
4	504
5	324
6	187
7	107
8-18	211
Potential DDI (n=4693)	**Number of prescriptions**
Moderate	3792 (80.8%)
Minor	679 (14.5%)
Major	222 (4.7%)

Table 2. Drug class combinations of major interactions, potential adverse events and their frequency

Potential Adverse Event	DDI	N (%)
Increased risk of hyperkalemia (36.9%)	Amiloride + ARBs (Losartan, Valsartan)	30 (13.5)
	Amiloride + ACEIs (Lisinopril, Enalapril)	25 (11.3)
	Potassium Chloride + ARBs (Valsartan, Losartan)	13 (5.9)
	Spironolactone + Losartan	6 (2.7)
	Potassium Chloride + Lisinopril	4 (1.8)
	Spironolactone + Enalapril	4 (1.8)
Increased risk of Rhabdomyolysis/hepatotoxicity (20.7%)	Simvastatin + Amlodipine	46 (20.7)
Increased risk of severe allergic reactions and infections (4.5%)	Allopurinol + ACEIs (Lisinopril, Enalapril)	10 (4.5)
Increased risk of an irregular heart rhythm (4.5%)	Clopidogrel + Esomeprazole	6 (2.7)
	Haloperidol + Quetiapine	4(1.8)

DISCUSSION

This is the first study of its kind to be carried out at the University Heath Centre Pharmacy. Our study revealed that approximately half of the patients that have prescriptions with more than one drug have been exposed to potential DDIs; this is within the range identified from previous studies of non-hospitalised patients in other countries which have yielded a prevalence of DDI ranging from 26.53% to 63.00%.[6-8] Most of the potential DDIs identified were moderate, but 4.7% were major potential DDI and therefore clinically significant.

It is known that DDIs can compromise therapy, for example, by increasing the length of hospitalization, and therefore specific measures that can ensure that healthcare professionals increase their awareness/recognition of potential DDIs may improve the quality of health care.[9] Easy access to drug interaction databases, such as Drugs.com may be an integral tool in assisting both physicians and pharmacists in detecting these potential DDIs during the prescription writing and dispensing process to minimize the DDI risks to patients. This would have to be combined with pharmacological expertise, knowledge of individual patients, and close monitoring to ensure that the most suitable drugs are prescribed.

Choosing suitable alternatives in the case of major potential DDIs and closer patient monitoring in the case of moderate, as well as minor potential DDIs are ways in which physicians can minimize the risk or prevent AEs. While it may be impossible to totally eliminate potential DDIs based on the need for poly-pharmacy especially in patients with multiple chronic diseases, it is the responsibility of health care professionals to weigh risk versus benefit when prescribing and dispensing. In cases where the prescribed drugs have the potential of causing adverse events, the pharmacist may inform patients of the signs and symptoms that may be manifested and may urge patients to seek immediate medical attention if these symptoms are experienced.The most frequently occurring major potential DDI in this study was simvastatin and amlodipine. According to Drugs.com, co-administration with amlodipine may significantly increase the plasma concentrations of simvastatin, potentiating the risk of hepatoxicity and rhabdomyolysis. The mechanism associated with these AEs relates to amlodipine inhibition of cytochrome P450 enzyme CYP3A4, especially in the gut, the enzyme that metabolizes simvastatin to its inactive metabolite; this would thus increase the bioavailability of and hence the accumulation of simvastatin. Physicians have the option of prescribing pravastatin, rosuvastatin or fluvastatin, as these statins are not metabolised by CYP3A4 and thus reducing the risk of hepatotoxicity and rhabdomyolysis.[10]

It is important to note that there is no gold standard reference available for detecting potential DDIs. In assessing the potential DDIs on prescriptions filled at the University Health Centre Pharmacy, the use of only one database limited access to information that might be available on other DDI checkers. Another limitation of the study is that it did not involve immediate follow-up of the patients whose prescriptions possessed potential DDIs. The intervention was made on completion of the study by means of consultation with the prescribing physicians, and in other cases the findings and recommendations were documented and placed in the patient's docket. As part of the intervention, a detailed report was made to the healthcare professionals at the Health Centre detailing the nature and prevalence of the potential DDIs that were detected. The researchers therefore do not know if the potential AEs were experienced or if an intervention was made on the part of the doctors to counter these events.

Further studies to determine the effect of this intervention was recommended, to determine if there are changes in the prescribing habits and by extension the prevalence of potential DDIs among prescriptions filled at the University Health Centre Pharmacy.

CONCLUSIONS

In conclusion, DDIs are common among patients who fill prescriptions with more than one drug at the University Health Centre. While it may be impossible to totally eliminate potential DDIs based on the need for poly-pharmacy especially in patients with multiple chronic diseases, it is the responsibility of health care professionals to use all education tools available to ensure drug benefits always outweigh risk for each patient.

CONFLICT OF INTEREST

None to declare.

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PREVALENCIA DE INTERACCIONES POTENCIALES MEDICAMENTO-MEDICAMENTO EN UNA FARMACIA DE CENTRO DE SALUD UNIVERSITARIO EN JAMAICA

RESUMEN
Objetivo: Identificar interacciones potenciales medicamento-medicamento (DDI) en las prescripciones atendidas en la farmacia del centro de salud de Universitario del campus de Mona, Jamaica.
Métodos: Esta investigación utilizó un análisis transversal de todas las prescripciones con más de un medicamento que fueron atendidas en el centro de salud universitario entre noviembre de 2012 y febrero de 2013. Las DDI potenciales se identificaban en el Drug Interactions Checker de la base de datos Drugs.com.
Resultados: Durante el periodo de estudio, se analizaron a la busca de DDI un total de 2.814 prescripciones. La prevalencia de DDI potenciales encontrada durante el estudio fue del 49,82%. Las DDI *major* potenciales totalizaron el 4,7% del total de interaciones detectadas, mientras que las moderadas y *minor* fueron el 80,8% y el 14,5%, respectivamente. Las tres DDI potenciales *major* que aparecieron más frecuentemente fueron amlodipina y simvastatina (n=46), amilorida y losartan (n=27), y amilorida y lisinopril (n=16).
Conclusión: Este estudio ha remarcado la necesidad de iniciativas educativas para asegurar que los médicos y los farmacéuticos colaboren en el esfuerzo de minimizar los riesgos de los pacientes. Estas interacciones eran evitables en su mayor parte, ya que el uso de herramientas *online* puede facilitar la selección de tratamientos alternativos o guiar decisiones para monitorizar más de cerca a los pacientes, y así reducir el riesgo de eventos adversos.

Palabras clave: Interacciones medicamentosas; Errores de medicación; Seguridad del Paciente; Farmacéuticos; Jamaica

References

1. Klepper MJ, Cobert B. Drug Safety Data: How to Analyze, Summarize and Interpret to Determine Risk. Sudbury, MA: Jones & Bartlett Learning; 2010. ISBN: 978-0763769123
2. Chatsisvili A, Sapounidis I, Pavlidou G, Zoumpouridou E, Karakousis VA, Spanakis M, Teperikidis L, Niopas I. Potential drug-drug interactions in prescriptions dispensed in community pharmacies in Greece. Pharm World Sci. 2010;32(2):187-193. doi: 10.1007/s11096-010-9365-1
3. Sepehri G, Khazaelli P, Dahooie FA, Sepehri E, Dehghani MR. Prevalence of potential drug interactions in an Iranian general hospital. Indian J Pharm Sci. 2012;74(1):75-79. doi: 10.4103/0250-474X.102548
4. Obreli Neto PR, Nobili A, Marusic S, Pilger D, Guidoni CM, Baldoni Ade O, Cruciol-Souza JM, Da Cruz AN, Gaeti WP, Cuman RK. Prevalence and predictors of potential drug-drug interactions in the elderly: a cross-sectional study in the brazilian primary public health system. J Pharm Pharm Sci. 2012;15(2):344-354.
5. Peng CC, Glassman PA, Marks IR, Fowler C, Castiglione B, Good CB. Retrospective drug utilization review: incidence of clinically relevant potential drug-drug interactions in a large ambulatory population. J Manag Care Pharm. 2003;9(6):513-522.
6. Moura CS, Prado NM, Belo NO, Acurcio FA. Evaluation of drug-drug interaction screening software combined with pharmacist intervention. Int J Clin Pharm. 2012;34(4):547-552. doi: 10.1007/s11096-012-9642-2
7. Secoli SR, Figueras A, Lebrão ML, de Lima FD, Santos JL. Risk of potential drug-drug interactions among Brazilian elderly: a population-based, cross-sectional study. Drugs Aging. 2010;27(9):759-770. doi: 10.2165/11538460-000000000-00000
8. Cruciol-Souza JM, Thomson JC.Prevalence of potential drug-drug interactions and its associated factors in a Brazilian teaching hospital. J Pharm Pharm Sci. 2006;9(3):427-433.
9. Moura C, Prado N, Acurcio F. Potential drug-drug interactions associated with prolonged stays in the intensive care unit: a retrospective cohort study. Clin Drug Investig. 2011;31(5):309-316. doi: 10.2165/11586200-000000000-00000
10. Schreiber DH, Anderson TR. Statin-induced rhabdomyolysis. J Emerg Med. 2006;31(2):177-180.